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Nutritional and health benefits and risks of plant-based substitute foods

François Mariotti
Université Paris-Saclay, AgroParisTech, INRAE, UMR PNCA, 91120 Palaiseau, France

Plant-based substitutes (PBS) are seen as a convenient way to transition to a more plant-based diet, but their potential health benefits and nutritional concerns remain debated. Based on a review of the literature, it is concluded here that the primary risk of insufficient nutrient intake with PBS concerns iron and calcium, which are critical to the nutritional value of PBS. Other risks were identified but these would depend on the characteristics of the overall diet, as is the case for iodine in a diet containing no seafood or dairy, and vitamin B12 in a vegetarian/vegan diet. Conversely, the use of PBS is also expected to confer some benefits for long-term health because it would result in higher fibre intakes (in the case of meat PBS) and lower SFA intakes (but higher PUFA/MUFA intakes), but attention should be paid to a potential increase in sodium intake with PBS of meat products. In fact, a recurring finding in this review was that PBS is a very heterogeneous food category involving considerable variations in ingredient and nutrient composition, and whose design could be improved in order to foster nutritional and health benefits. The latter also depend on the animal food that is being replaced and are only deemed likely when PBS replace red meat. The fortification of PBS with key nutrients such as iron and calcium may constitute an actionable public health solution to further shift the balance in favour of PBS in the context of the current dietary transition in western countries.

Meat: Dairy products: Dietary proteins: Iron: Zinc: Calcium: Iodine: Vitamin B12: Diet: Vegetarian

In higher income countries, there is growing interest in diets that might improve human and planetary health. There are also a growing number of people who are concerned by animal welfare. There is therefore a marked trend towards the adoption of diets that are more plant-based, which indeed cover a broad spectrum, ranging from those which are simply lower in meat, to a 'flexitarian' diet (with very occasional meat/fish consumption, similar to a semi-vegetarian diet), and vegetarian diets (which comprise lacto-ovo vegetarian and vegan diets)[1]. This spectrum of diets thus involves a partial or total reduction in meat, fish and dairy products, associated with either a complete revision of the diet in favour of traditional plant-based food categories (grains, legumes, vegetables, nuts, seeds, etc.) or the utilisation of plant-based food analogues that usually facilitate the direct substitution of animal food products. The two ways to adopt a plant-based diet also coexist; either that seen in traditional vegetarian populations, e.g.[2] or a second way whose popularity has been increasing, as indicated by a change to the foods offered to the general population[3]. Plant-based substitutes (PBS) have indeed been developed for vegetarians[4]. More recently, PBS have moved out the vegetarian market niche to enter the mainstream market and be proposed to a variety of consumers[5]. The market trend is surprisingly high, especially in countries with little tradition of vegetarianism and a food culture largely built on animal products, such as France. By contrast, in countries where vegetarianism has long been non-anecdotal, such as the UK, this

Abbreviations: PBMA, plant-based milk alternative; PBS, plant-based substitute; UPF, ultra-processed food.
Corresponding author: François Mariotti, email francois.mariotti@agroparistech.fr

trend is not new, and a wide variety of PBS are entering a growing market and becoming increasingly popular among consumers[6,7].

People concerned by animal welfare may find that the benefits of using PBS are trivial. The benefits regarding environmental impact have been discussed, and may depend on the production systems used for animal products and the ingredients and degree of processing of PBS, but overall it is considered that using PBS results in lower environmental pressures, and particularly lower greenhouse gas emissions, land use and water use[8–11]. By contrast, the benefits of PBS regarding nutrition and health have been and remain the subject of much debate. Recent studies have shed some light on the benefits and risks of PBS. Here, when for discussing the benefits and risks of plant-based milk alternatives (PBMA), the review will first focus on the potential impact of PBS on nutritional status, based on the expected effects on nutrient displacement. Then the review will deal with essential nutrients whose requirements need to be covered and the nutrients with upper references that must not be exceeded; focusing on nutrients that may affect health, either in the short term (deficiency) or over the long term (regarding the risk of chronic diseases). Then, the review will address the issue of changes to other characteristics of the overall dietary pattern, such as the type of substitutions, potential increases in the share of ultra-processed foods (UPF) and changes to the consumption of food categories that might enable improvements in compliance with food-based dietary guidelines.

Potential impact on the adequacy of intake of indispensable nutrients

Because of the marked increase in PBS availability on the market, there have been many reports on their nutrient content compared to the animal foods they are designed to replace. These reports usually concern PBS as sold in specific countries or geographic areas. One limitation to these studies is that the information on nutrient contents is usually restricted to the information shown on the package[12]; i.e. the standard mandatory nutrient list (depending on national regulations) and any additional information linked to the use of a nutrient-content claim.

