

# *Animal board invited review: dietary transition from animal to plant-derived foods: are there risks to health?*

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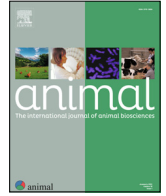
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## Animal board invited review: Dietary transition from animal to plant-derived foods: Are there risks to health?



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### ABSTRACT

Animal-derived foods (ADFs) are a very varied group of foods, but many are nutrient rich and contain higher quality protein than provided by plant-derived foods such that a simple replacement of ADF protein is likely to lead to a reduction in overall protein quality. In addition, many ADFs are richer in some nutrients than plant-based foods (e.g. Fe, Ca) and these often have a higher bioavailability. ADFs also provide nutrients that plants cannot supply (e.g. vitamin B<sub>12</sub>) and some provide beneficial health functionality (e.g. hypotensive) which is not explained by traditional nutrition. However, there remains a good health reason to increase the proportion of plant-derived food in many diets to increase the intake of dietary fibre which is often consumed at very sub-optimal levels. It seems logical that the increased plant-derived foods should replace the ADFs that have the least benefit, the greatest risk to health and the highest environmental impact. Processed meat fits these characteristics and should be an initial target for replacement with plant-based based protein-rich foods that additionally provide the necessary nutrients and have high-quality dietary fibre. Processed meat covers a wide range of products including several traditional foods (e.g. sausages) which will make decisions on food replacement challenging. There is therefore an urgent need for research to better define the relative health risks associated with the range of processed meat-based foods. The aim of this review is to examine the evidence on the benefits and risks of this dietary transition including the absolute necessity to consider initial nutrient status before the replacement of ADFs is considered.

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### Implications

Animal-derived foods contain high-quality protein and a range of nutrients that plants do not contain or contain at lower concentrations. A simple replacement of animal protein by plant-based foods will lead to an overall lower protein quality and lower intakes of key nutrients. This is a particular concern for adolescents who already consume very suboptimal amounts of nutrients that are typically supplied by animal-derived foods. A key concern is for bone health since 80% of bone mineralisation occurs in adolescent years, which if impaired increases the risk of weaker bones in later life as already seen with vegans.

### Introduction

Concerns about the consumption of animal-derived foods (ADFs) because of their believed negative effects on the environment and human health have given rise to an increased interest

in replacing at least a proportion of dietary protein of animal origin with that from plants. Despite this trend, in 2022, only 10 and 3% of the European population followed vegetarian and vegan dietary patterns, respectively (Meticulous Research, 2024). Nevertheless, the same report predicts that within Europe, the demand for plant-derived protein will rise to €7.16 billion by 2030 at an annual compound growth rate of 8.9% from 2023 to 2030. There is also increasing demand for plant-based milk alternatives (PBMA) and plant-based meat substitutes (PBMS) which presumably will at least partially replace the ADFs (Statistica, 2023). There has however been considerable concern about the nutritional adequacy of many PBMA (Clegg et al., 2021; Antunes et al., 2023; Moore et al., 2024), and Tso and Forde (2021) suggest that the health benefits of novel PBMS lack adequate evidence from longitudinal and randomised controlled trials (RCTs).

Those advocating a need to replace ADFs with those from plants have tended not to recognise that ADFs represent a highly diverse range of foods varying substantially in nutritional composition, nutrient quality, and functionality. There has also been a tendency to consider only the replacement of protein, ignoring the fact that replacing animal-derived protein may also lead to a reduction in

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other important nutrients that ADFs contain. This was acknowledged by the review of [Viroli et al. \(2023\)](#) and shown in the 12-week RCT of [Pellinen et al. \(2021\)](#) involving partial replacement of animal protein foods with plant protein foods which led to a lower status of vitamin B<sub>12</sub> and iodine. There are therefore many uncertainties surrounding the replacement of ADFs by plant counterparts.

The impact of dietary transition from ADFs to plant-derived foods will clearly depend on the extent of the transition and crucially, on which ADF is targeted and the nutrient status of the consumer at the start of the transition. This review aims to review and summarise the key issues associated with this transition with some focus on populations with sub-optimal initial nutrient status.

### Variability of nutrient composition and bioavailability of animal-derived foods

Animal-derived foods vary not only in the animal providing the food but also in the food type (meat, eggs, milk etc), its nutritional composition and quality and its association with diet-responsive chronic diseases. [Table 1](#) illustrates the substantial variability in nutritional composition both between and within a selection of ADFs. Further variability will exist between for example, different cuts of beef, breast and leg meat of chicken and the wide range of different dairy products. Nevertheless, [Table 1](#) does show beef, milk, eggs and mackerel to be rich sources of Fe, Ca, vitamin A and vitamin B<sub>12</sub>, respectively. Yet nutrient composition alone does not indicate the proportion of a nutrient that is bioavailable for absorption. For example, the data in [Table 1](#) do not show that much of the Fe in beef is in the haem form which has a considerably higher bioavailability than non-haem Fe found in plant-derived foods ([Fairweather-Tait, 2023](#)) or that Ca in milk (and dairy products) becomes bioavailable in the digestive tract whilst phytate in some plant-derived foods can substantially limit the absorption of Ca ([Shkempi and Huppertz, 2021](#)), Fe ([Ravindran, 1991](#)) and Zn ([Lönnerdal, 2000](#)). Other plant-derived compounds including oxalates can inhibit Zn absorption ([Agte et al., 1994](#)), and tannins reduce the absorption of Fe ([Delimont et al., 2017](#)). The potential substantial effects of these and other plant-produced nutrient absorption inhibitors need to be considered when replacing ADFs with plant-derived foods.

**Table 1**

Typical variability of energy and nutrient concentrations in typical animal-derived foods<sup>1</sup> (source [Pinchen et al., 2021](#)).

| Energy and nutrient concentration / 100 g | Meat |         | Fish |          | Eggs <sup>2</sup> | Milk  |      |
|---|------|---------|------|----------|-------------------|-------|------|
|   | Beef | Chicken | Cod  | Mackerel |                   | Whole | S-sk |
| Energy (kJ)                               | 542  | 457     | 320  | 968      | 547               | 265   | 195  |
| Protein (g)                               | 22.5 | 22.3    | 17.5 | 18.0     | 12.6              | 3.4   | 3.5  |
| Fat (g)                                   | 4.3  | 2.1     | 0.60 | 17.5     | 9                 | 3.6   | 1.7  |
| SFA <sup>3</sup> (g)                      | 1.7  | 0.60    | 0.16 | 3.9      | 2.5               | 2.3   | 1.1  |
| MUFA <sup>4</sup> (g)                     | 1.9  | 1.0     | 0.14 | 6.7      | 3.4               | 0.96  | 0.40 |
| PUFA <sup>5</sup> (g)                     | 0.23 | 0.40    | 0.11 | 4.5      | 1.4               | 0.09  | Tr   |
| Calcium (mg)                              | 5    | 6       | 12   | 20       | 46                | 120   | 120  |
| Magnesium (mg)                            | 22   | 26      | 25   | 37       | 13                | 11    | 11   |
| Iron (mg)                                 | 2.7  | 0.7     | 0.10 | 1.0      | 1.7               | 0.02  | 0.02 |
| Zinc (mg)                                 | 4.1  | 1.2     | 0.30 | 0.5      | 1.1               | 0.5   | 0.4  |
| Selenium (µg)                             | 7    | 13      | 23   | 42       | 23                | 1     | 1    |
| Iodine (µg)                               | 10   | 7.0     | 196  | 29       | 50                | 31    | 30   |
| Vitamin A (µg)                            | Tr   | 11      | 2.0  | 54       | 126               | 36    | 1    |
| Vitamin D (µg)                            | 0.5  | 0.1     | Tr   | 8        | 3.2               | Tr    | Tr   |
| Vitamin B <sub>12</sub> (µg)              | 2.0  | Tr      | 1.5  | 9        | 2.7               | 0.9   | 0.8  |

Abbreviations: S-sk = Semi-skimmed; Tr = Trace.

<sup>1</sup> The beef, chicken, cod, mackerel, eggs, whole milk, semi-skimmed milk are Foods 18–468, 18–488, 16–373, 16–393, 12–937, 12–596, 13–313 respectively in [Pinchen et al. \(2021\)](#).

<sup>2</sup> Hen eggs.

<sup>3</sup> Saturated fatty acids.

<sup>4</sup> Monounsaturated fatty acids.

<sup>5</sup> Polyunsaturated fatty acids.

Similarly, the protein concentration of foods does not indicate the quality of the protein. Protein quality is a function of its amino acid composition and their bioavailability. The current internationally agreed system for ascribing protein quality is the Digestible Indispensable Amino Acid Score ([FAO, 2013](#)). Essentially, the most limiting digestible indispensable (essential) amino acid content defines the Digestible Indispensable Amino Acid Score of a protein with digestible indispensable amino acid ratios set according to reference pattern scores for infants (0–6 months), children (0.5–3 years), children older than 3 years, adolescents, and adults. [Table 2](#) shows some Digestible Indispensable Amino Acid Scores for a selection of protein sources based mainly on [Herreman et al. \(2020\)](#). A Digestible Indispensable Amino Acid Score > 75 defines the protein as high quality and overall, [Table 2](#) shows that animal proteins have a higher quality than plant proteins although there is considerable variability between different plant protein sources. Because much of the plant-based protein fed to food-producing animals is human-inedible and that protein quality of animal proteins is usually higher than plant proteins, [Ertl et al. \(2016\)](#) proposed that protein quality should be included when assessing the net contribution of livestock to human food supply. Similarly, [Pikosky et al. \(2022\)](#) highlight that protein quality must be considered at a time of food systems transition to avoid unintended health consequences. The issue of protein quantity and quality is particularly important in relation to the increased availability of PBMA since except for soya-based drinks, most have extremely low protein concentrations (e.g. [Moore et al., 2024](#)) which has led to serious kwashiorkor-related illness in a number of infants and toddlers ([Walsh and Gunn, 2020](#)).

[McAuliffe et al. \(2023\)](#) have proposed that protein quality should be included as a complementary functional unit in the life cycle assessment of ADFs when compared with those from plants.

### Sources of protein in the diet and should this change?

#### The contribution of food groups

As an example, data from the UK National Diet and Nutrition Survey (NDNS) Years 9–11 ([NDNS, 2020](#)) extracted into [Table 3](#) indicate for all age groups, that ADFs (including fish and eggs) make the largest contribution (57–59%) to protein intake. Cereals

**Table 2**

Digestible indispensable amino acid scores (DIAAS) for a selection of plant and animal protein sources (source [Herreman et al., 2020](#)).

| Protein source    | DIAAS Score <sup>1</sup> | Limiting amino acid  |
|-------------------|--------------------------|----------------------|
| <b>Plants</b>     |                          |                      |
| Wheat             | 40                       | Lysine               |
| Fava/Faba bean    | 55                       | Methionine + Cystine |
| Pea               | 70                       | Methionine + Cystine |
| Soya bean         | 91                       | Methionine + Cystine |
| <b>Animals</b>    |                          |                      |
| Whey protein      | 85                       | Histidine            |
| Casein            | 117                      | NA <sup>2</sup>      |
| Eggs              | 101                      | NA                   |
| Pork              | 117                      | NA                   |
| Beef <sup>3</sup> | 114                      | NA                   |

<sup>1</sup> According to the 0.5–3 years old reference pattern score.

<sup>2</sup> Not applicable to DIAAS scores > 100.

<sup>3</sup> Source [Ertl et al. \(2016\)](#).

and cereal products were the major plant sources (24–29%). Meat contributed the greatest proportion of protein of all ADFs (29–37%) followed by milk and dairy foods (13–20%) with the higher value for milk understandably seen for the youngest age group. Within meat, red and processed meat provided somewhat more protein than white meat. Using the definitions of red and processed red meat defined by [Hobbs-Grimmer et al. \(2021\)](#), processed red meat contributed slightly more protein than red meat for the youngest age group with the opposite for the other two age groups. The level of detail in the current NDNS summary data makes further differentiation of red meat/processed red meat difficult but in an earlier detailed study of 1758 adults (19–64 years of age) in the NDNS data for 2008–2012, [Hobbs-Grimmer et al. \(2021\)](#) showed that mean intakes of red meat ( $36.8 \pm 48.8$  g/day) and processed red meat ( $34.8 \pm 48.9$  g/day) were very similar and the similarity was retained across low and high tertiles of intake. No data on the relative protein contribution were reported. They also showed that overall, only 57% of the population achieved the target

**Table 3**

Sources of protein in the diet of three age groups in the UK (source [NDNS, 2020](#)).

| Protein source                     | Age range (years) |       |       |
|------------------------------------|-------------------|-------|-------|
|                                    | 4–10              | 11–18 | 19–64 |
| <b>All sources (%)</b>             |                   |       |       |
| Cereals/cereal products            | 29                | 29    | 24    |
| Milk and dairy products            | 20                | 13    | 13    |
| Meat and meat products             | 29                | 37    | 34    |
| Vegetables and nuts                | 8                 | 7     | 9     |
| Fish and fish dishes               | 5                 | 5     | 7     |
| Eggs and egg dishes                | 3                 | 2     | 5     |
| Miscellaneous <sup>1</sup>         | 6                 | 7     | 8     |
| Total                              | 100               | 100   | 100   |
| <b>Animal vs plant sources (%)</b> |                   |       |       |
| Animal sources                     | 57                | 57    | 59    |
| Plant sources                      | 37                | 36    | 33    |
| <b>Within meat (%)</b>             |                   |       |       |
| White meat                         | 45                | 46    | 45    |
| Red meat                           | 26                | 31    | 33    |
| Processed red meat                 | 29                | 23    | 22    |
| Red + processed red meat           | 55                | 54    | 55    |
| <b>Within dairy (%)</b>            |                   |       |       |
| Whole milk                         | 21                | 13    | 10    |
| Semi-skimmed milk                  | 32                | 33    | 30    |
| Skimmed milk                       | 1                 | 2     | 4     |
| Other milk and cream               | 5                 | 10    | 6     |
| Cheese                             | 22                | 31    | 34    |
| Yogurt                             | 15                | 8     | 14    |
| Ice cream                          | 4                 | 3     | 2     |

<sup>1</sup> Not included in the calculations below

of consuming < 70 g/day of red meat plus processed meat as proposed by the [Scientific Advisory Committee on Nutrition \(2010\)](#) and this fell to zero in the highest tertile of intake.

Interestingly, [NDNS \(2020\)](#) also reported that mean protein intake for the three age groups in [Table 3](#) were 2.2, 1.7 and 1.3 times the reference nutrient intake (**RNI**) for the 4–10 years, 11–18 years and 19–64 years age groups, respectively. This may suggest that a reduction of protein intake could be achieved without any health risk. Currently, the RNI for protein in the UK ([Dorrington et al., 2020](#)) and the EU ([EFSA, 2024](#)) is based solely on BW with surprisingly, no consideration of protein quality, so any reduction should ensure that the remaining protein is of adequate quality especially at critical life stages such as childhood, pregnancy, and lactation. In addition, there is now building evidence that protein requirements for the elderly should be increased to help reduce the loss of skeletal muscle mass and thus the risk of sarcopenia ([Lonnie et al., 2018](#); [Dorrington et al., 2020](#)), although the type of protein for stimulating muscle protein synthesis is important and is discussed below.

#### *The impact of animal-derived protein-rich foods on cardiometabolic health, cancer, and dementia*

A key factor that should be considered when a dietary transition from ADFs to those from plants is contemplated is the association/-effect of the ADFs on health and mortality. Like nutrient composition, the risk of diet-responsive chronic diseases varies between ADFs and is often misunderstood. There have been several reviews on this subject recently including those for meat ([Geiker et al., 2021](#); [Girromini and Givens, 2022](#); [Wood et al., 2024](#)) and dairy foods ([Soedamah-Muthu and de Goede, 2018](#); [Givens, 2023](#)). As a result, the following sections will only summarise the findings but will concentrate on the two major protein-rich food groups milk/dairy foods and meat and meat products with emphasis on meat/meat products which present a more complex association with chronic disease risk and have a higher environmental impact.

#### *Eggs and fish*

Overall, eggs and fish make only a small contribution to UK protein intake ([Table 3](#)) although there is evidence that egg consumption has increased since 2006 ([Egg Info, 2023](#)). Eggs are nutrient dense ([Table 1](#)) and are not now subject to intake limits in some dietary guidelines ([Mason, 2023](#)), with the possible exception of subjects with familial hypercholesterolaemia. [Mason \(2023\)](#) also estimates that eggs should be considered as a replacement for less healthy ADFs or those with a higher environmental impact such as red meat and particularly processed red meat. Eggs have been associated with an increased risk of type 2 diabetes and of cardiovascular diseases in subjects with type 2 diabetes ([Shin et al., 2013](#)) but the work of [Geiker et al. \(2018\)](#) concluded that factors such as overall dietary pattern, exercise and genotype would have a greater impact on risk of cardiovascular diseases and type 2 diabetes than typical egg consumption. They recommended that consuming up to seven eggs per week was safe, although those with established cardiovascular diseases or type 2 diabetes should pay particular attention to a healthy lifestyle. The prospective study with three US cohorts plus a systematic review and meta-analysis of [Drouin-Chartier et al. \(2020\)](#) found no association between moderate egg consumption and the risk of type 2 diabetes. In a pooled analysis of 15 prospective studies, [Wu et al. \(2016\)](#) showed that those who consumed  $\geq 25$  g/day vs < 5 g/day of eggs had a significant + 14% risk of advanced ( $P$ -trend 0.01) and fatal ( $P$ -trend 0.01) prostate cancers although subsequently the [World Cancer Research Fund and the American Institute for Cancer Research \(2018\)](#) update review reported that

the evidence on this association was limited leading to no conclusion.