Nutrients of little concern: the case of protein

Meat, and dairy, make an important contribution to protein intake in the general population in western countries[13,14]. Many reports on PBS for meat, milk and cheese have emphasised their lower protein contents than the animal foods they are intended to replace[15–17]. The protein content varies considerably depending on the type of milk substitute, with soya-based drinks containing similar amounts to milk, while others such as almond or rice drinks contain very low levels[18,19]. Likewise, the protein content in meat substitutes also varies and is often higher in PBMA designed to mimic meat because those PBMA are often made of protein isolates, which are concentrated sources of protein. The protein content in PBMA may also be a marketing argument, presented as a claim such as ‘rich in protein’ or highlighting the amount of protein in a serving of the product. This could be seen as a simplified way to tell consumers that the PBMA is nutritionally equivalent to meat; consumers mostly represent meat as protein, and protein as strength and vitality, connected to masculinity[20,21], although this may also vary according to cultural background. Cutroneo *et al.* estimated that 68 % of PBMA in Italy displayed a protein content claim while this figure could be as high as 94 % in the USA[16,22]. Although the protein content in some PBMA may be similar to that of red meat, it is somewhat lower in most products and this has been viewed as a nutritional drawback. Yet a simple comparison of the substitutes and substituted products offers very limited and indeed biased information. This simplistic approach does not take account of the impact of product substitution on the overall diet and the baseline situation regarding the nutrients at issue. If a PBMA that is lower in protein replaces meat, the resulting decrease in protein intake is not anticipated to be a problem because the high-protein intake seen in high- and middle-income countries actually far exceeds the reference value for adults[23,24]. For instance, in France, the proportion of adults with insufficient protein intake in their usual diet is <0·5 %[25]. Therefore, substituting meat with PBMA, even completely, cannot be expected to result in protein insufficiency[26]. One reason is that PBMA remains a source of protein, and indeed, as shown by diet modelling studies, the removal of meat tends to reduce protein intake but does not result in a protein shortage if the remainder of the diet includes other sources of protein (of whatever origin)[27]. The substitution of milk is unlikely to have a significant effect on protein intake, even with low-protein milk analogues, because milk contributes little to protein intake (about 6 % in France, *v.* about 38 % for the contribution of meat to protein intake)[13,25]. Insufficient protein intake may be anticipated if all animal protein foods are replaced with plant-based foods that are low in protein, but not if the plant-based protein sources are diverse and include legumes, whole-grain, nuts and seeds[25]. Likewise, we have shown that lowering the animal:plant protein intake in a nutrient-adequate diet is limited (to about 15 %, without food fortification or alternate plant-based food sources) but not because of the total level of protein in the diet[28]. Indeed, the protein intake from different food groups mediates the benefits and risks of transiting towards a more plant-based diet because of the nutrient package that is conveyed[29]. Finally, reports on protein intake in lacto-ovo vegetarian and even vegan diets (as observed in dietary surveys) have not revealed any insufficient intakes[23,30]. This could be ascribed to the fact that people eating a more plant-based diet and vegetarians classically use legumes and PBMA where others would classically eat meat[31].

It should be noted that the risk of protein insufficiency is very low in adults and virtually null in children, but it

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is higher in the elderly and important in the frail elderly with low energy and protein intakes[32]. In these populations, such as those in low-income countries, there remains a risk of protein-energy undernutrition, which contrasts with the situation pertaining to the general population in western countries.

Analysing which nutrients matter

Meat, and dairy, are sources of protein and are also associated with clusters of nutrients that are directly supplied by these food groups (known as the 'protein package') or indirectly associated with the overall dietary pattern[13,29]. Replacing meat or dairy can cause marked changes to the nutrient profile of the diet. The risks (or benefits) associated with these changes depend on the amount of nutrients provided by the rest of the diet, the effect size of the replacement (i.e. the difference in nutrient content conveyed by the substitution, which itself depends on the level of consumption of the animal food and the degree of replacement), and lastly the importance to health that a given nutrient is consumed in quantities that comply with reference values. No direct simple answer can therefore be obtained from a direct comparison between some PBS and the animal foods they are intended to replace. As observed for protein, such decreases are not expected to result in insufficient intakes. The same applies to other nutrients, despite important differences between PBS and the corresponding animal foods. For instance, the vitamin B3 content in meat is about ten times higher than that in PBMA, but virtually the entire population consumes sufficient vitamin B3 when account is taken of the conversion of tryptophan into niacin in populations in western countries with a very high tryptophan intake[25], so using PBMA would have no effect on the virtually null probability of an insufficient vitamin B3 intake[26]. As for vitamin B5, the content in meat is about twice that found in PBMA, resulting in a decrease in vitamin B5 intake as compared to the reference value when simulating replacement[26]. However, this reference value for vitamin B5 is an *adequate intake* based on observed intakes, and no signs of deficiency being found within the range of vitamin B5 intakes among adults in western countries[33].

By contrast, when the animal foods that are replaced are important contributors to nutrient intake and the nutrient status is marginal in the population, then significant differences between PBS and the animal foods are expected to result in a nutritional risk.

Vitamin B12 and riboflavin

The nutritional risk may depend on the specificity of the animal food category as a contributor to nutrient intake and, again, of the overall diet profile. Since vitamin B12 is high in meat and absent in unfortified PBMA, using the latter will result in a lower vitamin B12 intake[34] whatever the PBMA; although in the observed population vitamin B12 intakes are above the requirement, this would ultimately increase the proportion of people not reaching the reference value[26]. Such an effect would depend on the overall diet profile and in particular of the consumption of other important sources of vitamin B12, such as seafood which, with offal, are the richest sources of vitamin B12. In the lower meat or meat-free diets modelled by Dussiot *et al*., concurrent increases in seafood resulted in high vitamin B12 levels in these diets. By contrast, in diets devoid of meat and fish, such as lacto-ovo-vegetarian diets, a low intake of vitamin B12 can result in higher plasma homocysteine concentrations, which can be expected to translate into an increase in the risk of CVD[35]. Under a scenario that replaced all meat and dairy with plant-based analogues and some other alternative foods, Seves *et al*. found about 35 % decrease in vitamin B12 intake, despite the fact that some PBS were fortified with this vitamin[36]. In the general population, when simulating the full replacement of meat with PBMA, the risk of overt vitamin B12 deficiency increased slightly, on average by about 5 %[26]. This suggests that, apart from vegetarians and vegans, there may be a risk of inadequate vitamin B12 status in that part of the general population with low seafood intakes and using unfortified PBMA. The fortification of PBMA with vitamin B12 appears to be rare; Melville *et al*. found a proportion of 15 % in an Australian survey[37].