Fish has been traditionally regarded as a healthy food with consistent evidence of an association with a reduction of cardiovascular diseases, particularly for oily fish which supply the long chain n-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) (Raatz et al., 2013; Ricci et al., 2023). This is supported by a recent umbrella review of meta-analyses of prospective studies and RCTs (Zhao et al., 2023). This identified 17 beneficial health associations including those for cardiovascular disease mortality, acute coronary syndrome, cerebrovascular disease, and all-cause mortality. A further eight non-significant associations were seen for conditions including colorectal and prostate cancers and hypertension. Using dose–response analyses, Zhao et al. (2023) estimated fish consumption of one–two servings per week, especially of oily fish, appears to be safe and may provide health protective effects.

There has also been considerable interest in the potential role of DHA in particular as a risk moderator for dementia and Alzheimer's disease. For example, a meta-analysis of Zhang et al. (2016) found that a 100 mg/day increase in DHA intake was associated with 14 and 37% reduced risks of dementia and Alzheimer's disease respectively. Pontifex et al. (2018) reviewed the evidence on the effect of the APOE genotype on risk of Alzheimer's disease and how this might be influenced by DHA status. They concluded that a higher tissue status of DHA was associated with a lower risk of Alzheimer's disease with APOE-ε4 carriers probably requiring a higher dose. More recently, Liu et al. (2022) reported a study with data on 215 083 subjects (mean age 64.1 ± 2.9 years) without dementia in the UK Biobank with a mean follow–up period of 7.92 years. The results showed that compared with non-user, fish oil use was associated with a 13% lower risk of all-cause dementia (Hazard ratio 0.87, 95% confidence interval: 0.79–0.96). However, fish oil use was not associated with any dementia sub-types including Alzheimer's disease and vascular dementia. This may be surprising considering that Alzheimer's disease is typically by far the most frequent form of dementia.

#### *Milk and dairy foods*

Across many studies the association between dairy foods and cardiovascular diseases is generally neutral but with some studies showing a reduced risk, especially for stroke (Soedamah-Muthu and de Goede, 2018). This is regardless of milk and dairy products being the main dietary contributor of saturated fatty acids. This creates considerable uncertainty that the traditional diet–heart hypothesis remains valid since it predicts that rising saturated fatty acid intake will increase the concentration of serum cholesterol which in turn will promote more cardiovascular diseases. Research that has measured serum cholesterol tends to confirm that increased intake of saturated fatty acids gives rise to higher concentration of low-density lipoprotein cholesterol, yet with no consistent rise in risk of cardiovascular diseases, even though low-density lipoprotein has been confirmed a causal component of atherosclerotic cardiovascular diseases. Recent research findings are beginning to provide some explanations for this, particularly in relation to dairy foods. These include the potentially counteractive benefits of saturated fatty acid–related increases in high-density lipoprotein cholesterol and food matrix lowering effects on fat absorption which lead to smaller increases in low-density lipoprotein cholesterol. Other evidence includes saturated fatty acids being associated with the less atherogenic large, buoyant low-density lipoprotein particles and possible counterbalancing hypotensive actions of dairy proteins (Givens, 2023).

Prospective studies and RCT show that dairy foods are not generally associated with the risk of type 2 diabetes, although there is a reasonably consistent negative association between yogurt con-

sumption and risk of type 2 diabetes (Soedamah-Muthu and de Goede, 2018). Given the rapidly rising prevalence of type 2 diabetes in many populations this topic needs considerably more research attention. This should include identifying biochemical mechanisms which may explain the association as they are not known with any certainty. Furthermore, since the composition of yogurt is highly variable, there is a pressing need to know if there is an optimum type for type 2 diabetes protection.

In relation to dairy foods and the risk of cancer, the most recent evidence from the World Cancer Research Fund/American Institute for Cancer (2018) reports only limited or indecisive findings on the association of dairy foods and cancers of the mouth-pharynx-larynx, gall bladder, liver, pancreas, bladder, oesophagus, endometrium, stomach, kidney, ovary, and lung. However, World Cancer Research Fund/American Institute for Cancer (2018) does confirm that 'Consumption of dairy products probably protects against colorectal cancer'. For premenopausal cancer of the breast World Cancer Research Fund/American Institute for Cancer (2018) reports 'Limited-suggestive' evidence that dairy foods can decrease its risk, whilst for postmenopausal breast cancer, the report says 'the picture is less clear, and no conclusion was possible'. The findings in relation to prostate cancer are somewhat uncertain with the overall World Cancer Research Fund/American Institute for Cancer (2018) conclusion being 'For a higher consumption of dairy products, the evidence suggesting an increased risk of prostate cancer is limited'.

The meta-analysis of Wu and Sun (2016) reported that the highest consumption of milk was associated with decreased risk of cognitive disorders (odds ratio 0.72, 95% confidence interval: 0.56–0.93) although only seven papers could be found, and subgroup analysis showed that the benefit was only seen in Asian subjects with overall high heterogeneity. More recently Baliyan et al. (2023) showed in a study with old rats that a supplement of concentrated milk fat globule membrane led to enhanced spatial working memory. The supplement also led to higher concentrations of EPA, DHA, and plasmalogens in the synaptosomes isolated from the hippocampus and frontal cortex. Although the use of a rodent model has limitations, the same group (Calvo et al., 2023) fed a milk drink fortified with milk fat globule membrane to healthy or mildly cognitively impaired subjects aged > 65 years in a 14-week placebo-controlled RCT. Female participants on the milk fat globule membrane treatment showed improved episodic memory and early life recall. Males showed a similar tendency, but the effect was not significant. Clearly, it is early days for this work, but it definitely has promise and should be expanded particularly starting with subjects before any clinical symptoms are evident.

#### *Meat and meat products*

An early systematic review and meta-analysis found that intake of processed meat, but not red meat, was associated with an increased risk of ischaemic heart disease (Micha et al., 2010). A further analysis of 13 prospective studies showed that the highest intake of processed meat had 22 and 18% higher risk of all-cause mortality and cardiovascular diseases, respectively. Red meat was associated with a 16% higher risk of death from cardiovascular diseases whilst white meat was not associated with any of the disease or mortality outcomes (Abete et al., 2014).

To rationalise the findings of several systematic reviews, Jakobsen et al. (2021) published an umbrella review of three systematic reviews and meta-analyses (18 cohorts) published in 2017–2019. This found no obvious association between unprocessed red meat or processed meat and the risk of cardiovascular diseases overall, although processed meat was positively associated with of ischaemic heart disease (+27% per 50 g/day) and stroke (+16–17% per 50 g/day). Unprocessed white meat was asso-

ciated with reduced risk of stroke (−13% in high vs low consumers). These findings were supported by the Prospective Urban Rural Epidemiology Study (Iqbal et al., 2021) involving a cohort of 134 297 individuals from 21 low-middle, and high-income countries. No significant associations between unprocessed red meat and poultry meat and mortality or major cardiovascular disease events were seen. A higher intake of processed meat ( $\geq 150$  g/wk vs 0 g/wk) was however associated with a considerably higher risk of mortality (+51%) and major cardiovascular disease events (+46%) including stroke (+56%). A meta-analysis of Schwingshackl et al. (2017) reported that red meat and processed meat were both associated with an increased risk of hypertension, but the risk associated with processed meat was almost double that for red meat (+12% per 50 g). This is consistent with the increased risk of stroke as observed by Jakobsen et al. (2021) and Iqbal et al. (2021).

Wang et al. (2022) studied the association between red meat consumption and cardiovascular diseases-caused mortality using data from the UK Biobank. This involved analysis of data for 180 642 subjects with a median follow-up period of 8.6 years using covariates including processed meat, poultry meat and fish such that the findings applied only to red meat. The results showed that the highest consumption of red meat ( $\geq 3.0$  times/week) was associated with increased risks of 20, 53, and 101% for mortality caused by cardiovascular diseases, coronary heart disease, and stroke respectively, compared with the lowest consumption ( $< 1.5$  times/week). There was no association between red meat consumption and all-cause mortality. These results differ from some others which have found an association of processed meat with all-cause and cardiovascular disease mortality but with not with red meat (e.g. Abete et al., 2014; Larsson and Orsini, 2014). Wang et al. (2022) discussed the possible causes of this heterogeneity between studies including the possibility that unprocessed and processed meat may contain different types of meat that have different effects on mortality risk, but they did concede that generally, the association between processed meat and mortality risk was more consistent than for unprocessed red meat. Wang et al. (2022) also showed using substitution analysis that replacing dietary red meat with poultry meat or cereal was associated with a 9–16% reduction in cardiovascular diseases or coronary heart disease mortality.

In relation to the association of meat intake and type 2 diabetes, a meta-analysis of 12 prospective studies found that the risk of high vs low consumers was +17, +21 and +41% for total, red, and processed meat respectively (Aune et al., 2009). A similar outcome was reported by Pan et al. (2011) with three US cohorts. They confirmed that both unprocessed and processed red meat were positively (P-trend 0.001) associated with the risk of type 2 diabetes with a meta-analysis showing that unprocessed red meat and processed red meat were associated with an increased risk of +19% per 100 g/day and + 51% per 50 g/day respectively. A recent study (Gu et al., 2023) reported that intakes of total, processed, and unprocessed red meat were all positively and significantly associated (highest vs lowest quintile) with risks of type 2 diabetes of +62, +51 and +40% respectively. Gu et al. (2023) also estimated that replacing one portion/day of total red meat, processed red and unprocessed red meat with one portion/day of nuts plus legumes would reduce the type 2 diabetes risk by 22, 33 and 20% respectively. Replacement with one portion of dairy foods (type not specified) also produced a risk reduction although slightly smaller than for nuts plus legumes.

The World Cancer Research Fund/American Institute for Cancer (2018) update review of 19 studies on meat and colorectal cancer concluded that consumption of red meat is probably a cause of colorectal cancer, and that processed meat is a convincing cause. The

relative risks of colorectal cancer were +12% per 100 g/day of red meat and +16% per 50 g/d of processed meat. As a result, the expert committee recommended 'For people who eat meat, eat no more than moderate amounts of red meat, such as beef, pork and lamb, and eat little, if any, processed meat' although the current World Cancer Research Fund (2023) website adds that 'This recommendation is not to completely avoid eating meat. Meat can be a valuable source of nutrients, in particular protein, iron, zinc, and vitamin B<sub>12</sub>'. The recommendation not to avoid meat appears wise given the key nutrients some meat provides but additional guidance on what meat type to consume to obtain these nutrients would have been helpful. Based to a large degree on the World Cancer Research Fund data, the Scientific Advisory Committee on Nutrition (2010) confirmed that there was an association between red and processed meat and colorectal cancer, and this led to the UK government advice 'that adults who regularly consume more than 90 g per day of red and processed meat reduce their consumption to no more than the population average of 70 g per day of red and processed meat'. This advice is confusing as it suggests that those consuming 90 g per day of any combination of red and processed meat need do nothing which is certainly not in line with the World Cancer Research Fund findings. There should be separate guidelines for red and processed meat.

Zeraatkar et al. (2019) undertook a systematic review of 12 RCTs which studied lower vs higher red meat intake on several outcomes including colorectal cancer but proposed that only a single trial of 48 835 women met their criteria for being at low risk of bias and thus provided the most credible evidence. The results showed low-very low certainty that diets lower in red meat may have little or no effect on total cancer and colorectal cancer incidence (Hazard ratio 1.04, 95% confidence interval: 0.90–1.20). The authors did report that there were few relevant trials and the one selected only involved women. These limitations may have restricted the widespread interpretation of the findings and this and other points have been discussed in various commentaries on the study including Koretz (2020).

Recently, Niedermaier et al. (2023) reported the findings of a simulation study which estimated the impact of reducing intake of red and processed meat on colorectal cancer incidence in Germany from 2020 to 2050. Removing processed meat from the diet predicted a reduction in colorectal cancer cases by some 205 000 (9.6%) whereas eliminating red meat the equivalent reduction would be about 63 000 cases (2.9%). In both cases, there would be a greater reduction in males than females. It was also estimated that simply reducing intake of both processed and red meat by one or two servings (each 11 or 22 g) per day would reduce case numbers by 3.1 and 6.5% respectively. This study used the relative risk factors of the World Cancer Research Fund and the American Institute for Cancer Research (2018) which explains the substantially greater case number reduction for processed meat than red meat but highlights the potentially large impact that removing processed meat would have at least in Germany where consumption of red and particularly processed meat is high with median intakes of 38 g/day and 46 g/day respectively. These compare with mean UK intakes of 37 g/day and 35 g/day, respectively (Hobbs-Grimmer et al., 2021).

Wu et al. (2016) concluded that the results of their pooled analysis of 15 prospective studies did not support a major effect of red meat, unprocessed red meat, and processed meat on any of the prostate cancer outcomes examined, apart from a small positive association between unprocessed red meat and advanced stage tumours although this examination had several studies excluded. Moreover, poultry meat was significantly associated with a reduced risk of advanced (−17%) and fatal (−31%) prostate cancers. The World Cancer Research Fund and the American Institute for

Cancer Research (2018) update reported that there was only limited evidence for an association of red, processed and poultry meat such that no conclusion could be reached.

There is evidence (e.g. Hur et al., 2019; Zaoui et al., 2024) that in addition to meat processing, the cooking and preservation of meat may increase the cancer risk due to the creation of potentially carcinogenic compounds including heterocyclic amines, polycyclic aromatic hydrocarbons, and N-nitroso compounds. These compounds or their derivatives have been shown to cause DNA damage, a key step in cancer development. Typically, heterocyclic amines are formed in a temperature-dependent manner by cooking meat at high temperatures (175–300 °C) although the non-IQ-type of heterocyclic amines are generated at temperatures > 300 °C. Polycyclic aromatic hydrocarbons are associated with cooking time and temperature by methods such as grilling, roasting and frying but also smoking and drying (Hur et al., 2019). N-nitroso compounds comprise nitrosamine and nitrosamide and are typically produced during food storage when nitrite/nitrate compounds have been added as preservatives. Higher concentrations have been seen following long-term storage. In addition, directly consumed nitrates and nitrites can be converted to N-nitroso compounds in the digestive system (Chazelas et al., 2022) as can haem (Cross et al., 2003). Current advice from the World Cancer Research Fund (2023) cautions against high-temperature cooking of processed meat such as when grilling or barbecuing.

There is concern that the worldwide prevalence of dementia, predominantly Alzheimer's disease, is rising and while an increasing age of many populations accounts for some of the rise, dementia is not a specific part of biological ageing and genotype, lifestyle and dietary factors are known to contribute to dementia risk. Some earlier studies including Grant (2014) have shown a positive association between meat consumption and dementia prevalence but perhaps the most convincing evidence available relates to a cohort study of some 490 000 subjects in the UK Biobank with a mean ( $\pm$  SD) follow-up period of  $8 \pm 1.1$  years (Zhang et al., 2021). This showed that an increase of 25 g/day of processed meat was associated with an increased risk of all-cause dementia by 44% ( $P$ -trend < 0.011) and an increased risk of Alzheimer's disease by 52% ( $P$ -trend = 0.001). Interestingly, red meat was associated with a 30% reduction in the risk of Alzheimer's disease ( $P$ -trend = 0.009) and unprocessed poultry meat had no association with the risk of all-cause dementia or Alzheimer's disease.