Some potential impacts of using PBS have been suggested regarding other nutrients that have been much less explored. This is the case for riboflavin when using either PBMA or milk analogues. Riboflavin intakes are quite high in the general population but it is largely conveyed by animal products (meat, fish, eggs and dairy)[38,39]. Plant-based milk alternatives are naturally low in riboflavin (legume-based alternatives) or very low (grains or coconut-based), and fortification has been very rare in Europe until recently when adopted by a few brands. Based on food composition data from the Australian market, as reported by Zhang *et al*., it can be calculated that although 250 ml milk would supply 33 % of the reference value for riboflavin, using (unfortified) legume-based alternatives would only supply 6 % and mixed milk alternatives just 1 %[40]. Using PBMA has been shown to largely reduce riboflavin intakes, leading to a suggested insufficient intake in part of the population, including a slight increase in the risk of overt deficiency[26]. This risk varies depending on the type of substitute, and was lower with PBS that included legumes[26]. The prevalence of overt deficiency, namely ariboflavinosis, is virtually null in high-income countries, and the characterised adverse effect on health of milder forms of riboflavin remains uncertain. However, riboflavin plays an important role in one-carbon metabolism, and riboflavin subdeficiency has been associated with hypertension, especially in individuals with the MTHFR 677TT genotype[41,42]. Therefore further studies are needed to better characterise the adverse effects of low riboflavin intake in high-income countries.

The review will now turn to nutrients for which a risk of shortfall has long been identified when using PBS; namely calcium and iodine for dairy product analogues and iron and zinc for meat analogues.

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Calcium and iodine

Dairy is well known as an important contributor to calcium intake and a significant part of the general population has a calcium intake below their estimated requirements[43]. Among people consuming no dairy products, there is a very high risk of shortfall[44]. Although this has long been disputed, recent findings pointed out that vegans have a higher risk of osteoporotic fractures, and this could be ascribed to insufficient calcium intake[45]. Indeed, the risk was high among vegans who are not taking calcium supplements, whereas it was not significant in those using calcium supplements[45]. The risk to bone health in vegans may be due to insufficient intakes of the many nutrients and foods that can affect bone mineral density and/or the risk of fracture, which of course include calcium from sources other than dairy, such as fortified plant-based milks (e.g. soya milk, firm calcium-set tofu), other fortified foods such as fortified breakfast cereals, natural foods such as dark leafy greens or mineral water or blackstrap molasses[46]. When fortified with calcium, dairy analogues such as plant-based 'milk' usually contain the same level of calcium as their dairy counterpart, so no important impact on calcium intake is expected. However, in many countries, milk analogues are rarely fortified and cheese analogues almost never, especially in countries such as France[19,40,47]. In the Netherlands, Seves *et al.* found that a scenario involving no meat and dairy would decrease calcium intake by 25 %, even though some dairy analogues were fortified with calcium[36]. When simulating the replacement of milk with PBS in France, we found a marked increase in inadequacy and a risk of deficiency for calcium when considering the total set of milk analogues studied but, as expected, this risk was almost null when considering the smaller (one-third) subset of fortified milk analogues[26]. It is interesting to mention that conversely, we also found that using meat analogues resulted in a reduction in the level of inadequacy for calcium, so such meat analogues could compensate for the adverse effects of milk and dairy dessert analogues[26]. However, it might be expected that using also other unfortified dairy analogues, such as plant-based alternatives to cheese, and not using plant-based alternative sources of calcium could result in a marked increase in calcium inadequacy, with a resulting risk to long-term bone health.

Less emphasis has been placed on iodine when considering the nutritional quality of dairy analogues in general surveys. Dairy products are an important source of iodine in the general population[48]. The importance of dairy is less specific regarding iodine than it is for calcium because another important contributor is seafood. When diets are low in or devoid of both dairy and seafood, as in the case of vegan diets, few specific products high in iodine are consumed, such as fortified salt and seaweed, and soils are poor in iodine, its intake can be very low and clearly inadequate[49–51]. The contribution of dairy products to iodine nutrition can be important, as shown recently by Nicol *et al.* who reported that three portions of dairy products (milk/yoghurt/cheese) daily supply 124 μg iodine (close to the reference intake of 150 μg) whereas three portions of alternative dairy products including two, one or zero iodine-fortified products only provide 84, 51 and 3 μg iodine[52]. Although this marked contrast is the result of extreme scenarios, it suggests the potential magnitude of the effect of replacing dairy with analogues because few of them are fortified with iodine. Iodine was one of the nutrients showing the greatest decrease in scenarios concerning an increased use of milk analogues[53]. We also showed that there was an increased risk of iodine deficiency when simulating the utilisation of milk analogues or, to a lesser extent, dairy dessert analogues[26]. The prevailing risk for iodine indeed constitutes one of the highest risks of overt deficiency in the general population at baseline[54] and the simulated increase with milk substitute was the greatest of all nutrients[26]. This situation is probably due to a combination of factors, including an insufficient consumption of seafood, the insufficient fortification of iodine in salt (both because iodine is incorporated at a low level in France and fortification is restricted to household salt, not that used as an ingredient in the food chain), suboptimal levels of iodine in soils which result in low intakes of iodine from plant products, and, finally, the anecdotal consumption of seaweed[48]. Dineva *et al.* reported that the population exclusively consuming milk-alternative drinks could be classified as iodine deficient based on median urinary concentrations, whereas non-exclusive consumers of milk analogues and milk consumers were not classified as deficient[55]. Again, this could be explained by the same series of reasons, to which it should also be added that although 70 % of the consumers of milk analogues in this cross-sectional study in the UK were eating fish[55], they may have had lower intake of iodine from seafood. Also, in both the UK and in France, the salt iodisation programme is little effective[56].

As far as iodine in milk or dairy analogues is concerned, it should be noted that the iodine fortification of dairy products is very rare. Iodine-fortified milk analogues such as soya drinks have been commercialised in recent years in the UK, with levels differing little from those in milk (although iodine levels in milk vary considerably depending on areas and seasons)[57,58]. A recent UK survey found that, not even accounting for organic products (which cannot be fortified in the European Union and UK), 28 % of milk alternatives and 6 % of yoghurt alternatives were fortified with iodine[52]. However, in other European countries such as France, milk analogues fortified with iodine do not appear to be on the market. For instance, a well-known brand of soya milk fortified with vitamins B2, B12 and D is available in France, Portugal, Spain and Italy, but not the version fortified with iodine that is on the UK market (based on the information found in company's national websites and the O*penFoodFact* database).

Iron and zinc

Iron and to a lesser extent zinc, have been the focus of numerous studies because their intakes are largely provided by meat consumption. However, iron is also high in many plant-based products and comparisons between meat and plant-based meat substitutes have often

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reported similar amounts of total iron, or even higher amounts in PBMA[59] which led to a higher iron intake when simulating the substitution of meat and dairy with PBS[36]. However, this did not take account of the well-known differences in absorption (often referred to as 'bioavailability') of plant and animal sources, which were only alluded to in these studies (and indeed not in all cases). Few studies have compared the levels of bioavailable iron in meat and PBMA. Some attempts have been made using average estimates of absorbable iron from animal-based or plant-based meals/diets, such as 16 % absorption from meals/diets containing meat and 10 % absorption from plant-based meals/diets[60]. However, there remain many uncertainties in those estimates, because iron bioavailability can vary markedly depending on the content of the meal and whether the equation or algorithm used to estimate iron absorption take into account multiple factors in a variable manner[61–63]. Taking account of changes in bioavailability and using simulation techniques on all individuals in a French representative survey, we were able to show that replacing all meat with varied plant-based meat analogues would decrease absorbed iron from the diet, and therefore raise the risk of insufficient intake and result in a slight increase in the probability of over-deficiency (i.e. iron-deficiency anaemia)[26]. Because the bioavailability of zinc is also dependent on animal sources such as meat, zinc bears many similarities with iron. In this simulation study, we found decrease in absorbed zinc from the diet when PBMA replaced meat, but no increase in the risk of overt deficiency[26].

Recent findings in the literature have shown that iron nutrition, and to a lesser extent zinc nutrition, are critical when considering a general shift towards a plant-based diet. Again, this was revealed in studies accounting for the bioavailability of iron and zinc, using equations or algorithms to estimate iron absorption[62]. In this context, we showed using optimisation models that imposing a modelled healthy diet conveying sufficient bioavailable iron to cover the estimated physiological requirements of the population markedly limited the healthiness of the modelled diet, as it led to incomplete reductions in red meat consumption (conveying bioavailable iron) and incomplete increases in whole-grain products (conveying phytates which inhibit iron absorption)[64]. This resulted in suboptimal reductions in morbidity/mortality risks as assessed as disability-adjusted life years using a comparative risk assessment model. By contrast, when the constraint on dietary absorbable iron was relaxed, the optimally healthy modelled diet was almost devoid of red meat and all grain products were whole grains, leading to further important reductions in the long-term health risk. This was at the price of a projected increase in iron-deficiency anaemia (from 2 % in the observed population to 5 % in the flexible optimal model) but the increase in morbidity (as daily-adjusted life years) due to anaemia was much lower than the reduction due to benefits on long-term health[64]. During this study, bioavailable iron and bioavailable zinc were dually constraining modelled diets, since iron and zinc were found to mostly to be contributed by the same sources and their bioavailability was influenced similarly. Recently, van Wonderen *et al*. showed convincingly that taking account of bioavailable iron was important when modelling diets. Using meal-planning optimisation from a selection of meals, and applying several methods to estimate total iron absorption from these meals, they showed that modelled diets with constant absorption factors (as is usually done) finally conveyed much less absorbed iron than diets modelled using specific diet-dependent absorption equations[63].

The question of insufficient iron intake is specific to diets containing no meat. Meatless diets that are healthy tend to lead to critical levels of bioavailable iron, since other classical healthy food categories convey iron with low bioavailability (such as legumes and whole grains) or are not consumed enough to make a sufficient contribution to intakes of iron of good bioavailability (such as seafood)[27]. Vegetarian diets can be designed to supply enough bioavailable iron[65], but the iron status of vegetarians is low, although evidence of iron deficiency, such as a higher risk of iron-deficiency anaemia, is lacking[66]. The relationship between vegetarian diets and iron status appears to vary considerably, and one source of variation might be the nature of the food consumed instead of meat, which in traditional vegetarian populations (such as in the UK and among north-American Adventists) is legumes and vegetarian alternatives[31,67]. In populations that have turned more recently towards a meatless diet in western countries, PBMA is probably a more common alternative[4], raising possible concerns about nutritional quality in general[68]. A second source of variation might be the level of iron fortification in the food chain (such as flour being fortified with iron) and the fortification of food items, and of course, particularly PBMA. In Europe, the UK is the only country to fortify flour with iron.

Because the composition of PBMA is variable, as discussed earlier, so is the amount of iron and absorbable iron they contain. We found that the simulated impact of using PBMA on the risk of iron deficiency in the population varied according to the type of PBMA (being higher with plant-based breaded foods than with plant-based patties) and the nature of the main protein ingredient (being higher with cereal-based analogues rather than with soya-based analogues)[26]. Few data are available on the potential contribution of PBMA to dietary bioavailable iron because reports based on a composition survey included limited information on vitamins and minerals as the information was missing from the pack, and there was no information regarding the bioavailability of iron. Therefore, most reports have simply mentioned that PBMA contain higher amounts of total iron than meat[59,69] or that the replacement of meat and dairy with PBS will lead to increases in population iron intake[70]. Some studies have however taken account of expected differences in bioavailability, such as 45 % less absorption (meaning an 80 % higher dietary requirement or reference value) reported by Pointke and Pawelzik, who nevertheless found that PBMA sold in Germany made a potential contribution to iron nutrition that was similar to meat[17]. Labba *et al*. went one step further