Overall, the evidence is building that processed meat is associated with substantially increased risks of cardiovascular diseases, type 2 diabetes, colorectal cancer and possibly dementia whilst red meat has a somewhat varied association with cardiovascular diseases, type 2 diabetes, colorectal cancer and dementia but does provide high-quality protein and is rich in several important micronutrients including haem Fe, Zn, and vitamin B<sub>12</sub>. This adds more evidence to the proposal that processed and unprocessed meat should have separate public dietary guidance as proposed by Hobbs-Grimmer et al. (2021). However, if this guidance was linked with replacing processed meat protein with plant-based sources the benefits would be twofold, reduction of the health risks associated with processed meat and an increase in dietary fibre intake which has been shown to provide protection against colorectal cancer. For example, 10 g/day of protein from processed meat could be replaced by 167 g of faba beans (fresh, raw) which would also give about 13 g/day of dietary fibre, a sizeable increase for many. In the prospective study of Bingham et al. (2003) the highest vs the lowest fibre intake was associated with a 40% reduction in risk of colorectal cancer whilst Murphy et al. (2012) reported a risk reduction of 13% per 10 g/day. It is however worth noting that in the EPIC-Oxford study with 64 000 participants, vegetarians had a significantly higher (+39%) incidence of colorectal cancer than meat eaters for no clear reason. No data on fibre intake

were given (Key et al., 2009). In a case-control study, Song et al. (2015) found that the controls consumed more total fibre than the cases and an overall inverse association between total fibre and colorectal cancers, representing a 56% risk reduction in the highest vs lowest intakes. Overall, the evidence indicates that dietary fibre is a highly desirable dietary component, and it is concerning that in the UK a low percentage of all age groups consume the recommended intake of dietary fibre (Fig. 1).

#### *The functionality of milk proteins in key life processes*

Whilst milk and dairy products are known to be rich sources of key nutrients, milk proteins in particular, have certain functionalities that would not be explained by a classical consideration of nutrient supply. These do contribute to the overall health impact and should be considered when assessing dairy protein replacement. Two examples are briefly discussed here although there are others including hypotensive effects and related improvement in vascular endothelial function (Fekete et al., 2016).

#### *Growth of children*

The benefits of milk in childhood diets have been known for many years. For example, a report of Corry Mann (1926) showed that giving an additional 568 mL/day of milk to boys in a children's residential home led to a marked increase in growth, and Leighton and Clark (1929) showed that daily feeding to children aged 6 to 13 years of 426–568 mL/day (according to age) led to a mean height and weight increase of 23.5 and 45.3% respectively compared to the non-milk treatment. A range of studies over a long period have shown milk to be an important food for reducing stunting in children. The effect of milk on linear growth is now understood to be mainly driven by the stimulation of hepatic IGF-1 by milk proteins (Watling et al., 2021), especially by caseins but not my meat or vegetable proteins (Hoppe et al., 2009). The reasons for this differential effect on IGF-1 stimulation are unclear but may be related to different amino acid profiles. IGF-1 is essential for longitudinal bone growth, with its regulation of bone length associated with changes in chondrocytes of the proliferative and hypertrophic zones of the growth plate (Yakar et al., 2018). IGF-1 is also involved in the maintenance of bone in adult life. Dietary protein-activated IGF-1 production is mediated by peroxisome proliferator-activated receptor gamma activation. This therefore plays a big role in the regulation of hepatic IGF-1 secretion and gene expression in response to dietary proteins (Wan et al., 2017).

#### *Reducing skeletal muscle loss in the elderly*

Sarcopenia is a condition characterised mainly by a chronic loss of muscle mass and muscle strength with advancing age. Sarcopenia can have far-reaching consequences since, for example, it reduces bone protection increasing the risk of breakage in a fall leading to reduced mobility, disability, and lower quality of life. A less well-recognised outcome of reduced muscle mass and possibly associated reduced exercise ability, is the increased risk of hyperglycaemia. This is because skeletal muscle has a key role in the regulation of postprandial blood glucose concentration, with some 80% of circulating glucose being taken up by the skeletal muscles for oxidation (Hulett et al., 2022). Impairment in this process can lead to insulin resistance and hence type 2 diabetes which increases the risk of mortality in sarcopenic subjects (Takahashi et al., 2021).

There has been considerable research on the relative anabolic effects of amounts of protein and protein types (Givens, 2024) with the primary conclusion that whey protein, which is rapidly digested and absorbed, leads to greater muscle protein synthesis than from slower-digested proteins like casein and from plant proteins (van Vliet et al., 2015). This is primarily attributed to the



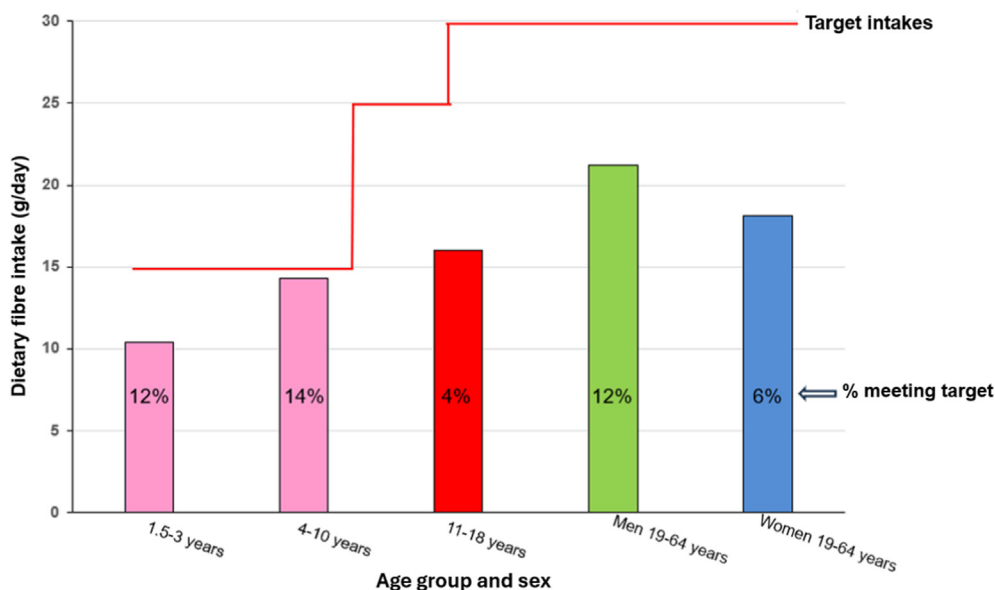


Fig. 1. Dietary fibre intake in the UK, comparison with targets and % achieving targets ( source NDNS, 2020).

higher leucine content of whey protein which has also been seen in studies using leucine supplements. The anabolic effect of leucine is complex. It is an important activator of the mammalian target of rapamycin (mTOR), a nutrient-sensing signalling pathway which promotes skeletal muscle synthesis (Rehman et al., 2023). In addition, leucine is insulinotropic and additional insulin enhances muscle protein synthesis.

### Summary

Across the range of ADFs commonly consumed, fish, eggs, milk/milk products and white meat generally have neutral or beneficial associations with cardiometabolic health. Yet there remains a lack of knowledge on some of the mechanisms involved and the relative impacts of the various products derived from these foods. The situation with red meat is more complex with a good deal of conflicting evidence, in part likely due to its inherent heterogeneity. There is no doubt however that most ADFs provide higher quality protein than plant sources and ADFs are often rich in several important micronutrients with high bioavailability and these nutrients need to be considered when assessing protein replacement. The evidence for processed meat of an association with increased risk of cardiometabolic diseases and colorectal cancer is increasing as is the case for having separate dietary guidance for red and processed meat. The proposition that replacing protein from processed meat with plant-sourced protein has strong foundations giving health benefits from reduced processed meat and increased dietary fibre intake. There is considerably less evidence for associations of ADFs with dementia although the evidence from the study of Zhang et al. (2021) with typical processed meat products is concerning although not a cause-and-effect study. Clearly, more evidence is needed.

### Dietary transition and micronutrient status: Risks to health

As noted earlier it is important to consider the nutritional status of populations and individuals before dietary transition is considered. It is therefore concerning that the UK NDNS (2020) reported that 49, 16, 40, 16, 41 and 28% of adolescent females (aged 11–18 years) had dietary intakes of Fe, Ca, Mg, Zn, Se and I respectively, below the Lower Reference Nutrient Intakes (LRNI) for these nutri-

ents and there are also some concerns for male adolescents and older women. (Table 4). The LRNI represents the nutrient requirements adequate for only the bottom 2.5% of the population and therefore intakes less than the LRNI represent a serious risk to health. Many of the low nutrient intakes are predominantly the result of a progressive reduction in red meat (Stewart et al., 2021; Giromini and Givens 2022; Fe, Zn, Se) and dairy (predominantly milk, Givens, 2020; Ca, I) consumption, whilst some nutrients are likely to have been affected by combined reductions in intake of red meat and dairy (Mg), and dairy and fish (I).

The tendency for reduced dairy consumption during adolescence is not new nor only found in the UK. Larson et al. (2009) reporting on the US Eating Among Teens study (1998–2004) found that during the transition to young adulthood, mean daily Ca intakes decreased by a mean of 153 mg and 194 mg of females and males, respectively, linked to reductions in dairy food consumption (mainly milk) from baseline at a mean age of 15.9 years to early adulthood at a mean age 20.5 years. Similar findings were seen in children from the Raine birth cohort in Australia followed up at ages 14 and 17 years over a three-year period starting in 2003 and 2006, respectively (Parker et al., 2012). Mean intakes of dairy decreased from 536 to 464 g/day ( $P < 0.01$ ) from 14 to 17 years of age mostly due to reduced milk consumption. The reduction was considerably greater in girls than boys.

The low intakes of red meat and milk are particularly notable for adolescent females, and whilst the reasons for this are not fully understood, it does mean that this cohort has already undergone a progressive form of dietary transition away from ADFs with the  $P$  that they have been replaced by products of poorer nutritional and health characteristics. For example, in the UK, dietary fibre intake data (NDNS, 2020; Fig. 1.) show that only 4% of teenage females achieve the recommended intake suggesting there has not been a concerted effort to replace red meat and milk by little-processed plant-based alternatives. Indeed, NDNS (2020) data show that only 7% of adolescents (11–18 years old) consume less than the recommended maximum amount of free sugars (5% of energy intake) with the mean intake being 12.5% of energy intake (i.e. 250% above the recommended intake). It is also perhaps worth noting that free sugars are dietary components of plant origin. A dietary transition of this type is very undesirable since there is good evidence of an association of sugar-sweetened beverage

**Table 4**Percentage of three UK populations with dietary micronutrient intakes less than the LRNI<sup>1</sup> and as a percentage of RNI<sup>2</sup> for dietary vitamin D (source NDNS, 2020).

| Population          | % with intakes less than the LRNI for: |    |    |    |    |    | %RNI<br>Vitamin D |
|---------------------|--|----|----|----|----|----|-------------------|
|                     | Fe                                     | Ca | Mg | Zn | Se | I  |                   |
| Males 11–18 years   | 11                                     | 14 | 33 | 20 | 24 | 19 | 21                |
| Females 11–18 years | 49                                     | 16 | 40 | 16 | 41 | 28 | 19                |
| Females 19–64 years | 25                                     | 9  | 11 | 7  | 46 | 12 | 26                |

<sup>1</sup> Lower Reference Nutrient Intake.<sup>2</sup> Reference Nutrient Intake, values for vitamin D are median intake as %RNI.

intake and obesity in adolescents (Hu et al., 2023) which can be the precursor of cardiometabolic diseases in later life. In addition, the low intakes of micronutrients in adolescence may also be the precursor of a range of other health problems. This emphasises that the replacement of ADFs requires a well-defined and nutritionally balanced substitution.

### Micronutrient intake and anaemia

Sub-optimal dietary Fe intakes leading to some degree of Fe deficiency-related conditions, predominantly anaemia, have been recognised for a considerable time with teenage girls and women of childbearing age being the most affected although the elderly have also been affected. The prevalence and causes of Fe deficiency anaemia in the UK population and notably in teenage females have recently been extensively reviewed by Fairweather-Tait (2023). This review highlights the role of red meat as a dietary source of highly bioavailable haem Fe and considers the role of PBMS. As a result, the topic will not be extensively covered in the current review but the key messages predominantly from Fairweather-Tait (2023) are summarised below.

According to the NDNS (2020), only 9 and 7% of teenage females and women aged 19–64 years, respectively, had blood haemoglobin concentrations below the threshold of < 120 g/L although the women group include many that are postmenopausal. However, Fe status assessed as plasma ferritin concentration (a measure of body Fe stores) showed that 17% of adolescent girls had low concentrations (< 15 µg/L) compared with only 6% for the boys partly reflecting the differences in Fe intake.

Haem Fe in meat is present mainly in haemoglobin in blood and myoglobin in muscle but with contributions from ferritin and haemosiderin. Whilst it is often believed that about 40% of Fe in red meat is in the haem Fe form, this can vary considerably depending on the source of the meat and factors such as method of cooking. The study of Latunde-Dada and Neale (1986) reported that the haem content of total Fe in beef, lamb, pork, and chicken meat was respectively 77, 68, 55 and 42%. A recent systematic review of Fe intakes in Europe (Bakaloudi et al., 2021) showed that this was generally higher in vegan diets than other dietary patterns, but this did not always lead to higher ferritin concentrations, likely due to lower bioavailability of Fe in the vegan diet. Very few RCTs are reported on the effect of excluding dietary meat on Fe status and many that exist are of inadequate length although a 12-week intervention in men showed that whilst Fe intake was similar in the vegetarian and beef-containing treatments the latter led to significantly higher values for haemoglobin and haematocrit (Wells et al., 2003).

The vast importance of Fe in many body functions including the developing brain and nervous system where inadequate Fe supply can have lifelong ill-effects including impairment of the synthesis of haemoglobin for O<sub>2</sub> transport, and vitamin D activation is given (Mogire et al., 2022). It is vital that Fe status of the adolescent females and women of child-bearing age is monitored to counter any further risk associated with continued reduction in red meat

consumption. It is also vital that more research attention is given to measuring and potentially increasing the bioavailability of Fe from plant-derived foods. As reported by Craig et al. (2021), Fe is listed as a nutrient of concern in a plant-based diet.

### Micronutrient intake and bone health

Bone is a composite tissue with inorganic and organic components. The inorganic part is approximated as hydroxyapatite [Ca<sub>10</sub>(PO<sub>4</sub>)<sub>6</sub>(OH)<sub>2</sub>] but has a somewhat different Ca:P ratio due to the presence of other anionic (e.g. CO<sub>3</sub><sup>2-</sup>) and cationic (e.g. Mg<sup>2+</sup>) species. Although Mg concentration in bones is much lower than for Ca and P, about 60% of total body Mg is stored in the bones. Mg deficiency contributes to osteoporosis, and low serum Mg concentrations have been associated with increased bone fracture risk (Dominguez et al., 2023). Mg is now known to have an important role in the first and second stages of activation of vitamin D (Uwitonze and Razzaque, 2018) which also has implications for bone health. The role of diet in supplying all the bonetrophic nutrients is critical, and the low intakes of Mg by adolescent females noted earlier are particularly concerning.

It is now known that bone mineral accretion rate increases rapidly at puberty and 90% of adult bone mineral content is created by the end of adolescence and 40% of adult bone mineral content is achieved during the 4 years of maximum speed of bone mineral content accretion (Cashman et al., 2023). Weaver et al. (2016) reported that in children with European ancestry, the maximum bone mineral accretion rate is seen at ages of 12.5 ± 0.90 years for girls and 14.1 ± 0.95 years for boys. Crucially, if adequate bone mineralisation is not achieved during adolescence, there follows an increased risk of osteoporosis and bone fractures in later life. This represents a bigger risk for postmenopausal women with reduced circulating oestrogen which is important for maintaining bone formation homeostasis (Baker and Benayoun, 2023).

Milk and dairy products are key sources of dietary Ca and to some extent Mg which is reflected in the study of Kalkwarf et al. (2003) which showed in white females who had milk consumption during childhood and adolescence, was positively associated with bone mass in later life and negatively associated with osteoporotic fracture rate after 50 years of age. Perhaps surprisingly, milk intake in childhood and fracture rate were more closely associated than fracture rate and milk consumption during adolescence. A key conclusion of the study was that women with low milk intake during childhood and adolescence have less bone mass in adulthood and greater risk of bone fracture. A more recent 12-month RCT in Chinese adolescent girls (Ma et al., 2014) found that those with a high Ca intake (mean 1 243 mg/day) had higher bone mineral density of the femoral neck than girls with a low Ca intake (mean 706 mg/day) with a similar effect in boys. Ma et al. (2014) suggested Ca supplementation is more effective in early than late puberty for increasing bone mineral mass. The systematic review of Kouvelioti et al. (2017) of RCTs examined the effect of dairy consumption on bone characteristics in children and adolescents. They reported that eight of the 11 RCTs found significant increases

( $P < 0.05$ ) in bone mineral content and bone mineral density. Five of these with adolescent boys and girls and data on Ca intake showed a mean increase in bone mineral density of 8% after 16 months of dairy (milk, yogurt, cheese) with Ca intakes of about 1 000 mg/day. Ca intakes of the non-dairy control groups were not summarised but were reported to be lower than in the dairy treatments.

The strength of evidence for effects of milk/bonetrophic micronutrients on bone development in adolescents is strong and by implication, bone properties would be weaker in populations with lower consumption of these micronutrients. A systematic review and meta-analysis of the associations between vegan and vegetarian diets and bone mineral density provides additional information on the chronic effect of diets containing low or zero milk and dairy products with attendant low intakes of Ca and potentially Mg and vitamin D (Iguacel et al., 2018). Twenty studies involving 33 131 subjects with data on fracture rate and 4 003 with data on bone mineral density were used. Compared with omnivores, vegetarians and vegans had significantly lower bone mineral density at the femoral neck, lumbar spine, and whole body, with vegans generally exhibiting lower bone mineral density than vegetarians. Vegans also had a 55% higher risk of fracture particularly in subjects aged over 50 years. These findings are supported by the prospective EPIC-Oxford study of Tong et al. (2020) which also found that after adjustment for socio-economic factors, lifestyle confounders, and body mass index, vegans had significantly increased risks for total fractures (+50%), hip (+39%) and leg fractures (+50%) relative to meat eaters. Vegetarians only had an increased risk for hip fractures (+25%). Details of this study are shown in Table 5.

These findings highlight the absolute need for careful, detailed, and long-term planning of vegetarian and vegan diets to reduce the risk of negative effects on bone health. As concluded by Veronese and Reginster (2019) 'individuals who decide to follow these diets (vegetarian and particularly vegan) should be aware of the risk of osteoporosis and of bone fractures and should introduce dietary sources of calcium and vitamin D and/or supplementation'.

### Iodine status during pregnancy

Whilst iodine is an essential nutrient for thyroid hormone synthesis at all life stages, it is doubly essential during pregnancy to ensure adequate production of maternal and foetal thyroid hormones which are critical for development of the foetal brain and nervous system.

**Table 5**  
Risks of total and site-specific fractures by diet type in the EPIC-Oxford study with subjects with adequate Ca intake (source Tong et al., 2020).

| Fracture site/diet group | Hazard ratio | 95% CI <sup>1</sup> | n cases |
|--------------------------|--------------|---------------------|---------|
| <b>Total fractures</b>   |              |                     |         |
| Meat eaters              | Reference    |                     | 2 077   |
| Fish eaters              | 0.92         | 0.82–1.03           | 377     |
| Vegetarians              | 1.08         | 0.98–1.19           | 700     |
| Vegans                   | 1.50         | 1.12–1.99           | 49      |
| <b>Hip fractures</b>     |              |                     |         |
| Meat eaters              | Reference    |                     | 507     |
| Fish eaters              | 1.21         | 0.96–1.52           | 95      |
| Vegetarians              | 1.25         | 1.02–1.54           | 136     |
| Vegans                   | 2.39         | 1.39–4.11           | 14      |
| <b>Leg fractures</b>     |              |                     |         |
| Meat eaters              | Reference    |                     | 191     |
| Fish eaters              | 0.98         | 0.68–1.42           | 38      |
| Vegetarians              | 1.00         | 0.73–1.37           | 61      |
| Vegans                   | 2.50         | 1.15–5.42           | 7       |

<sup>1</sup> Confidence interval.

In many countries, milk and milk products are the largest source of iodine in the diet by a substantial amount. The NDNS (2020) shows that these foods contribute 40 and 32% of iodine intake for UK adolescents and adults aged 19–64 years respectively with milk supplying the majority. Milk and dairy products were also the major determinants of iodine status in US men and women, despite the availability of iodised salt (Lee et al., 2016). There have been several studies (e.g. Stevenson et al., 2018) showing that milk from organic production systems has a lower iodine concentration than conventionally produced milk although there are indications that this may have been resolved in the UK (Stergiadis et al., 2021). Fish are the next largest contributor to dietary intake at approximately 10% for both adolescents and adults, although it is now known that the iodine content of fish and other seafoods can vary considerably (Sprague et al., 2022).

Until recently, it was thought that the UK population had adequate iodine status. Doubts on this were raised following a study with schoolgirls where measurements of urinary iodine concentration showed that 51% were mildly iodine deficient (Vanderpump et al., 2011). As shown in Table 4, the NDNS (2020) recorded that 28% of adolescent females (aged 11–18 years) had iodine intakes below the LRNI (70 µg/day), with 12% for females aged 19–64 years. With recent trends in milk consumption according to age (Givens, 2020), it is likely that women of childbearing age now substantially exceed this value. Results from a cohort study in pregnant women support this contention finding consistent mild-to-moderate iodine deficiency (Bath et al., 2014) with similar findings in Norway for pregnant women (Brantsæter et al., 2013) and recently in mothers of young children (Aarsland et al., 2023). Bath and Rayman (2015) reviewed the current evidence on the iodine status of pregnant women in the UK and concluded that a substantial proportion were iodine deficient with similar findings in non-pregnant women of childbearing age. More recently urinary iodine concentration was used to assess the iodine status of teenage girls on the island of Ireland which indicated that they were at 'the low end of sufficiency' (Mullan et al., 2019), a status which gives concern for future progression into pregnancy. There has been uncertainty about the value of urinary iodine concentration needed to predict thyroid function, but Zha et al. (2023) confirmed in pregnant women that low urinary iodine concentration: urinary creatinine ratio was significantly associated with lower serum thyroid-stimulating hormone concentration with a trend towards higher serum free thyroxine (FT4). They also showed that low iodine status was a predictor of low birth weight.

There is now increasing evidence that sub-optimal maternal iodine status during pregnancy is associated with poorer cognitive performance/neurological development in the offspring (Bath et al., 2013). A systematic review and meta-analysis of RCT, non-RCT and prospective studies on the relationship mainly between maternal iodine status and mental development of children 5 years old and younger (Bougma et al., 2013) concluded that independent of study type, low iodine status had a substantial effect on mental development of the children.

Given that iodine intake is already low in UK adolescent females and older women of childbearing age, further dietary transition away from ADFs, especially milk, is likely to reduce iodine intake further increasing the risks outlined above (Qin et al., 2023). This has been shown in the study with women (mean age 31.6 years) by Fallon and Dillon (2020) who reported iodine intakes of 112.6, 90.8 and 24.4 µg/day for omnivores, vegetarians and vegans, respectively. Groufh-Jacobsen et al. (2020) reported median urinary iodine concentrations of 43, 67 and 96 µg/L in vegans, vegetarians and pescatarians, respectively, indicating that vegans were moderately iodine deficient. The vegetarians and the pescatarians had significantly ( $P = 0.03$ ) higher urinary iodine concentrations than the vegans but were still classified as mildly defi-

cient. It was concluded that there is an urgent need for dietary guidance for those in all three dietary patterns. A study with children aged 0–18 years reported that those on vegetarian and vegan diets had significantly lower median urinary iodine concentrations than those on omnivorous diets although were above the WHO cut-off of 100 µg/L. However, the presence of anti-thyroglobulin antibodies was more common in the vegetarian and vegan diet-consuming children than the omnivores suggesting that the former were at higher risk of iodine deficiency (Světničková et al., 2023).

A comparison of breast milk iodine concentration in US women consuming vegetarian, vegan and omnivore diets was reported by Pawlak et al. (2023) with mean values (range) of 89 µg/L (32–194), 116 µg/L (62–189), and 276 µg/L (62–1 719), for milk from vegans, vegetarians, and omnivores, respectively. When the data from vegans and vegetarians were combined, this was significantly ( $P = 0.0405$ ) lower than for milk from omnivores. A similar study by Perrin et al. (2023) found median iodine concentrations in breast milk of 62, 80 and 93 µg/L from vegan, vegetarian and omnivore mothers, although there was considerable variability within each and the overall effect was not significant.

Overall, the evidence indicates that the prevalence of marginal to low iodine status of UK pregnant women is likely to be substantial with greater risk for those on vegetarian and especially vegan diets. Indeed, there was a case of goitre in a 10-day-old infant whose mother was a vegan with an extremely low dietary iodine intake and who also had a goitre (Shaikh et al., 2003). Given the potentially serious implications of sub-optimal iodine status on child development, there is a clear need for more awareness of the problem and more dietary guidance especially for those on plant-based diets. It is of concern that Nicol et al. (2023) reported that most plant-based dairy and fish alternatives sold in the UK are not iodine-fortified putting consumers at risk. It is also concerning that Mansilla et al. (2024), using shopping transaction data reported that relative to milk, replacement by PBMA would lead to a 44% reduction in iodine intake.

#### Micronutrients that plants cannot supply

There are very few nutrients that plant-based foods simply do not contain but there are others that are present in low concentrations or in rare plants such that plant-based foods cannot supply enough. An example is iodine, where Nicol et al. (2024) showed that an 80 g portion of fruit and vegetables would only supply 3 µg of iodine. These authors also reported that if milk was replaced with unfortified PBMA, iodine intake would only be 54 µg/day and provide only 22–27% of the required iodine intake for pregnancy (Nicol et al., 2024). This section will briefly review the situation for vitamins B<sub>12</sub> and D<sub>3</sub>, and long-chain n-3 fatty acids which plants cannot provide.

#### Vitamin B<sub>12</sub>

Whilst it is recognised that vitamin B<sub>12</sub> has been found in edible duckweed (*Wolffia globosa*), it is probably from endophytic bacteria resident inside the plant tissues (Kaplan et al., 2019), for the vast majority vitamin B<sub>12</sub> is only provided by ADFs and from supplements. In UK adults (19–64 years) 36, 30 and 18% of vitamin B<sub>12</sub> dietary intake is from milk/dairy foods, meat/meat products and fish, respectively (NDNS, 2020). An earlier study showed that the concentration of plasma vitamin B<sub>12</sub> was associated with increasing intakes of vitamin B<sub>12</sub> from dairy products and fish but not from meat or eggs. This suggested that the bioavailability of vitamin B<sub>12</sub> from dairy products was higher than from the other foods (Vogiatzoglou et al., 2009).

The UK RNI for vitamin B<sub>12</sub> for males and females ≥ 15 years of age is 1.5 µg/d. This includes during pregnancy but a higher value

of 2 µg/day is advised during lactation. A 200 mL serving of milk will typically provide 2 µg. As would be predicted, intakes of vitamin B<sub>12</sub> are lower in those who partially or completely exclude ADFs from their diet. Sukumar et al. (2016), using data from women of childbearing age (19–39 years), found that those with vitamin B<sub>12</sub> intakes < 1.5 (mean 1.29) and ≥ 1.5 (mean 3.86) µg/day had serum vitamin B<sub>12</sub> concentrations of 169 and 244 pmol/L, respectively ( $P = 0.05$ ). They also reported that a small subgroup of vegetarians had significantly lower serum vitamin B<sub>12</sub> concentrations than the non-vegetarians (192 vs 248 pmol/L,  $P < 0.01$ ). Serum vitamin B<sub>12</sub> concentrations < 133 pmol/L (< 180 pg/mL) are regarded as possibly deficient (NHS, 2024a).

Derbyshire (2017) using data from females aged 11–64 years concluded that those who consumed < 40 g/day of total red meat were more likely to have intakes below the LRNI for vitamin B<sub>12</sub> (given as 1.0 µg/day) although there was no significant difference in serum vitamin B<sub>12</sub> concentrations of low (< 40 g/day) and higher (40–69 g/day) meat intakes possibly a result of greater supplementary vitamin B<sub>12</sub> use in the lower meat consumers. Indeed, this effect was shown in a German study (Storz et al., 2023). Mean vitamin B<sub>12</sub> intakes of 2.14, 0.98 and 0.43 µg/day ( $P < 0.001$ ) were recorded for omnivores, lacto-ovo-vegetarians, and vegans respectively but overall vitamin B<sub>12</sub> status was adequate for the omnivores and vegans but poorer in the lacto-ovo-vegetarians with respective plasma vitamin B<sub>12</sub> concentrations of 377, 405 and 310 pg/mL ( $P = 0.023$ ). Although the value for the lacto-ovo-vegetarians appeared normal this group also had a plasma holotranscobalamin concentration much lower ( $P = 0.001$ ) than the other two groups at 40.1 pmol/L, the lowest point of adequacy (Nexo and Hoffmann-Lücke, 2011). Storz et al. (2023) suggested that holotranscobalamin may be the most sensitive biomarker to measure vitamin B<sub>12</sub> status in subjects that have plant-based diets. Fewer of the lacto-ovo-vegetarians used vitamin B<sub>12</sub> supplements than vegans (51 vs 90%) showing that high supplementation (median 250 µg/day for 2 years) provided an adequate status for healthy vegans in accordance with the recommendations of Niklewicz et al. (2023) for consumers of plant-based diets. Similarly, Pawlak et al. (2018) showed that vegan lactating women who consumed vitamin B<sub>12</sub> supplements can have breast milk vitamin B<sub>12</sub> concentrations like non-vegetarians.

The efficiency of B<sub>12</sub> absorption from food decreases in older adults, and over time can lead to mild vitamin B<sub>12</sub> deficiency but at greater risk of severe deficiency. The main reason for lower absorption efficiency is reduced gastric acid secretion which lowers the ability to extract vitamin B<sub>12</sub> bound to food proteins. Vogiatzoglou et al. (2009) found that milk provided the most bioavailable vitamin B<sub>12</sub> even in older (aged 71–74 years) people of low vitamin B<sub>12</sub> status. Milk therefore may be helpful for maintaining adequate status in the elderly, but this will not apply milk excluders and vegans who would need to consider using supplements.

The importance of vitamin B<sub>12</sub>, in metabolic association with folate, for red blood cell formation, synthesis of DNA/RNA, optimum nerve function and maintaining normal concentrations of blood homocysteine has been known for some time but its functionality is now known to be more extensive. There has been considerable interest in the association of vitamin B<sub>12</sub> status and cognitive function. Rutjes et al. (2018) concluded that giving supplements of B vitamins (folic acid, vitamins B<sub>12</sub>, B<sub>6</sub>) together or alone to cognitively healthy adults mostly aged 60–79 years probably has little or no effect on cognitive function for at least 5 years. However, Zhou et al. (2023) found that vitamin B<sub>12</sub> supplementation with subjects aged > 45 years with cognitive impairment led to a significant improvement, notability in attention, calculation ( $P < 0.01$ ) and visual-constructional ability ( $P < 0.05$ ) compared with the matched control group. This study did involve giving very

large doses of vitamin B<sub>12</sub> (500 mg/day for 7 days) by intramuscular injection. It is therefore doubtful that typical dietary supplementation would have achieved the same outcome but is clearly an area to be further explored.

It has been known for some time that neural tube defects such as spina bifida can be largely prevented by taking folic acid supplements (typically 400 µg/day) before conception and for the first 12 weeks of pregnancy. However, the metabolism of folic acid is dependent on an adequate supply of vitamin B<sub>12</sub> and it has been shown that low maternal vitamin B<sub>12</sub> status can result in a 3-fold increase in the risk for neural tube defects even when folic acid supplements were used (Ray et al., 2007). Similarly, Molloy et al. (2009) found that pregnant women not taking a folic acid supplement but with a pregnancy blood vitamin B<sub>12</sub> concentration < 250 ng/L were associated with 3-fold greater risk of neural tube defects compared with those with the highest status. Molloy (2018) has also confirmed that in countries with a high prevalence of vitamin B<sub>12</sub> deficiency, consideration of adding vitamin B<sub>12</sub> to folic acid fortification regimes should be a top priority.

There is little doubt that ensuring an adequate intake of vitamin B<sub>12</sub> from an acceptable source will be one of the most demanding challenges that vegetarians and vegans face. However, given the fundamental necessity of vitamin B<sub>12</sub> (and folic acid), achieving this is vital and cannot be overlooked.

#### Vitamin D

It is now understood that sub-optimal vitamin D status is extensive in adults and children with dark-skinned and obese individuals being particularly vulnerable. Many believe that it has reached pandemic levels. Cashman et al. (2016) confirmed that within Europe, the prevalence of vitamin D deficiency represents a major health risk requiring a major public health initiative to resolve it.

The Scientific Advisory Committee on Nutrition (2016), in a change to earlier recommendations, proposed an RNI for vitamin D of 10 µg/d throughout the year, for everyone in the general population aged 4 years and above including pregnant and lactating women. This is the mean amount needed by 97.5% of the population to ensure a serum 25(OH)D concentration ≥ 25 nmol/L when exposure to UVB (λ 280–315 nm) sunshine is very limited. The RNI was based on evidence related to benefits for musculoskeletal health, with serum 25(OH)D concentration < 25 nmol/L being associated with increased risk of rickets in infants/children and osteomalacia in adults. The recommendation that the RNI was applicable all year was to some extent a precautionary measure to ensure sections of the population most at risk were covered but assumed minimal sunshine exposure. Despite this precaution, there is now evidence that dark-skinned populations probably require at least 20 µg/day to ensure the maintenance of adequate serum 25(OH)D concentrations in all seasons (Cashman et al., 2022). Lifestyle changes in recent decades have reduced sunshine exposure and increased use of sunscreen preparations in hot weather.