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by analysing the iron and phytate contents in a series of PBMA on the Swedish market and used this information to categorise the PBMA according to their expected bioavailability, determined using the phytate:iron content in the PBMA[71]. Their results showed that except for a few items, PBMA contained very high phytate:iron ratio, indicating very low bioavailability. It is noteworthy that these authors found one exception among the PBS, tempeh, for which they estimated a high content in bioavailable iron, because of both its high iron content (similar to meat) and low phytate content; this could be explained by the fact that tempeh is a food fermented with a fungus that produces the phytate-degrading enzyme phytase. Similar results were found for zinc, with probably low bioavailable zinc as assessed from the phytate:zinc estimates. Here also there was one notable exception, found with the mycoprotein product analysed as being very high in zinc and virtually devoid of phytate. Finally, the literature data do not provide a clear and uniform answer regarding the risk of insufficient levels of bioavailable iron in the PBS on the market, but this generally appears to be considerable when products are not fortified, and may vary depending on the type of product and the country/area market.

Overall, PBS with the potential to be valuable sources of iron and zinc are either very traditional products (such as tempeh) or highly innovative products such as the recent PBMA that incorporate iron in a form that is not sensitive to inhibitors such as phytate and tannins. This is the case of PBMA that incorporate haem-iron from plant sources (soya leghaemoglobin) as a bioengineered ingredient. Although this ingredient is used to better imitate the colour and taste of meat in these PBMA[69,72,73], the haem-iron form is expected to supply highly bioavailable iron, irrespective of the amounts of phytate in the PBMA[74]. Likewise, there are many reports on how food products could include large amounts of bioavailable iron and zinc, including but not limited to the case of phytate, and using biofortification, ingredient selection and a broad range of treatments (germination, soaking, fermentation, enzymatic treatment)[75–77].

However, on average, and within the current range of products on the market, absorbable iron levels appear to be low in PBMA. This raises the question whether a PBMA could be designed with the usual ingredients to be sufficiently rich in iron, or would it need to be fortified with iron? In a model that minimised environmental impacts, Van Mierlo *et al.* found that iron fortification was necessary when seeking to match the nutritional composition of beef (but not chicken), although it appeared to be limited to the non-haem-iron content, and that the result could be sensitive to changes in the bioavailability of iron due to interactions with the inhibitors and enhancers of iron absorption found in the diet[78]. We searched for the best theoretical recipe for a pulse-based meat analogue to improve overall diet quality using a list of ingredients and technological constraints[79]. The final recipe resulted in a marked improvement in nutrient-based diet quality, which was about 4-fold higher than the effect of the best of the PBMA found in our benchmark database. However using this overall 'optimal' PBMA would lower the absorbable iron content in the diet and increase the probability of an insufficient iron intake, although the increase in the risk of deficiency (when compared to the threshold for the risk of iron-deficiency anaemia) was almost unchanged. Indeed, the absorbable iron content of the PBMA, although relatively high, remained lower than that found in the meat it was entirely replacing under our scenario. Among the binding constraints for optimisation, we found higher levels of herbs, spices, nuts and seeds that were good sources of iron but had to be restricted in the recipe for the sake of their expected acceptability. In a subsequent work, we further elaborated on the importance of iron (and zinc) fortification in PBMA in the perspective of building healthiest diets that included lowering red meat levels[80]. As the general aim was to investigate the nutritional benefits of plant-based meat substitutes and covered different alternatives, various dietary changes were allowed, both within a food category (such as the partial or total replacement of any type of meat with plant-based meat substitutes) and between food categories; however, the latter were hampered by the search for a healthier dietary pattern that would remain close to current eating habits[80]. Without fortification, the average meat substitute was not incorporated in the model diet to any significant extent, showing that its nutrient composition was insufficient to act as a nutritional lever. By contrast, fortification with iron and zinc resulted in introducing more PBMA in the modelled diets, along with major reductions to the levels of red meat, processed meat and poultry. The PBMA that we had already optimised on a nutrient basis was more readily introduced into these modelled diets, but not so much at the expense of meat, whereas when it was fortified with iron and zinc, a higher level of inclusion were reached together with marked decreases in beef[80]. As in our study, Mertens *et al.* modelled substitutions for meat under the background hypothesis that PBMA were taken as substitutable for meat with no cost regarding acceptability[81]. In their model designed to improve adherence to dietary guidelines and then maximally reduce green-house gas emissions, these authors also found that theoretical fortifications in iron (and some vitamins) led to larger quantities of meat substitutes and smaller quantities of meat in the modelled diets compared to those involving non-fortified meat substitutes. Interestingly, with the same objectives of achieving the highest diet quality, the amount of PBMA in modelled diets varied between countries[81], which may reflect differences in the background diet and associated nutrient intake.

The case for the fortification of meat analogues with iron and dairy analogues with calcium

From the above, it appears that nutrient security related to the use of PBS by the general population mostly concerns calcium and iron. But as discussed earlier, these are not the only nutrients at issue, although for others the risk would be less specific as dependent on the

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consumption of other food categories (such as seafood for iodine) and vary according to the background diet (e.g. animal products for vitamin B12). Although this does not mean that they should be disregarded (but rather that they should be further studied), the hazard characterised and hence the estimated risk is also lower for other nutrients where overt deficiency has been poorly characterised or is rare in western countries with no protein energy undernutrition, such as zinc or riboflavin. By contrast, the calcium intake in the general population is insufficient while iron intake appears to be marginal in some women with high requirements, leading to a greater risk of deficiency if calcium and iron decrease following the use of PBS. As also illustrated, although the fortification of PBS varies between countries, it remains low inasmuch as it would be insufficient to alleviate the risk. Fortification requires an in-depth knowledge of the technological issue of acceptability and the optimum form to achieve high bioavailability, but considerable progress has already been achieved[82,83]. PBS fortification would seem to be the most appropriate method to avoid decreases in nutrient intakes when shifting from animal products, but, if this is not made mandatory by regulations, it would be necessary to determine solutions so that more manufacturers will adopt this measure. Alternatively, fortification could be introduced as a general public health initiative based on the fortification of agricultural commodities (e.g. flour) or staple/mass market foods (e.g. salt), including PBS, which would thus improve the nutrient status of the entire population[84,85]. And indeed, the two approaches could be interestingly combined. However, fortification scenarios need to be closely monitored beforehand to ensure that the goals are attained while not causing any excessive exposure to nutrients of concern in this respect. In particular, iron fortification should reduce rates of iron-deficiency anaemia in at-risk females without leading to iron exposure that would become excessive in male meat eaters[86,87]. PBMA is the food fortification vehicle that could be prioritised to avoid this risk. However, for calcium, multiple vehicles could be considered in order to ensure more general improvements to intake, given the absence of an upper level. As we have argued elsewhere, in view of the development of PBMA as one way to move towards a more plant-based diet would be to take the opportunity of using PBMA as a vehicle for fortification with nutrients that tend to be too low in plant-based diets[4]. If fortification is not made mandatory, rendering effective in the general population remains an issue[88]. On the one hand, because consumer attitudes have been shown to depend on the perceived appropriateness of fortifying a given food product[89], and notably the perceived healthiness of the food vehicle[90]. Since PBS are seen as replacing animal products, fortification of PBS could be legitimate from the consumers' perception. This could indeed be the rationale for the marketing of the nutritional equivalence, which however today mostly limited to protein for PBMA and calcium for plant-based dairy analogues. However, the perceived relevance for consumers is also related to perceived personal benefits and problem awareness[89], which may explain why the protein claim has gained popularity (although it is less relevant to public health nutrition) and may hinder the promotion of other nutrient claims, such as iron in PBMA or iodine in dairy PBS, because of they are less recognised, despite their greater public health importance. The promotion of fortification could also be fostered by the structure–function claims (in the USA) or standard health claims (Article 13 in the European Union) but, as expected, these claims are mostly used for marketing purposes and involve multiple pitfalls from a public health nutrition perspective[91,92]. The appeal for fortified products varies; some consumers consider that fortification shifts the plant-based product away from the naturalness spontaneously attached to it, unless it is assured using natural ingredients[90]. There is therefore a risk that the voluntary fortification of PBS will fail to secure the nutrient status of a large proportion of people who would prefer PBS to be devoid of any ingredients and supplements which they deem are not natural, or consume organic foods, which cannot be fortified in the European Union and UK.

Nutrients with a potential impact on long-term health

Fibre is only found in plant-based products and it is a clear and consistent dimension of the nutrient cluster associated with plant:animal protein or, more generally, a plant-rich dietary pattern[93,94]. While there is no fibre in the animal foods that they are replacing, most PBS contain fibre, although in variable amounts. For instance, Labba *et al.* reported on analysed total fibre contents and found values ranging from 3·5 to 9·5 g per 150 g PBMA[71]. Cutroneo *et al.* also reported a very broad range but the average fibre content was not high among red meat or poultry analogues (1·9 g/100 g), whereas average values were high in analogues of burgers or meatballs (4·7 and 4·5 g/100 g)[16]. Similar figures were reported in Australia, with burger analogues containing 4·5 g/100 g, meatball analogues 3·8 g/100 g and plain poultry analogues 4·7 g/100 g[37], and in other countries[15]. The variability was considerable, as shown by the 95 % CI in fibre content, e.g. [2·4, 7·1] in the latter category[37]. The amount of fibre was found to be much lower in plant-based milk or dairy analogues, at about 0·5 g/100 g in milk analogues and about 1 g/100 g in yoghourt analogues in Norway and France[15,26]. As expected, given the virtually null level of fibre in meat products, the significant levels in PBMA, and the high levels of meat consumption in observed diets, we found that replacing meat with PBMA led to a significant reduction in the risk of inadequacy for fibre, and the effect was maximal when using pulse-based substitutes or plain cooked pulses (which were taken as a reference)[26]. By contrast, this reduction remained very small when milk and yoghurt/desserts were replaced with their PBS counterparts[26]. Under a scenario that reduced or replaced both meat and dairy with PBS, the fibre intake rose markedly, by up to one-third in the replacement scenario[36].

The importance of fibre to human health is now widely acknowledged[95]. Insufficient fibre intake has been rated

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as an important contributor to the burden of diet-related disease in high-income countries; its impact is less than that of most dietary factors but greater than that of a high consumption of sugar-sweetened beverages or a low consumption of vegetables[96]. Therefore, given the importance of fibre per se, and the projected increase in fibre when using PBS instead of their animal-based counterparts, they could have a favourable impact on long-term health.

Like fibre, amounts of SFA are usually largely associated with the level plant:animal content in the diet. As expected, SFA contents are usually low in PBMA and, on average in country markets, SFA content in PBMA are between half[37] and one-third[6,17,97]. More specifically, the SFA content in PBMA varies markedly as a function of product type, and also depends on specific items within this type. For instance, Labba *et al.* reported SFA values of 0·2 g/100 g in a mycoprotein filet and 3·5 g/100 g in a pea burger[71]. The SFA content varied considerably depending on the type of added fat, being much higher when shea butter or coconut or palm oil was used, compared to rapeseed oil or sunflower oil[6,71]. High levels of fat and the use of coconut oil can lead to high SFA levels in some PBMA products[98]. Finally, generally marked effects on the SFA intake can be expected from the use of PBMA rather than their animal counterparts, inasmuch as the differences in contents are significant, meat intake is high and SFA intake is excessive in a large part of the population. Accordingly, in a simulation study, we found that such a substitution would lower the risk of excessive SFA intake in the population[26].