The RNI clearly relates to all dietary sources including normal foods, fortified foods, and supplements. There are few foods that are naturally rich in vitamin D<sub>3</sub> and those that contain valuable amounts are exclusively of animal origin (e.g. meat, oily fish, and egg yolk). It is however noteworthy that these will also contain varying amounts of 25(OH)D (Jakobsen and Christensen, 2021) which may be more effective than D<sub>3</sub> for increasing circulating 25(OH)D concentration (Guo et al., 2018). There are no known plant sources of vitamin D, although some mushrooms (a type of fungi) grown under specific conditions are a source of vitamin D<sub>2</sub> although this is considerably less potent than D<sub>3</sub> (Tripkovic et al., 2017). In the UK, the top four dietary sources of vitamin D for adults (19–64 years) are meat/meat products, eggs/egg dishes, fish/fish dishes and fortified cereals which provide 30, 20, 17 and

15% of dietary vitamin D, respectively (NDNS, 2020). However, total dietary intake remains low with approximate median values of 2.1, 1.9, and 2.6 µg/day, representing 21, 19 and 26% of the RNI respectively for males aged 11–18 years, females aged 11–18 years and females aged 19–64 years (Table 4). These data strongly support the advice of UK National Health Service that 'everyone should consider taking a daily vitamin D supplement during the autumn and winter. People at high risk of not getting enough vitamin D, all children aged 1 to 4 years, and all babies (unless they're having more than 500 ml of infant formula per day) should take a daily supplement throughout the year' (NHS, 2024b).

Whilst infant formula is by law fortified in the UK liquid milk is not, unlike Canada where PBMA must also contain the amount found in milk. Other countries voluntarily fortify milk and biofortification of vitamin D in eggs has been shown to occur in organically produced eggs (Guo et al., 2017) and by increasing the vitamin D concentration in the birds' diet, although a study doing the same with dairy cows was unsuccessful in changing milk vitamin D concentration (Guo et al., 2019).

As part of a systematic review, Neufingerl and Eilander (2022) examined 15 studies with adults in which vitamin D intake was assessed according to diet type. They reported mean intakes of 5.25, 4.17, 2.67 and 1.52 µg/day for pesco-vegetarians, meat eaters, vegetarians, and vegans, respectively. Similarly, Hedegaard et al. (2024) reported vitamin D intakes of 3.3, 4.2, 1.7 and 1.1 µg/day by non-supplemented pregnant Danish women following omnivorous, vegetarian/fish/poultry, vegetarian/lacto/ovo and vegan dietary patterns, respectively. The vegan diets were also associated with low birthweight (< 2.5 kg, *P* < 0.05) which the authors speculated might be due to the lower protein intake from the vegan diets. All the above vitamin D intakes were substantially lower than 10 µg/day, predicably with the lowest intakes in vegetarian and vegan diets although Hedegaard et al. (2024) showed that those taking vitamin D supplements had mean vitamin D intakes > 10 µg/day except the vegans whose value was only 6.2 µg/day.

In terms of vitamin D status based on serum/plasma 25(OH)D concentrations, Neufingerl and Eilander (2022) found in 11 studies, that status was higher in pesco-vegetarians (72.3 nmol/L), meat eaters (65.5 nmol/L), and semi-vegetarians (64.5 nmol/L), than vegetarians (57.0 nmol/L) and vegans (54.8 nmol/L) although there was only one study each for pesco- and semi-vegetarians. Four studies found that vitamin D deficiency (< 25 nmol/L) was low in meat-eaters and pesco-vegetarians (0–6%) but higher in vegetarians (0–33%) and especially vegans (3–67%). Overall, it was concluded that the highest rate of vitamin D deficiency was in vegetarians and vegans. This was also reported in a study in Finnish women (Outila et al., 2000) that also showed significantly lower bone mineral density in the lumber spine region and femur neck in vegans compared with omnivores.

Buttriss and Lanham-New (2022) reviewed knowledge on vitamin D and how it had evolved since 1922 when a study in Austrian children showed that rickets could be prevented or cured by consumption of cod liver oil (Chick et al., 1922). Subsequently the hormonal function of vitamin D regulating circulating concentrations of Ca and phosphorus and its promotion of bone mineralisation has been researched in detail. Also, a range of additional functions of vitamin D and associations with health have emerged. These include evidence that exposure to vitamin D supplementation is associated with reduced dementia rate (40% reduction; Ghahremani et al., 2023), the potential to moderate blood cell count-based (but not C-reactive protein) markers of a systemic inflammatory response (Sha et al., 2023), and the role of vitamin D in the immune response with indications that vitamin D deficiency has been associated with increased incidence of SARS-CoV-2 infection although without adequate evidence for its use as a therapeutic treatment (Lordan, 2021).

As highlighted by [Uwaezuoke \(2017\)](#), there has been evidence building for some time of a relationship between vitamin D deficiency and risk of anaemia. It is now known that there is an interaction between Fe and vitamin D such that higher vitamin D status may increase Fe status via suppressing hepcidin, a key hormone inhibitor of Fe absorption. In addition, Fe deficiency may contribute to vitamin D deficiency by decreasing the activity of haem-containing 25- and 1 $\alpha$ -hydroxylase enzymes involved in vitamin D activations ([Mogire et al., 2022](#)). [Mogire et al. \(2022\)](#) recommended that the link between vitamin D and Fe deficiency strongly implies that both conditions should be assessed in public health strategies where both nutrient deficiencies are known to coexist. This recommendation was targeted on children in Africa, but it may have implications for UK adolescent females that are known to have low Fe intakes and marginal vitamin D status. Perhaps more concerning is the very low intakes of Mg in this cohort because Mg is now known to be also involved in vitamin D activation and hence status suggesting that optimal Mg status may be vital to ensure optimal 25(OH)D status ([Dai et al., 2018](#); [Erem et al., 2019](#)). A recent example of this association was shown by [Kettig et al. \(2023\)](#). In older subjects (mean age 75.7 years) in geriatric rehabilitation, increased Mg status may enhance grip strength in vitamin D sufficient but not deficient individuals. Also, Mg was not associated with fatigue, regardless of vitamin D status. Interestingly, [Erem et al. \(2019\)](#) highlighted the 'profound lack of awareness of the insufficient intake of Mg in the US population and worldwide...'

#### Long-chain n-3 fatty acids

Whilst it has been known since the late 1920s that  $\alpha$ -linoleic acid (18:3n-3) is a dietary essential nutrient, there has been uncertainty whether the functionally important long-chain n-3 fatty acids EPA and DHA should also be classified as dietary essential nutrients due to the low efficiency of their synthesis from  $\alpha$ -linoleic acid ([Burdge and Wootton, 2002](#)). Largely because of evidence that fish oil improves cardiovascular health mediated by its EPA and DHA content, the [Scientific Advisory Committee on Nutrition/Committee on Toxicology \(2004\)](#) recommended the consumption of two portions of fish per week, one of which should be oily to supply 450 mg EPA+DHA/day. At about the same time, several other organisations proposed EPA+DHA intakes of 500–680 mg/day although [Givens and Gibbs \(2008\)](#) estimated the average adult intake in the UK to be only 244 mg/day. The target intake recommendations have become regarded as a requirement for EPA+DHA as essential nutrients leading to a range of research focused on ways of increasing their intake, for e.g. by enriching poultry meat. Recently however, [Burdge \(2022\)](#) concluded that the synthesis of EPA and DHA from  $\alpha$ -linolenic acid is indeed sufficient for human needs such that plant-based diets providing only  $\alpha$ -linolenic acid are not detrimental to health including cognitive development. [Burdge \(2022\)](#) did confirm that there will still be value in preformed EPA and DHA for dealing with some diseases notably those linked to chronic inflammation. In this regard, [O'Keefe et al. \(2024\)](#) recently published a harmonised analysis of 183 291 subjects from 29 prospective studies and reported that higher circulating EPA+DHA was associated with significantly reduced risk of total (–17%) and ischaemic (–18%) but not haemorrhagic stroke.

Dietary EPA and DHA are essentially only present in fish and some meat but not in plant sources. [Neufingerl and Eilander \(2022\)](#) reported a systematic review and meta-analysis of 141 studies with adults of which nine and eight reported intakes of  $\alpha$ -linolenic acid and EPA/DHA, respectively. Plant-based diets led to higher intakes of total n-3 fatty acids which was primarily due to higher intakes of  $\alpha$ -linolenic acid by vegans (2.01 g/day), compared with vegetarians (1.78 g/day) and meat-eaters

(1.38 g/day). EPA and DHA intakes were lowest in vegans (27 and 4 mg/day) and vegetarians (16 and 31 mg/day) than meat eaters (94 and 172 mg/day). EPA and DHA status was measured in 13 studies and as expected vegans had the lowest status followed by vegetarians and meat eaters. A meta-analysis of a small number of studies with children found essentially the same outcomes as for adults ([Neufingerl and Eilander, 2023](#)).

Lower intakes of EPA and DHA from vegetarian and especially vegan diets than meat and fish-eaters were also seen in the EPIC Norfolk study ([Welch et al., 2010](#)). However, when the dietary  $\alpha$ -linolenic acid to plasma long-chain n-3 fatty acid ratio was calculated as an indicator of  $\alpha$ -linolenic acid conversion efficiency, vegan diets had values 209 and 184% higher ( $P < 0.001$ ) than fish eaters for men and women respectively despite vegans having higher circulating n-6 linoleic acid concentrations. There were also indications of higher  $\alpha$ -linolenic acid: plasma long-chain n-3 fatty acid ratio for both vegetarian and meat eaters than for fish eaters and overall conversion efficiency was greater in women than men ( $P < 0.001$ ). Other studies have noted that for vegetarian and vegan diets, DHA from  $\alpha$ -linolenic acid is generally the only source with plasma DHA concentrations lower than omnivores, yet rates of neurological disease and brain function are like omnivores suggesting that DHA from  $\alpha$ -linolenic acid is sufficient ([Domenichiello et al., 2015](#)). These findings support the recent contentions of [Burdge \(2022\)](#), yet other reviews remain clear that vegetarians and vegans should regularly consume EPA and DHA supplements ([Lane et al., 2022](#)). In the future, a plant-based source of EPA and DHA may be commercially available since the genetically modified plant *Camelia sativa* produces oils rich in EPA and DHA which have been shown to be as effective as fish oil for increasing EPA and DHA status in humans ([West et al., 2020](#)).

#### Summary

There are clearly nutrition and related health risks involved in dietary transition from animal to plant-derived foods. The impact will depend on the extent of the transition and the initial nutrient status. For the latter, there are serious concerns for adolescent girls and young women since many already consume substantially sub-optimal amounts of a range of nutrients. The low intakes of Ca and Mg, together with poor vitamin D status increase the risk of inadequate bone mineralisation which can increase the risk of bone weakness in later life. Indeed, vegetarian, and vegan diets have already been shown to be associated with increased risk of bone breakage. Obtaining an adequate intake of vitamin B<sub>12</sub> is a major challenge for the elderly and vegetarians and vegans. It is therefore a concern that the recent study of women in high-income countries (UK, Singapore, New Zealand; [Godfrey et al., 2023](#)) showed that preconception, 29% had marginal or low plasma status of folate (< 13.6 nmol/L), 82% for riboflavin ( $\geq 265.5$  nmol/L), 9% for vitamin B<sub>12</sub> (< 221 pmol/L) and 49% for vitamin D (< 50 nmol/L). Also, many women developed markers of vitamin B<sub>6</sub> (pyridoxine) deficiency in late pregnancy. It was also seen that non-prescription supplements substantially reduced the prevalence of low status before and during pregnancy ([Godfrey et al., 2023](#)).

#### Aspects of plant-rich diets and health

There is evidence that the increased interest in plant-rich diets is based on several factors. These include purported benefits for human health, lower environmental impact, and several so-called qualities of life domains. These can include the adoption of a morally correct attitude and an increased sense of belonging to a like-minded community ([Hargreaves et al., 2021](#)). Whilst there are six reasonably well-defined types of plant-rich diets i.e. lacto-

ovo-vegetarian, lacto-vegetarian, ovo-vegetarian, flexitarian, pescatarian and vegan, there are other more complex categorisations (e.g. [Minimalistic vegan, 2024](#)). There will also be others whose desire is only to make a moderate transition from animal- to plant-derived foods. In the context of the present paper, these may be the majority and are likely to consume rather heterogeneous diets. Nevertheless, some aspects of vegetarian/vegan diets are worthy of discussion.

#### Aspects of health

[Key et al. \(2022\)](#) reviewed the data from EPIC-Oxford study on the impact of plant-based diets and long-term health. All-cause mortality did not differ between vegetarians (Hazard ratio 1.00, 95% confidence interval: 0.93–1.08), vegans (Hazard ratio 1.14, 95% confidence interval: 0.97–1.35) and meat-eaters (reference) although the combined risk of ischaemic heart disease in vegetarians and vegans was 22% less than for meat-eaters although this was attenuated to 17% following adjustment for body mass index. Similarly, the risk of type 2 diabetes in vegans was 47% lower than for meat eaters but was reduced to 1% (and non-significant) after accounting for body mass index. Unlike for ischaemic heart disease, vegetarians had a 17% higher risk of predominantly haemorrhagic stroke than meat eaters and this was not changed by body mass index adjustment. Adjusting for body mass index also reduced the differences in favour of non-meat eaters for low-density lipoprotein cholesterol and systolic blood pressure. [Watling et al. \(2022\)](#) reported that whilst postmenopausal vegetarian women had a significantly lower risk of breast cancer, this was attenuated to non-significance after body mass index adjustment. Thus, whilst non-meat-eaters are often shown to be healthier than the general population, the difference can be much smaller when comparing vegetarians with health-conscious non-vegetarians, at least as expressed by body mass index. There has been much debate about whether lower body mass index is caused by plant-based diets which would nullify adjustment for body mass index or whether it is a function of broader lifestyle choices.

#### Aspects of diet

It is becoming clear that greater consumption of plant-based diets rich in healthy plant-derived foods tend to be associated with improved health whilst those containing less healthy plant-derived foods lead to poor health, plant-derivation alone not being an adequate health-related characteristic. [Li et al. \(2022\)](#) created three plant-based diet indices including an overall plant-based diet index, a healthful plant-based diet index and an unhealthful plant-based diet index (UPDI). They examined the association between these three indices and mortality in a prospective study involving ~ 40 000 participants with a median follow-up period of 7.8 years. The results showed a negative association of healthful plant-based diet index with all-cause mortality (Hazard ratio 0.86, 95% confidence interval: 0.77–0.95,  $P$  trend 0.001) whilst the opposite for the UPDI (Hazard ratio 1.33, 95% confidence interval: 1.39–1.48,  $P$  trend < 0.001). The UPDI was also positively associated with cardiovascular disease mortality (Hazard ratio 1.42, 95% confidence interval: 1.12–1.79,  $P$  trend 0.015). The healthful plant-based diet index was not associated with cardiovascular disease mortality and neither index was associated with cancer mortality. The key ingredients of the healthful plant-based diet index were rich in legumes, fruit and whole grain and fruit juices whilst those of UDPI were low in legumes and fruit and high in sugar-sweetened drinks and more refined grains. Some ADFs were included, with dairy foods being the main one in the healthful plant-based diet index with more meat in the UPDI. The high sucrose content of the UPDI was probably a key component of its

unhealthfulness despite being of plant origin. As concluded by [Wang et al. \(2023\)](#), this highlights the importance of defining 'which vegetarian dietary compositions provide better health outcomes and which components are detrimental to human health'.

There are also some increasing concerns that industrial PBMS and PBMA may be classified as ultra-processed foods with attendant health risks ([Monteiro et al., 2018](#)). [Gehring et al. \(2021\)](#) studied this in a cross-sectional study of subjects in the French NutriNet-Santé cohort. This involved 19 812 meat eaters, 646 pesco-vegetarians, 500 vegetarians and 254 vegans, which showed that increasing avoidance of ADFs was associated with greater consumption of ultra-processed foods ( $P < 0.001$ ). The highest contribution of ultra-processed foods was seen in the vegan diet (39% energy intake) and the lowest in the pesco-vegetarian diet (32.5% energy intake). Diet quality was also linked to ultra-processed food consumption with the highest UPDI (59.9) in the vegan diet and the lowest in the meat eater diet (54.0). [Gehring et al. \(2021\)](#) also concluded that a greater number of vegans and vegetarians preferred unhealthy plant-based foods than the meat eaters.

Interestingly, an earlier prospective study with 105 000 subjects in the same cohort with a median follow-up period of 5.2 years showed that intake of ultra-processed foods was associated with an increased risk of cardiovascular diseases with a hazard ratio of 1.12 (95% confidence interval: 1.05–1.20) per 10% increase of ultra-processed foods. Similar associations were seen for coronary heart disease and cerebrovascular disease risks ([Srouf et al., 2019](#)).