As for dairy and SFA, dairy is usually an important contributor to SFA intakes but SFA levels in dairy products vary considerably. SFA contents in plant-based drinks are often one-third or one-quarter of those found in semi-skimmed milk[15,26]. The SFA content varies little in plant-based drinks, with the notable exception of coconut drinks where amounts similar to, or even much higher than, those in whole milk have been reported[15,99]. Nonetheless, because the average SFA content is low, substituting milk with plant-based drinks does not appear to change significantly the risk of excessive SFA intake at the population level[26]. The issue may be slightly different where other PBS are concerned, such as analogues of dairy desserts and cheese, but the composition (and SFA levels) of both dairy products and plant-based analogues varies considerably. For instance, we found that replacing dairy desserts with sweet plant-based desserts would markedly lower excessive SFA intakes whereas replacing them with a plant-based mousse would in fact result in the opposite[26]. Comparisons based solely on SFA contents may remain difficult since fat consumed in the form of cheese has a differential effect on blood lipid responses relative to some other dairy food structures, although there is considerable heterogeneity and relatively few comparisons with other varied matrices of dairy products[100] and obviously with cheese PBS.

When simulating the combined substitution of meat and dairy with PBS, Temme *et al.*[70] showed a marked decrease in SFA, from 13·2 % of the population average energy intake to 9·2 %Energy, which would mean that the proportion of the population complying with the recommendation (<10 %Energy) would increase from 20 to 62 %. Such a change is consistent with the known contribution of meat and dairy to excessive SFA intake[101] and it would be expected to have an important impact on long-term health.

We will only make rapid reference to the expected effects of PBS on the profile and overall intake of fatty acids other than SFA. The aforementioned trends seen for improvements in SFA levels are associated with similar trends regarding MUFA + PUFA, resulting from the fact that the fatty acid composition of PBS is naturally strongly reflected by the utilisation of vegetable oils in the recipes. Indeed, even for PBMA that might contain SFA levels similar to those of meat, the fatty acid profile was (4-fold) richer in PUFA[98]. So alongside the improvement in SFA levels, PBS could be viewed as a way to replace animal fats with vegetable oil. The type of vegetable oil is of course important when defining PBS. In a modelling study, we found that the optimal recipe for a PBMA-integrated rapeseed oil, and sensitivity analysis revealed that this ingredient was by itself one of the most important in improving diet quality[79]. Higher levels of α-linolenic acid, resulting from the use of rapeseed oil, proved to be important for incorporating a PBMA in a healthy diet containing lower quantities of red meat[80].

Lastly, sodium levels in PBS have been a matter of debate. Many reports have warned about the high level of sodium in PBMA, which are higher than in meat and meat-based products[6,17], but some reports have found similar or lower levels[37,102]. In more detail, studies have found that the sodium content varied depending on the PBMA category[6,59]. For instance, sodium in plant-based mince has been reported to be twice or even 6-fold higher than in meat mince, while conversely meat sausages contained about 66 % more sodium than plant-based sausages[6,12]. Because processed meat is usually high in added salt, it is not surprising that the plant-based analogue displayed lower levels. By contrast, sodium levels were found to be consistently higher in PBS for unprocessed meat. Nevertheless, sodium contents do not account for the salt added by consumers, which is expected to be higher with meat than with PBMA, where salt has been added beforehand into the recipe. The amount of salt probably added by consumers cannot be estimated and thus taken into account, even in simulation/modelling studies[26,36,79]. In our simulation study which did not take account of salt added to meat, the substitution of meat by PBMA resulted in an average increase in sodium intake from initially 3200 mg/d to 3400 mg/d[26]. Although such levels are far higher than the recommended upper level of 2300 mg/d, such an increase would further worsen the situation of excessive intake, which is indeed known as an important public health nutrition issue, because excessive sodium is both the usual situation and is detrimental to health, leading to a very high contribution to the burden of diseases. Being the most binding constraint in diet modelling[27,28], appropriate levels of sodium in the diet require an in-depth reorganisation of the dietary pattern, which would not be expected from limited and simple swaps with PBS.

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It remains difficult to determine how far the use of PBS will result in changes to nutrient intake that will achieve effects on long-term health. In addition, the nutrient compositions of all PBS are quite varied(103). However, an important and consistently higher fibre intake and lower SFA intake, and a probable higher PUFA intake would be expected to result in major benefits to health, although these might be somewhat limited by a potential increase in sodium intake. We are currently investigating how these factors may weight in the final health benefit.

Impact of using plant-based substitutes on the healthiness of the dietary pattern

The benefits of using PBS should also be considered at the overall dietary level, in terms of changes to the intake of food categories that are related to long-term health. Although the use of PBS leads to relatively specific changes in the diet which facilitate the prediction of possible benefits, their ultimate effect may depend on the subtype of food they replace, leaving open the eternal question for nutritionists: 'instead of what?'(104). Given the adverse effects of red meat (total and processed) on health(105), its replacement by PBMA should result in a benefit. However, PBMA are also made to replace other types of meat, including poultry, and poultry has not been shown to be associated with a higher risk of disease(105,106). Replacing poultry with PBS would also be expected to have much less impact on SFA intake (as reviewed earlier), because poultry contributes less SFA than red meat. However, the final impact on atherogenic lipoprotein may remain high with poultry(107).

In contrast, there is limited evidence on which to base speculation regarding the expected effects of decreasing dairy products, and indeed milk and yogurt have been associated with reductions in some health risks(108). The overall benefit may outweigh the detrimental effect of their contribution to SFA intake(109). Cheese could be a better subtype to be decreased by replacing it with PBS, based on current dietary guidelines, but the reasoning is mostly based on the level of nutrients (with the high contribution of cheese to SFA and sodium) and the energy density of higher-fat dairy(110). However, cheese analogues are not yet well developed, and their composition varies considerably(103). While some plant-based cheese analogues are UPF that include palm oil, others are traditional tofu-based products or based on simple fermented nuts (such as cashew)(47,111,112). The latter may offer a more valuable option given the health benefits of nuts, not to mention their good nutrient quality(112). Clearly, there is insufficient information to describe the potential health effects of substituting cheese with plant-based analogues.