In 2019, The EAT-Lancet Commission on Food, Planet and Health published its report on Healthy Diets from Sustainable Food Systems ([Willett et al., 2019](#)) which gave a new global reference diet intended to provide adequate nutrition whilst remaining within the earth's capacity to sustainably produce food. Inevitably, there have been several evaluations of the diet to assess its agreement with or divergence from other dietary guidelines. For example, [Blackstone and Conrad \(2020\)](#) reported that whilst there were some agreements with the Dietary Guidelines for Americans, there were also disagreements, notably the EAT-Lancet diet proposed a larger amount of protein-rich foods with some 47% of protein provided by beans and peas and with considerably less meat and most other ADFs. More recently, [Beal et al. \(2023a\)](#) reported that the EAT-Lancet diet does not provide adequate intakes of four micronutrients that are present in higher concentrations and in more bioavailable forms in ADFs. These were Ca, Fe, Zn and vitamin B<sub>12</sub> with the EAT-Lancet diet only providing 84, 55, 93 and 93% of the US recommended intakes for women aged 15–49 years, respectively. It was suggested that part of the reason was that the EAT-Lancet diet does not consider women of childbearing age separately from other adults. It is no surprise that these micronutrients are included in the discussion of dietary risks associated with dietary transition and vegetarian and vegan diets earlier in this paper.

#### Summary

Whilst many studies indicate health benefits associated with vegetarian and vegan diets, the plant food benefit may be considerably smaller when comparing vegetarians/vegans with health and lifestyle-conscious non-vegetarians. In addition, several studies have highlighted that not all vegetarian/vegan diets have health benefits possibly because of the ultra-processed nature of many meat and dairy alternatives and where diets contain a lot of sugar-sweetened beverages, despite sucrose being a plant product.

#### Overall conclusions

Animal-derived foods vary considerably in nutrient composition, but most are nutrient-dense, provide higher protein quality

than plant sources, and provide a range of nutrients some of which plants cannot supply e.g. vitamin B<sub>12</sub>. Some ADFs also have functionality of benefit to health beyond classical nutrient supply. They also vary in their chronic impact on health and this, along with nutrient issues needs to be considered when dietary transition from ADFs to plant-derived foods is planned. A simple replacement of protein will inevitably lead to a reduction in protein quality and supply of key nutrients. There is little doubt that environmental and related issues will require some dietary transition to happen, but this needs thoughtful planning and should be based on nutritional and health considerations in addition to traditional environment-related metrics. There are signs of increased interest in the more holistic approach (Beal et al., 2023b).

It seems logical, at least initially, to replace the animal-derived foods that have the least benefit or greatest risk to health and have a high environmental impact. As shown by Clark et al. (2019) who integrated the health and environmental impacts of various foods, processed meat fits these characteristics and should be the initial target for replacement with plant-based protein-rich foods that in addition to providing the necessary nutrients, can provide high-quality dietary fibre which is drastically missing in many diets. This is broadly in agreement with Auclair et al. (2024) who highlighted that this (together with red meat) would have a 5-times greater reduction in animal diet-related greenhouse gas emissions than replacing dairy. It is appreciated that processed meat covers a wide range of products including several traditional foods; there is an urgent need for research to better define the relative health risk associated with the range of processed meat-based foods. There is good evidence, that unless great care is taken, vegetarian and especially vegan diets can be associated with nutrient deficits and related health problems particularly low bone strength with increased risk of bone breakage. In addition, it is also clear that not all plant-based foods are healthy and some manufactured PBMA and PBMS lack key nutrients and can be defined as being ultraprocessed products. The impact and health risk of diet transition will depend on its extent and for many this will be small or medium. Nevertheless, the impact will depend substantially on initial nutrient status, and this is of great concern for UK female adolescents and women of childbearing age because many are already consuming very low intakes of some of the key nutrients that ADFs typically provide. So dietary transition from animal to plant-derived foods will indeed create health risks to these sections of the population especially. On the other hand, the replacement of protein in processed meat with plant-based foods that provide high-quality dietary fibre would have substantial health benefits.

There is an urgent need, however, to better define the health risks associated with the wide range of processed meat products bearing in mind that the impact of a specific product can depend on the overall dietary pattern and lifestyle. Therefore, efforts should be made to evaluate all these aspects together and define optimal dietary models according to the target population and the specific risks, without eliminating important sources such as ADFs but increasing good quality plant-based foods. This all needs considerable public awareness and guidance to avoid major health issues in the future.

### Ethics approval

Not applicable.

### Data and model availability statement

None of the data were deposited in an official repository. All of the data that support the review are publicly available in the references given.

### Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work the author(s) did not use any AI and AI-assisted technologies.

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### CRediT authorship contribution statement

D.I. Givens: Writing – review & editing, Writing – original draft, Conceptualization.

### Declaration of competing interest

The author declares the following financial interests/personal relationships which may be considered as potential competing interests: [The author has received travel expenses and honoraria in connection with lectures and meetings from the Dairy Council (now Dairy UK), Dutch Dairy Association, European Milk Forum, and the International Dairy Federation. He has also been a consultant to BioCC OÜ the Estonian Bio-Competence Centre of Healthy Dairy Products, and to the Dairy Council on fats in dairy products and cardiometabolic diseases.].

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### References

- Aarsland, T.E., Kaldenbach, S., Bakken, K.S., Solvik, B.S., Holten-Andersen, M., Strand, T.A., 2023. Inadequate iodine intake in mothers of young children in Innlandet County, Norway. *Current Developments in Nutrition* 7, 100047.
- Abete, I., Romaguera, D., Vieira, A.R., Lopez de Munain, A., Norat, T., 2014. Association between total, processed, red and white meat consumption and all-cause, CVD and IHD mortality: a meta-analysis of cohort studies. *British Journal of Nutrition* 112, 762–775.
- Agte, V., Chiplonkar, S., Joshi, N., Paknikar, K., 1994. Apparent absorption of copper and zinc from composite vegetarian diets in young Indian men. *Annals of Nutrition and Metabolism* 38, 13–19.
- Antunes, C., Bexiga, R., Pinto, C., Roseiro, L.C., Quaresma, M.A.G., 2023. Cow's milk in human nutrition and the emergence of plant-based milk alternatives. *Foods* 12, 99.
- Auclair, O., Eustachio Colombo, P., Milner, J., Burgos, S.A., 2024. Partial substitutions of animal with plant protein foods in Canadian diets have synergies and trade-offs among nutrition, health and climate outcomes. *Nature Food* published online 16 February 2024 <https://doi.org/10.1038/s43016-024-00925-y>.
- Aune, D., Ursin, G., Veierød, M.B., 2009. Meat consumption and the risk of type 2 diabetes: a systematic review and meta-analysis of cohort studies. *Diabetologia* 52, 2277–2287.
- Bakaloudi, D.R., Halloran, A., Rippin, H.L., Oikonomidou, A.C., Dardavesis, T.I., Williams, J., Wickramasinghe, K., Breda, J., Chourdakis, M., 2021. Intake and



- adequacy of the vegan diet: a systematic review of the evidence. *Clinical Nutrition* 40, 3503–3521.
- Baker, C., Benayoun, B.A., 2023. Menopause is more than just loss of fertility. *Public Policy & Aging Report* 33, 113–119.
- Baliyan, S., Calvo, M.V., Piquera, D., Montero, O., Visioli, F., Venero, C., Fontecha, J., 2023. Milk fat globule membrane concentrate as a nutritional supplement prevents age-related cognitive decline in old rats: a lipidomic study of synaptosomes. *Food Research International* 163, 112163.
- Bath, S.C., Rayman, M.P., 2015. A review of the iodine status of UK pregnant women and its implications for the offspring. *Environmental Geochemistry and Health* 27, 619–629.
- Bath, S.C., Steer, C.D., Golding, J., Emmett, P., Rayman, M.P., 2013. Effect of inadequate iodine status in UK pregnant women on cognitive outcomes in their children: results from the Avon Longitudinal Study of Parents and Children (ALSPAC). *Lancet* 382, 331–337.
- Bath, S.C., Walter, A., Taylor, A., Wright, J., Rayman, M.P., 2014. Iodine deficiency in pregnant women living in the Southeast of the UK: the influence of diet and nutritional supplements on iodine status. *British Journal of Nutrition* 111, 1622–1631.
- Beal, T., Ortenzi, F., Fanzo, J., 2023a. Estimated micronutrient shortfalls of the EAT–Lancet planetary health diet. *Lancet Planet Health* 7, e233–e237.
- Beal, T., Gardner, C.D., Herrero, M., Iannotti, L.L., Merbold, L., Nordhagen, S., Mottet, A., 2023b. Friend or Foe? The role of animal-source foods in healthy and environmentally sustainable diets. *The Journal of Nutrition* 153, 409–425.
- Bingham, S.A., Day, N.E., Luben, R., Ferrari, P., Slimani, N., Norat, T., Clavel-Chapelon, F., Kesse, E., Nieters, A., Boeing, H., et al., 2003. Dietary fibre in food and protection against colorectal cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC): an observational study. *The Lancet* 361, 1496–1501.
- Blackstone, N.T., Conrad, Z., 2020. Comparing the recommended eating patterns of the EAT–Lancet commission and dietary guidelines for Americans: implications for sustainable nutrition. *Current Developments in Nutrition* 4, nzaa015.
- Bougma, K., Aboud, F.E., Harding, K.B., Marquis, G.S., 2013. Iodine and mental development of children 5 years old and under: a systematic review and meta-analysis. *Nutrients* 5, 1384–1416.
- Brantsæter, A.L., Abel, M.H., Haugen, M., Meltzer, H.M., 2013. Risk of suboptimal iodine intake in pregnant Norwegian women. *Nutrients* 5, 424–440.
- Burdge, G.C., 2022.  $\alpha$ -linolenic acid interconversion is sufficient as a source of longer chain  $\omega$ -3 polyunsaturated fatty acids in humans: an opinion. *Lipids* 57, 267–287.
- Burdge, G.C., Wootton, S.A., 2002. Conversion of alpha-linolenic acid to eicosapentaenoic, docosapentaenoic and docosahexaenoic acids in young women. *British Journal of Nutrition* 88, 411–420.
- Buttriss, J.L., Lanham-New, S.A., 2022. Editorial: Vitamin D: One hundred years on. *Nutrition Bulletin* 47, 282–287.
- Calvo, M.V., Kohen, V.L., Díaz-Mardomingo, C., García-Herranz, S., Baliyan, S., Tomé-Carneiro, J., Colmenarejo, G., Visioli, F., Venero, C., Fontecha, J., 2023. Milk fat globule membrane-enriched milk improves episodic memory: a randomized, parallel, double-blind, placebo-controlled trial in older adults. *Journal of Functional Foods* 111, 105849.
- Cashman, K.D., Dowling, K.G., Skrabáková, Z., Gonzalez-Gross, M., Valtueña, J., De Henauw, S., Moreno, L., Damsgaard, C.T., Michaelsen, K.F., et al., 2016. Vitamin D deficiency in Europe: pandemic? *American Journal of Clinical Nutrition* 103, 1033–1044.
- Cashman, K.D., Kiely, M.E., Andersen, R., Grønberg, I.M., Tetens, I., Tripkovic, L., Lanham-New, S.A., Lamberg, A., Adebayo, F.A., Gallagher, J.C., Smith, L.M., Sacke, J.M., Huang, Q., Ng, K., Yuan, C., Giovannucci, E.L., Rajakumar, K., Patterson, C.G., Öhlund, I., Lind, T., Åkeson, P.K., Ritz, C., 2022. Individual participant data (IPD)-level meta-analysis of randomised controlled trials to estimate the vitamin D dietary requirements in dark-skinned individuals resident at high latitude. *European Journal of Nutrition* 61, 1015–1034.
- Cashman, K.D., Lewis, R., Weaver, C.M., 2023. Adolescence and acquisition of peak bone mass. In: Hewison, M., Bouillon, R., Giovannucci, E., Goltzman, D., Meyer, M., Welsh, J. (Eds.), *Feldman and Pike's Vitamin D 5th Edition, Volume One: Biochemistry, Physiology and Diagnostics*. Academic Press, Cambridge, MA, USA, pp. 801–829.
- Chazelas, E., Pierre, F., Druésne-Pecollo, N., Esseddik, Y., Szabo de Edelenyi, F., Agaesse, C., De Sa, A., Lutchia, R., Gigandet, S., Srour, B., Debras, C., Huybrechts, I., Julia, C., Kesse-Guyot, E., Allès, B., Galan, P., Hercberg, S., Deschasaux-Tanguy, M., Touvier, M., 2022. Nitrates and nitrites from food additives and natural sources and cancer risk: results from the NutriNet-Santé cohort. *International Journal of Epidemiology* 51, 1106–1119.
- Chick, H., Dalyell, E., Hume, M., Smith, H.H., Mackay, H.M., 1922. The ætiology of rickets in infants: prophylactic and curative observations at the Vienna University Kinderklinik. *The Lancet* 200, 7–11.
- Clark, M.A., Springmann, M., Hill, J., Tilman, D., 2019. Multiple health and environmental impacts of foods. *Proceedings of the National Academy of Sciences* 116, 23357–23362.
- Clegg, M.E., Ribes, A.T., Reynolds, R., Kliem, K., Stergiadis, S., 2021. A comparative assessment of the nutritional composition of dairy and plant-based dairy alternatives available for sale in the UK and the implications for consumers' dietary intakes. *Food Research International* 148, 110586.
- Corry Mann, H.C., 1926. Diets for boys during the school age. *Medical Research Council Special Report Series No. 105*. HMSO, London, UK.
- Craig, W.J., Mangels, A.R., Fresán, U., Marsh, K., Miles, F.L., Saunders, A.V., Haddad, E. H., Heskey, C.E., Johnston, P., Larson-Meyer, E., Orlich, M., 2021. The safe and effective use of plant-based diets with guidelines for health professionals. *Nutrients* 13, 4144.
- Cross, A.J., Pollock, J.R.A., Bingham, S.A., 2003. Haem, not protein or inorganic iron, is responsible for endogenous intestinal N-nitrosation arising from red meat. *Cancer Research* 63, 2358–2360.
- Dai, Q., Zhu, X., Manson, J.E., Song, Y., Li, X., Franke, A.A., Costello, R.B., Rosanoff, A., Nian, H., Fan, L., et al., 2018. Magnesium status and supplementation influence vitamin D status and metabolism: results from a randomized trial. *American Journal of Clinical Nutrition* 108, 1249–1258.
- Delimont, N.M., Haub, M.D., Lindshield, B.L., 2017. The impact of tannin consumption on iron bioavailability and status: a narrative review. *Current Developments in Nutrition* 1, 1–12.
- Derbyshire, E., 2017. Associations between red meat intakes and the micronutrient intake and status of UK females: a secondary analysis of the UK National Diet and Nutrition Survey. *Nutrients* 9, 768.
- Domenichiello, A.F., Kitson, A.P., Bazinet, R.P., 2015. Is docosahexaenoic acid synthesis from  $\alpha$ -linolenic acid sufficient to supply the adult brain? *Progress in Lipid Research* 59, 54–66.
- Dominguez, L.J., Veronese, N., Ciriminna, S., Pérez-Albela, J.L., Vázquez-López, V.F., Rodas-Regalado, S., Bella, G.D., Parisi, A., Tagliaferri, F., Barbagallo, M., 2023. Association between serum magnesium and fractures: a Systematic review and meta-analysis of observational studies. *Nutrients* 15, 1304.
- Dorrington, N., Fallaize, R., Hobbs, D.A., Weech, M., Lovegrove, J.A., 2020. A review of nutritional requirements of adults aged  $\geq 65$  years in the UK. *The Journal of Nutrition* 150, 2245–2256.
- Drouin-Chartier, J.-P., Schwab, A.L., Chen, S., Li, Y., Sacks, F.M., Rosner, B., Manson, J. E., Willett, W.C., Stampfer, M.J., Hu, F.B., Bhupathiraju, S.N., 2020. Egg consumption and risk of type 2 diabetes: findings from 3 large US cohort studies of men and women and a systematic review and meta-analysis of prospective cohort studies. *American Journal of Clinical Nutrition* 112, 619–630.
- EFSA, 2024. Dietary reference values for the EU. Retrieved on 27 May 2024 from: <https://multimedia.efsa.europa.eu/dvrs/index.htm#>.
- Egg Info, 2023. UK egg industry data. Available at: <https://www.egginfo.co.uk/egg-facts-and-figures/indus-try-information/data>, accessed 21 December 2023.
- Erem, S., Atfi, A., Razaque, M.S., 2019. Anabolic effects of vitamin D and magnesium in aging bone. *The Journal of Steroid Biochemistry and Molecular Biology* 193, 105400.
- Ertl, P., Knaus, W., Zollitsch, W., 2016. An approach to including protein quality when assessing the net contribution of livestock to human food supply. *Animal* 10, 1883–1889.
- Fairweather-Tait, S., 2023. The role of meat in iron nutrition of vulnerable groups of the UK population. *Frontiers in Animal Science* 4, 1142252.
- Fallon, N., Dillon, S.A., 2020. Low intakes of iodine and selenium amongst vegan and vegetarian women highlight a potential nutritional vulnerability. *Frontiers in Nutrition* 7, 72.
- FAO, 2013. Dietary protein quality evaluation in human nutrition: report of an FAO expert consultation. *Food and Nutrition Paper* 92, 1–66.
- Fekete, Á.A., Giromini, C., Chatzidiakou, Y., Givens, D.I., Lovegrove, J.A., 2016. Whey protein lowers blood pressure and improves endothelial function and lipid biomarkers in adults with prehypertension and mild hypertension: results from the chronic Whey2Go randomized controlled trial. *American Journal of Clinical Nutrition* 104, 1534–11154.
- Gehring, J., Touvier, M., Baudry, J., Julia, C., Buscaïl, C., Srour, B., Hercberg, S., Péneau, S., Kesse-Guyot, E., Allès, B., 2021. Consumption of ultra-processed foods by pesco-vegetarians, vegetarians, and vegans: associations with duration and age at diet initiation. *Journal of Nutrition* 151, 120–131.
- Geiker, N.R.W., Lytken Larsen, M., Dyerberg, J., Stender, S., Astrup, A., 2018. Egg consumption, cardiovascular diseases and type 2 diabetes. *European Journal of Clinical Nutrition* 72, 44–56.
- Geiker, N.R.W., Bertram, H.C., Mejborn, H., Dragsted, L.O., Kristensen, L., Carrascal, J. R., Bügel, S., Astrup, A., 2021. Meat and human health-current knowledge and research gaps. *Foods* 10, 1556.
- Ghahremani, M., Smith, E.E., Chen, H.-Y., Creese, B., Goodarzi, Z., Ismail, Z., 2023. Vitamin D supplementation and incident dementia: effects of sex, APOE, and baseline cognitive status. *Alzheimer's & Dementia* 15, e12404.
- Giromini, C., Givens, D.I., 2022. Benefits and risks associated with meat consumption during key life processes and in relation to the risk of chronic diseases. *Foods* 11, 2063.
- Givens, D.I., 2020. The importance of milk and dairy foods in the diets of infants, adolescents, pregnant women, adults, and the elderly. *Journal of Dairy Science* 103, 9681–9699.
- Givens, D.I., 2023. Dairy foods and cardiometabolic diseases: an update and a reassessment of the impact of saturated fatty acids. *Proceedings of the Nutrition Society* 82, 320–345.
- Givens, D.I., 2024. Dietary protein for the elderly: more attention needed? *Gerontology & Geriatric Studies* 8, GGS.000697.
- Givens, D.I., Gibbs, R.A., 2008. Current intakes of EPA and DHA in European populations and the potential of animal-derived foods to increase them. *Proceedings of the Nutrition Society* 67, 273–280.
- Godfrey, K.M., Titcombe, P., El-Heis, S., Albert, B.B., Tham, E.H., Barton, S.J., Kenealy, T., Chong, M.-F.-F., Nield, H., Chong, Y.S., et al., 2023. Maternal B-vitamin and vitamin D status before, during, and after pregnancy and the influence of supplementation preconception and during pregnancy: prespecified secondary analysis of the NiPPER double-blind randomized controlled trial. *PLOS Medicine* 20, e1004260.

- Grant, W.B., 2014. Trends in diet and Alzheimer's disease during the nutrition transition in Japan and developing countries. *Journal of Alzheimer's Disease* 38, 611–620.
- Grouff-Jacobsen, S., Hess, S., Aakre, I., Gjengedal, E.L.F., Pettersen, K.B., Henjum, S., 2020. Vegans, vegetarians and pescatarians are at risk of iodine deficiency in Norway. *Nutrients* 12, 3555.
- Gu, X., Drouin-Chartier, J.-P., Sacks, F.M., Hu, F.B., Rosner, B., Willett, W.C., 2023. Red meat intake and risk of type 2 diabetes in a prospective cohort study of United States females and males. *American Journal of Clinical Nutrition* 118, 1153–1163.
- Guo, J., Kliem, K.E., Lovegrove, J.A., Givens, D.I., 2017. Effect of production system, supermarket, and purchase date on the vitamin D content of eggs at retail. *Food Chemistry* 221, 1021–1025.
- Guo, J., Lovegrove, J.A., Givens, D.I., 2018. 25(OH)D3-enriched or fortified foods are more efficient at tackling inadequate vitamin D status than vitamin D3. *Proceedings of the Nutrition Society* 77, 282–291.
- Guo, J., Lovegrove, J.A., Givens, D.I., 2019. Food fortification and biofortification as potential strategies for prevention of vitamin D deficiency. *Nutrition Bulletin* 44, 36–42.
- Hargreaves, S.M., Raposo, A., Saraiva, A., Zandonadi, R.P., 2021. Vegetarian diet: an overview through the perspective of quality-of-life domains. *International Journal of Environmental Research and Public Health* 18, 4067.
- Hedegaard, S., Nohr, E.A., Olsen, S.F., Halldorsson, T.I., Renault, K.M., 2024. Adherence to different forms of plant-based diets and pregnancy outcomes in the Danish National Birth Cohort: A prospective observational study. *Acta Obstetrica Gynecologica Scandinavica*, <https://doi.org/10.1111/aogs.14778>, Published online by Wiley-Blackwell 24 January 2024.
- Herreman, L., Nommensen, P., Pennings, B., Laus, M.C., 2020. Comprehensive overview of the quality of plant- and animal sourced proteins based on the digestible indispensable amino acid score. *Food Science & Nutrition* 8, 5379–5391.
- Hobbs-Grimmer, D.A., Givens, D.I., Lovegrove, J.A., 2021. Associations between red meat, processed red meat and total red and processed red meat consumption, nutritional adequacy and markers of health and cardio-metabolic diseases in British adults: a cross-sectional analysis using data from UK National Diet and Nutrition Survey. *European Journal of Nutrition* 60, 2979–2997.
- Hoppe, C., Mølgaard, C., Dalum, C., Vaag, A., Michaelsen, K.F., 2009. Differential effects of casein versus whey on fasting plasma levels of insulin, IGF-1 and IGF-1/IGFBP-3: results from a randomized 7-day supplementation study in pre-pubertal boys. *European Journal of Clinical Nutrition* 63, 1076–1083.
- Hu, H., Song, J., MacGregor, G.A., He, F.J., 2023. Consumption of soft drinks and overweight and obesity among adolescents in 107 countries and regions. *JAMA Network Open* 6, e2325158.
- Hulett, N.A., Scalzo, R.L., Reusch, J.E.B., 2022. Glucose uptake by skeletal muscle within the contexts of type 2 diabetes and exercise: an integrated approach. *Nutrients* 14, 647.
- Hur, S.J., Yoon, Y., Jo, C., Jeong, J., Lee, K.T., 2019. Effect of dietary red meat on colorectal cancer risk - a review. *Comprehensive Reviews in Food Science and Food Safety* 18, 1812–1824.
- Iguacel, I., Miquel-Berges, M.L., Gómez-Bruton, A., Moreno, L.A., Julián, C., 2018. Veganism, vegetarianism, bone mineral density, and fracture risk: a systematic review and meta-analysis. *Nutrition Reviews* 77, 1–18.
- Iqbal, R., Dehghan, M., Mente, A., Rangarajan, S., Wielgosz, A., Avezum, A., Seron, P., AlHabib, K.F., Lopez-Jaramillo, P., Swaminathan, S., et al., on behalf of the PURE study, 2021. Associations of unprocessed and processed meat intake with mortality and cardiovascular disease in 21 countries [Prospective Urban Rural Epidemiology (PURE) Study]: a prospective cohort study. *American Journal of Clinical Nutrition* 114, pp. 1049–1058.
- Jakobsen, M.U., Bysted, A., Mejborn, H., Stockmarr, A., Trolle, E., 2021. Intake of unprocessed and processed meat and the association with cardiovascular disease: an overview of systematic reviews. *Nutrients* 13, 3303.
- Jakobsen, J., Christensen, T., 2021. Natural vitamin D in food: to what degree does 25-hydroxyvitamin D contribute to the vitamin D activity in food? *Journal of Bone and Mineral Research* plus 5, e10453.
- Kalkwarf, H.J., Khoury, J.C., Lanphear, B.P., 2003. Milk intake during childhood and adolescence, adult bone density, and osteoporotic fractures in US women. *American Journal of Clinical Nutrition* 77, 257–265.
- Kaplan, A., Zelicha, H., Tsaban, G., Meir, A.Y., Rinott, E., Kovsan, J., Novack, L., Thiery, J., Ceglarek, U., Burkhardt, R., et al., 2019. Protein bioavailability of *Wolffia globosa* duckweed, a novel aquatic plant - a randomized controlled trial. *Clinical Nutrition* 38, 2576–2582.
- Kettig, E., Kistler-Fischbacher, M., de Godoi Rezende Costa Molino, C., Bischoff-Ferrari, H.A., Frundi, D.S., 2023. Association of magnesium and vitamin D status with grip strength and fatigue in older adults: a 4-week observational study of geriatric participants undergoing rehabilitation. *Aging Clinical and Experimental Research* 35, 1619–1629.
- Key, T.J., Appleby, P.N., Spencer, E.A., Travis, R.C., Roddam, A.W., Allen, N.E., 2009. Cancer incidence in vegetarians: results from the European prospective investigation into cancer and nutrition (EPIC-Oxford). *American Journal of Clinical Nutrition* 89 (Suppl), 1620S–1626S.
- Key, T.J., Papier, K., Tong, T.Y.N., 2022. Plant-based diets and long-term health: findings from the EPIC-Oxford study. *Proceedings of the Nutrition Society* 81, 190–198.
- Koretz, R.L., 2020. JPEN Journal Club 52. What evidence will change minds? *Journal of Parenteral and Enteral Nutrition* 44, 1150–1152.
- Kouvelioti, R., Josse, A.R., Klentrou, P., 2017. Effects of dairy consumption on body composition and bone properties in youth: a systematic review. *Current Developments in Nutrition* 1, e001214.
- Lane, K.E., Wilson, M., Hellon, T.G., Davis, I.G., 2022. Bioavailability and conversion of plant based sources of omega-3 fatty acids - a scoping review to update supplementation options for vegetarians and vegans. *Critical Reviews in Food Science and Nutrition* 62, 4982–4997.
- Larson, N.I., Neumark-Sztainer, D., Harnack, L., Wall, M., Story, M., Eisenberg, M.E., 2009. Calcium and dairy intake: trends during the transition to young adulthood and correlates of calcium intake. *Journal of Nutrition Education and Behavior* 41, 254–260.
- Larsson, S.C., Orsini, N., 2014. Red meat and processed meat consumption and all-cause mortality: a meta-analysis. *American Journal of Epidemiology* 179, 282–289.
- Latunde-Dada, G.O., Neale, R.J., 1986. Pigeon (*Columba L.*) meat iron solubility and availability for absorption in rats. *British Journal of Nutrition* 55, 409–418.
- Lee, K.W., Shin, D., Cho, M.S., Song, W.O., 2016. Food group intakes as determinants of iodine status among us adult population. *Nutrients* 8, 325.
- Leighton, G., Clark, M., 1929. Milk consumption and the growth of school children. *Lancet* 1, 40–43.
- Li, H., Zeng, X., Wang, Y., Zhang, Z., Zhu, Y., Li, X., Hu, A., Zhao, Q., Yang, W., 2022. A prospective study of healthful and unhealthful plant-based diet and risk of overall and cause-specific mortality. *European Journal of Nutrition* 61, 387–398.
- Liu, X., Zhuang, P., Li, Y., Wu, F., Wan, X., Zhang, Y., Jiao, J., 2022. Association of fish oil supplementation with risk of incident dementia: a prospective study of 215,082 older adults. *Clinical Nutrition* 41, 589–598.
- Lönnerdal, B., 2000. Dietary factors influencing zinc absorption. *Journal of Nutrition* 130, 1378S–1383S.
- Lonnie, M., Hooker, E., Brunstrom, J.M., Corfe, B.M., Green, M.A., Watson, A.W., Williams, E.A., Stevenson, E.J., Penson, S., Johnstone, A.M., 2018. Protein for Life: review of optimal protein intake, sustainable dietary sources and the effect on appetite in ageing adults. *Nutrients* 10, 360.
- Lordan, R., 2021. Notable developments for vitamin D amid the COVID-19 Pandemic, but caution warranted overall: a narrative review. *Nutrients* 13, 740.
- Ma, X., Huang, Z., Yang, X., Su, Y., 2014. Calcium supplementation and bone mineral accretion in Chinese adolescents aged 12–14 years: a 12-month, dose-response, randomised intervention trial. *British Journal of Nutrition* 112, 1510–1520.
- Mansilla, R., Long, G., Welham, S., Harvey, J., Lukinova, E., Nica-Avram, G., Smith, G., Salt, D., Smith, A., Goulding, J., 2024. Detecting iodine deficiency risks from dietary transitions using shopping data. *Scientific Reports* 14, 1017.
- Mason, P., 2023. The importance of eggs in an environmentally sustainable diet. *Nutrition Bulletin* 48, 400–410.
- McAuliffe, G.A., Takahashi, T., Beal, T., Huppertz, T., Leroy, F., Buttriss, J., Collins, A.L., Drewnowski, A., McLaren, S.J., Ortenzi, F., van der Pols, J.C., van Vliet, S., Lee, M.R.F., 2023. Protein quality as a complementary functional unit in life cycle assessment (LCA). *The International Journal of Life Cycle Assessment* 28, 146–155.
- Meticulous Research, 2024. Europe Plant-Based Protein Market by Type, Crop Type, Source Process and Application - Forecast to 2030. Retrieved on 10 January 2024 from Europe Plant-based Protein Market by Size, Share, Forecast, & Trends Analysis ([meticulousresearch.com](https://www.meticulousresearch.com)).
- Micha, R., Wallace, S.K., Mozaffarian, D., 2010. Red and processed meat consumption and risk of incident coronary heart disease, stroke, and diabetes mellitus: a systematic review and meta-analysis. *Circulation* 121, 2271–2283.
- Minimalistic vegan, 2024. 12 Types of vegans and vegetarians explained. Retrieved on 12 January 2024 from: <https://theminimalistvegan.com/types-of-vegans-and-vegetarians/>.
- Mogire, R.M., Muriuki, J.M., Morovat, A., Mentzer, A.J., Webb, E.L., Kimita, W., Ndungu, F.M., Macharia, A.W., Cutland, C.L., Sirima, S.B., et al., 2022. Vitamin D deficiency and its association with iron deficiency in African children. *Nutrients* 14, 1372.
- Molloy, A.M., 2018. Should vitamin B12 status be considered in assessing risk of neural tube defects? *Annals of the New York Academy of Sciences* 1414, 109–125.
- Molloy, A.M., Kirke, P.N., Troendle, J.F., Burke, H., Sutton, M., Brody, L.C., Scott, J.M., Mills, J.L., 2009. Maternal vitamin B12 status and risk of neural tube defects in a population with high neural tube defect prevalence and no folic acid fortification. *Pediatrics* 123, 917–923.
- Monteiro, C.A., Cannon, G., Moubarac, J.-C., Levy, R.B., Louzada, M.L.C., Jaime, P.C., 2018. The UN decade of nutrition, the NOVA food classification and the trouble with ultra-processing. *Public Health Nutrition* 21, 5–17.
- Moore, S.S., Costa, A., Pozza, M., Weaver, C.M., De Marchi, M., 2024. Nutritional scores of milk- and plant-based alternatives and their difference in contribution to human nutrition. *LWT - Food Science and Technology* 191, 115688.
- Mullan, K., Hamill, L., Doolan, K., Young, I., Smyth, P., Flynn, A., Walton, J., Meharg, A.A., Carey, M., McKernan, C., Bell, M., et al., 2019. Iodine status of teenage girls on the island of Ireland. *European Journal of Nutrition* 59, 1859–1867.
- Murphy, N., Norat, T., Ferrari, P., Jenab, M., Bueno-de-Mesquita, B., Skeie, G., Dahm, C.C., Overvad, K., Olsen, A., Tjønneland, A., et al., 2012. Dietary fibre intake and risks of cancers of the colon and rectum in the European prospective investigation into cancer and nutrition (EPIC). *PLoS ONE* 7, e39361.
- NDNS, 2020. National Diet and Nutrition Survey Rolling programme, Years 9 to 11 (2016/2017 to 2018/2019). A survey carried out on behalf of Public Health England and the Food Standards Agency. PHE publications gateway number GW-1757, London, UK.