A final question at issue regarding the expected effects of plant-based food analogues on long-term health concerns their classification as mostly UPF, and particularly PBMA(103). The consumption of UPF, according to the NOVA classification, has received much attention, and there is a large body of evidence regarding its adverse effects on health. The consumption of UPF has reached high levels in western countries, reaching 55 % in the USA(113) and 31 % in France(114), and increasing the use of PBS would further increase the share of UPF in the diet. In France, when compared to non-vegetarians, the share of UPF is higher in vegetarians and vegans (about 6·5 % points higher), and notably as they are younger vegetarians(115). Likewise, we have estimated that substituting meat or dairy desserts with PBS would increase the share of UPF by up to about 10 % points, depending on the type of substitute, and replacing milk with analogues would increase it by about 5 % points. There has been much concern that a transition towards a plant-based diet using UPF PBS might result in 'missing the point' when compared to the recognised benefits of a traditional plant-based diet based on whole foods(68,116,117). However, although mostly classified as UPF(37,103), PBMA little share the features that have often been highlighted as potentially explaining the adverse effects of UPF; further, these features as potential mechanism still remain speculative(118). This topic was reviewed by Messina *et al.* who argued that soya-based meat and dairy alternatives do not have a higher energy density, glycaemic index and hyper-palatability, and do not have a lower satiety potential(119). Moreover, UPF are often criticised for their adverse nutrient content, but hardly applies to the PBS reviewed here, although some types of PBS do contain high levels of SFA, sugar or sodium. de las Heras-Delgado *et al.* found that, within UPF, most PBS had a better nutrient profile than their animal-based homologues, and their overall nutritional quality, assessed using the modified Food Standard Agency Nutrient Profiling System score, was only slightly lower than that of unprocessed animal-based foods(103). PBS are generally recognised as convenient and desirable plant-based foods to encourage dietary change and which, by means of their diversity, may help to maintain a plant-based diet with higher share of plant:animal protein(4,68). Attention should be paid to ensuring that PBS have a good nutritional composition, helping to reduce excessive amounts of some nutrients (such as SFA and sodium), increasing the amounts of nutrients with long-term impacts on health such as fibre and PUFA, and avoiding nutritional risks, such as those concerning iron and calcium(117). PBS which are as little '(ultra)processed' as possible should be considered as more desirable until we have gained further insight into the mechanisms underlying the adverse effects of UPF. Finally, it should be made clear that, all other things being equal, replacing animal foods with whole plant foods such as legumes, whole grains, nuts and seeds, offer clear evidence of beneficial effects on long-term health that is lacking when considering ultra-processed plant-based analogues.

Conclusion

PBS convey potential risks and benefits. Some risks may depend on the characteristics of the overall diet, as is the case for iodine in a diet devoid of seafood and dairy, and vitamin B12 in a vegetarian/vegan diet. Except in the

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frail elderly, the risk of an insufficient protein intake is deemed to be very low inasmuch as their diet includes alternatives that remain sources of protein, which is the case for PBMA. Some nutrients may be insufficiently consumed but the final health implications remain insufficiently clear, as is the case for riboflavin and zinc, which require further studies to characterise their impact. The most important concerns regarding nutrient shortages with PBS relate to iron and calcium, which are critical to the nutritional value of PBS. While some PBMA containing sufficient bioavailable iron exist or could be produced, the low bioavailable iron content in PBMA seems to limit their broad utilisation as a good substitute for meat in actual diets and modelled healthier diets, especially among women with high menstrual losses. Although there may be a risk of iron overload in other populations, this situation makes the case for fortifying PBMA with iron, and putting forward claims on iron rather than protein. The bioavailability of iron, and also zinc, in PBMA could also be improved by lowering levels of inhibitors such as phytate. While some dairy substitutes are fortified with calcium, the proportion of fortified products is very low in some countries. Insufficient calcium intake is a public health issue in the general population, causing a greater risk of osteoporosis in people following diets devoid of dairy products and not taking supplements. Attention should be paid to providing alternative foods that are rich in calcium. Again, a clear case is made for the calcium fortification of dairy substitutes, and other products, and even mandatory public health fortification, since, unlike iron, there is apparently no risk of a high calcium intake causing adverse effects on the population. Conversely, the use of PBS is also expected to convey some benefits for long-term health, because it would result in a higher fibre intake with PBMA, and a lower SFA intake (with a higher PUFA/MUFA intake), but attention should be paid to the possible increase in sodium intake with PBMA. As recently illustrated by others[103], a recurring finding of this literature review is that PBS are extremely heterogeneous, both within and between countries, in terms of their ingredients and nutrient composition – just as the nutritional profiles of consumers also vary – so it remains difficult to issue general statements about the quality of PBS. Health benefits could also derive from changes at the level of the dietary pattern, inasmuch as PBMA are specifically replacing red meat. PBMA that would convey healthy food categories as ingredients, such as legumes and vegetables, would offer further benefits for long-term health. The long-term benefits of dairy substitutes are much less evident, except maybe for cheese if legumes are used as a basis in fermented analogues. Lastly, PBS have also been criticised as being ultra-processed, although most of them do not share the attributes of UPF that might explain the adverse effects of UPF consumption on health. Although using whole plant foods remains the reference for nutrition and health, PBS in general are recognised as convenient and desirable plant-based foods that will encourage dietary change and through their diversity will help to maintain a plant-based diet. Attention should be paid to their composition in ingredients and nutrients so that any risks are restricted and the benefits can be the greatest. It is also necessary for fortification with iron and calcium to become an important public health nutrition consideration in our transitional diets, to the point of becoming a clear public policy objective.

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Authorship

The author had sole responsibility for all aspects of preparation of this paper.

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