- Neufingerl, N., Eilander, A., 2022. Nutrient intake and status in adults consuming plant-based diets compared to meat-eaters: a systematic review. *Nutrients* 14, 29.
- Neufingerl, N., Eilander, A., 2023. Nutrient intake and status in children and adolescents consuming plant-based diets compared to meat-eaters: a systematic review. *Nutrients* 15, 4341.
- Nexo, E., Hoffmann-Lücke, E., 2011. Holotranscobalamin, a marker of vitamin B-12 status: analytical aspects and clinical utility. *American Journal of Clinical Nutrition* 94, 359S–365S.
- NHS, 2024a. Vitamin B12 Haematinics Summary of Assay Change. Retrieved on 2 February 2024 from <https://www.nbt.nhs.uk/sites/default/files/document/Haematinics%20Summary%20of%20Assay%20Change.pdf>.
- NHS, 2024b. Vitamin D. Retrieved on 27 May 2024 from: <https://www.nhs.uk/conditions/vitamins-and-minerals/vitamin-d/>.
- Nicol, K., Thomas, E.-L., Nugent, A.P., Woodside, J.V., Hart, K.H., Bath, S.C., 2023. Iodine fortification of plant-based dairy and fish alternatives: the effect of substitution on iodine intake based on a market survey in the UK. *British Journal of Nutrition* 129, 832–842.
- Nicol, K., Nugent, A.P., Woodside, J.V., Hart, K.H., Bath, S.C., 2024. Iodine and plant-based diets: a narrative review and calculation of iodine content. *British Journal of Nutrition* 131, 265–275.
- Niedermaier, T., Gredner, T., Hoffmeister, M., Mons, U., Brenner, H., 2023. Impact of reducing intake of red and processed meat on colorectal cancer incidence in Germany 2020 to 2050-A simulation study. *Nutrients* 15, 1020.
- Niklewicz, A., Smith, A.D., Smith, A., Holzer, A., Klein, A., McCaddon, A., Molloy, A.M., Wolfenbuttel, B.H.R., Nexo, E., McNulty, H., et al., on behalf of CluB-12., 2023. The importance of vitamin B12 for individuals choosing plant-based diets. *European Journal of Nutrition* 62, pp. 1551–1559.
- O'Keefe, J.H., Tintle, N.L., Harris, W.S., O'Keefe, E.L., Sala-Vila, A., Attia, J., Garg, M., Hure, A., Bork, C.S., Schmidt, E.B., et al., 2024. Omega-3 blood levels and stroke risk: a pooled and harmonized analysis of 183291 participants from 29 prospective studies. *Stroke* 55, 50–58.
- Outila, T.A., Karkkainen, M.U., Seppanen, R.H., Lamberg-Allardt, C.J., 2000. Dietary intake of vitamin D in premenopausal, healthy vegans was insufficient to maintain concentrations of serum 25-hydroxyvitamin D and intact parathyroid hormone within normal ranges during the winter in Finland. *Journal of the American Dietetic Association* 100, 434–441.
- Pan, A., Sun, Q., Bernstein, A.M., Schulze, M.B., Manson, J.E., Willett, W.C., Hu, F.B., 2011. Red meat consumption and risk of type 2 diabetes: 3 cohorts of US adults and an updated meta-analysis. *American Journal of Clinical Nutrition* 94, 1088–1096.
- Parker, C.E., Vivian, W.J., Oddy, W.H., Beilin, L.J., Mori, T.A., O'Sullivan, T.A., 2012. Changes in dairy food and nutrient intakes in Australian adolescents. *Nutrients* 4, 1794–1811.
- Pawlak, R., Vos, P., Shahab-Ferdows, S., Hampel, D., Allen, L., Perrin, M.T., 2018. Vitamin B-12 content in breast milk of vegan, vegetarian, and nonvegetarian lactating women in the United States. *American Journal of Clinical Nutrition* 108, 525–531.
- Pawlak, R., Judd, N., Donati, G.L., Perrin, M.T., 2023. Prevalence and predictors of low breast milk iodine concentration in women following vegan, vegetarian, and omnivore diets. *Breastfeeding Medicine* 18, 2023.
- Pellinen, T., Päiväranta, E., Isotalo, J., Lehtovirta, M., Itkonen, S.T., Korkalo, L., Erkkola, M., Pajari, A.-M., 2021. Replacing dietary animal-source proteins with plant-source proteins changes dietary intake and status of vitamins and minerals in healthy adults: a 12-week randomized controlled trial. *European Journal of Nutrition* 61, 1391–1404.
- Perrin, M.T., Pawlak, R., Judd, N., Cooper, J., Donati, G.L., 2023. Major and trace mineral composition of milk from lactating women following vegan, vegetarian and omnivore diets. *British Journal of Nutrition* 130, 1005–1012.
- Pikosky, M.A., Ragalie-Carr, J., Miller, G.D., 2022. Recognizing the importance of protein quality in an era of food systems transformation. *Frontiers in Sustainable Food Systems* 6, 1012813.
- Pinchen, H., Powell, N., Church, S., Finglas, P., 2021. McCance and Widdowson's The Composition of Foods Integrated Dataset (CoFID). Public Health England, London, UK.
- Pontifex, M., Vauzour, D., Minihane, A.M., 2018. The effect of APOE genotype on Alzheimer's disease risk is influenced by sex and docosahexaenoic acid status. *Neurobiology of Aging* 69, 209–220.
- Qin, Y., Cifelli, C.J., Agarwal, S., Fugoni, V.L., 2023. Dairy food consumption is beneficially linked with iodine status in US children and adults: National Health and Nutrition Examination Surveys 2001–2018. *Public Health Nutrition* 26, 1828–1839.
- Raatz, S.K., Silverstein, J.T., Jahns, L., Picklo Sr., M.J., 2013. Issues of fish consumption for cardiovascular disease risk reduction. *Nutrients* 5, 1081–1097.
- Ravindran, G., 1991. Studies on millets: proximate composition, mineral composition, and phytate and oxalate contents. *Food Chemistry* 39, 99–107.
- Ray, J.G., Wyatt, P.R., Thompson, M.D., Vermeulen, M.J., Meier, C., Wong, P.-Y., Farrell, S.A., Cole, D.E.C., 2007. Vitamin B12 and the risk of neural tube defects in a folic acid-fortified population. *Epidemiology* 18, 362–366.
- Rehman, S.U., Ali, R., Zhang, H., Zafar, M.H., Wang, M., 2023. Research progress in the role and mechanism of leucine in regulating animal growth and development. *Frontiers in Physiology* 14, 1252089.
- Ricci, H., Gaeta, M., Franchi, C., Poli, A., Battino, M., Dolci, A., Schmid, D., Ricci, C., 2023. Fish intake in relation to fatal and non-fatal cardiovascular risk: a systematic review and meta-analysis of cohort studies. *Nutrients* 15, 4539.
- Rutjes, A.W.S., Denton, D.A., Di Nisio, M., Chong, L.Y., Abraham, R.P., Al-Assaf, A.S., Anderson, J.L., Malik, M.A., Vernooij, R.W.M., Martínez, G., Tabet, N., McCleery, J., 2018. Vitamin and mineral supplementation for maintaining cognitive function in cognitively healthy people in mid and late life (Review). *Cochrane Database of Systematic Reviews* 2018, Art. No. CD011906.
- Schwingshackl, L., Schwedhelm, C., Hoffmann, G., Knüppel, S., Iqbal, K., Andriolo, V., Bechthold, A., Schlesinger, S., Boeing, H., 2017. Food groups and risk of hypertension: a systematic review and dose-response meta-analysis of prospective studies. *Advances in Nutrition* 8, 793–803.
- Scientific Advisory Committee on Nutrition, 2010. Iron and Health. Published for the Department of Health under licence from the Controller of Her Majesty's Stationery Office. TSO, London, UK.
- Scientific Advisory Committee on Nutrition, 2016. Vitamin D and Health. Retrieved on 7 January 2024 from: <https://www.gov.uk/government/groups/scientific-advisory-committee-on-nutrition>.
- Scientific Advisory Committee on Nutrition/Committee on Toxicology, 2004. Advice on fish consumption: benefits and risks. TSO, Norwich, UK.
- Sha, S., Gwenzi, T., Chen, L.-J., Brenner, H., Schöttker, B., 2023. About the associations of vitamin D deficiency and biomarkers of systemic inflammatory response with all-cause and cause-specific mortality in a general population sample of almost 400,000 UK Biobank participants. *European Journal of Epidemiology* 38, 957–971.
- Shaikh, M.G., Anderson, J.M., Hall, S.K., Jackson, M.A., 2003. Transient neonatal hypothyroidism due to a maternal vegan diet. *Journal of Pediatric Endocrinology & Metabolism* 16, 111–113.
- Shin, J.Y., Xun, P., Nakamura, Y., He, K., 2013. Egg consumption in relation to risk of cardiovascular disease and diabetes: a systematic review and meta-analysis. *American Journal of Clinical Nutrition* 98, 146–159.
- Shkemi, B., Huppertz, T., 2021. Calcium absorption from food products: food matrix effects. *Nutrients* 14, 180.
- Soedamah-Muthu, S.S., de Goede, J., 2018. Dairy Consumption and cardiometabolic diseases: systematic review and updated meta-analyses of prospective cohort studies. *Current Nutrition Reports* 7, 171–182.
- Song, Y., Liu, M., Yang, F.G., Cui, L.H., Lu, X.Y., Chen, C., 2015. Dietary fibre and the risk of colorectal cancer: a case control study. *Asian Pacific Journal of Cancer Prevention* 16, 3747–3752.
- Sprague, M., Chau, T.C., Givens, D.I., 2022. Iodine content of wild and farmed seafood and its estimated contribution to UK dietary iodine intake. *Nutrients* 14, 195.
- Srouf, B., Fezeu, L.K., Kesse-Guyot, E., Allès, B., Méjean, C., Andrianasolo, R.M., Chazelas, E., Deschasaux, M., Hercberg, S., Galan, P., et al., 2019. Ultra-processed food intake and risk of cardiovascular disease: prospective cohort study (NutriNet-Santé). *British Medical Journal* 365, 1451.
- Statista 2023. Veganism and vegetarianism in the United Kingdom. Retrieved on 5 January 2024 from: <https://www.statista.com/study/67944/veganism-in-the-uk/>.
- Stergiadis, S., Qin, N., Faludi, G., Beauclercq, S., Pitt, J., Desnica, N., Pétursdóttir, Á., Newton, E.E., Angelidis, A.E., Givens, D.I., Humphries, D.J., Gunnlaugsdóttir, H., Juniper, D.T., 2021. Mineral concentrations in bovine milk from farms with contrasting grazing management. *Foods* 10, 2733.
- Stevenson, M.C., Drake, C., Givens, D.I., 2018. Further studies on the iodine concentration of conventional, organic and UHT semi-skimmed milk at retail in the UK. *Food Chemistry* 239, 551–555.
- Stewart, C., Piernas, C., Cook, B., Jebb, S.A., 2021. Trends in UK meat consumption: analysis of data from years 1–11 (2008–09 to 2018–19) of the National Diet and Nutrition Survey rolling programme. *Lancet Planet Health* 5, e699–e708.
- Storz, M.A., Müllera, A., Niederreiter, L., Zimmermann-Klemm, A.M., Suarez-Alvarez, M., Kowarschika, S., Strittmatter, M., Schlachtera, E., Pasluostad, C., Hubera, R., Hannibal, L., 2023. A cross-sectional study of nutritional status in healthy, young, physically-active German omnivores, vegetarians and vegans reveals adequate vitamin B12 status in supplemented vegans. *Annals of Medicine* 55, 2269969.
- Sukumar, N., Adaikalakoteswari, A., Venkataraman, H., Maheswaran, H., Saravanan, P., 2016. Vitamin B<sub>12</sub> status in women of childbearing age in the UK and its relationship with national nutrient intake guidelines: results from two National Diet and Nutrition Surveys. *BMJ Open* 6, e011247.
- Světnička, M., Heniková, M., Selinger, E., Ouařadová, A., Potočková, J., Kuhn, T., Gojda, J., El-Lababidi, E., 2023. Prevalence of iodine deficiency among vegan compared to vegetarian and omnivore children in the Czech Republic: cross-sectional study. *European Journal of Clinical Nutrition* 77, 1061–1070.
- Takahashi, F., Hashimoto, Y., Kaji, A., Sakai, R., Okamura, T., Kitagawa, N., Okada, H., Nakanishi, N., Majima, S., Senmaru, T., et al., 2021. Sarcopenia is associated with a risk of mortality in people with type 2 Diabetes Mellitus. *Frontiers in Endocrinology* 12, 783363.
- Tong, T.Y.N., Appleby, P.N., Armstrong, M.E.G., Fensom, G.K., 2020. Vegetarian and vegan diets and risks of total and site-specific fractures: results from the prospective EPIC-Oxford Study. *BMC Medicine* 18, 353.
- Tripkovic, L., Wilson, L.R., Lanham-New, S.A., 2017. Vitamin D<sub>2</sub> vs. vitamin D<sub>3</sub>: they are not one and the same. *Nutrition Bulletin* 42, 331–337.
- Tso, R., Forde, C.G., 2021. Unintended consequences: nutritional impact and potential pitfalls of switching from animal- to plant-based foods. *Nutrients* 13, 2527.
- Uwaezuoke, S.N., 2017. Vitamin D deficiency and anemia risk in children: a review of emerging evidence. *Pediatric Health, Medicine and Therapeutics* 8, 47–55.
- Uwitonze, A.M., Razaque, M.S., 2018. Role of magnesium in vitamin D activation and function. *Journal of the American Osteopathic Association* 118, 181–189.

- van Vliet, S., Burd, N.A., van Loon, L.J.C., 2015. The skeletal muscle anabolic response to plant- versus animal-based protein consumption. *Journal of Nutrition* 145, 1981–1991.
- Vanderpump, M.P.J., Lazarus, J.H., Smyth, P.P., Laurberg, P., Holder, R.L., Boelaert, K., Franklyn, J.A., 2011. Iodine status of UK schoolgirls: a cross-sectional survey. *The Lancet* 377, 2007–2012.
- Veronese, N., Reginster, J.-Y., 2019. The effects of calorie restriction, intermittent fasting and vegetarian diets on bone health. *Aging Clinical Experimental Research* 31, 753–758.
- Viroli, G., Kalmpourtzidou, A., Cena, H., 2023. Exploring benefits and barriers of plant-based diets: health, environmental impact, food accessibility and acceptability. *Nutrients* 15, 4723.
- Vogiatzoglou, A., Smith, A.D., Nurk, E., Berstad, P., Drevon, C.A., Ueland, P.M., Vollset, S.E., Tell, G.S., Refsum, H., 2009. Dietary sources of vitamin B-12 and their association with plasma vitamin B-12 concentrations in the general population: the Hordaland Homocysteine Study. *American Journal of Clinical Nutrition* 89, 1078–1087.
- Walsh, M.C., Gunn, C., 2020. Non-dairy milk substitutes: are they of adequate nutritional composition? In: Givens, D.I. (Ed.), *Milk and Dairy Foods: Their Functionality in Human Health and Disease*. Elsevier, Cambridge, MA, USA, pp. 347–369.
- Wan, X., Wang, S., Xu, J., Zhuang, L., Xing, K., Zhang, M., Zhu, X., Wang, L., Gao, P., Xi, Q., et al., 2017. Dietary protein-induced hepatic IGF-1 secretion mediated by PPAR $\gamma$  activation. *PLoS ONE* 12, e0173174.
- Wang, M., Ma, H., Song, Q., Zhou, T., Hu, Y., Heianza, Y., Manson, J.E., Qi, L., 2022. Red meat consumption and all-cause and cardiovascular mortality: results from the UK Biobank study. *European Journal of Nutrition* 61, 3543–12553.
- Wang, T., Masedunskas, A., Willett, W.C., Fontana, L., 2023. Vegetarian and vegan diets: benefits and drawbacks. *European Heart Journal* 44, 3423–3439.
- Watling, C.Z., Kelly, R.K., Tong, T.Y.N., Piernas, C., Watts, E.L., Tin Tin, S., Knuppel, A., Schmidt, J.A., Travis, R.C., Key, T.J., Perez-Cornago, A., 2021. Associations of circulating insulin-like growth factor-I with intake of dietary proteins and other macronutrients. *Clinical Nutrition* 40, 4685e4693.
- Watling, C.Z., Schmidt, J.A., Dunneram, Y., Tong, T.Y.N., Kelly, R.K., Knuppel, A., Travis, R.C., Key, T.J., Perez-Cornago, A., 2022. Risk of cancer in regular and low meat-eaters, fish-eaters, and vegetarians: a prospective analysis of UK Biobank participants. *BMC Medicine* 20, 73.
- Weaver, C.M., Gordon, C.M., Janz, K.F., Kalkwarf, H.J., Lappe, J.M., Lewis, R., O’Karma, M., Wallace, T.C., Zemel, B.S., 2016. The National Osteoporosis Foundation’s position statement on peak bone mass development and lifestyle factors: a systematic review and implementation recommendations. *Osteoporosis International* 27, 1281–1386.
- Welch, A.A., Shakya-Shrestha, S., Lentjes, M.A.H., Wareham, N.J., Khaw, K.-T., 2010. Dietary intake and status of n-3 polyunsaturated fatty acids in a population of fish-eating and non-fish-eating meat-eaters, vegetarians, and vegans and the precursor-product ratio of  $\alpha$ -linolenic acid to long-chain n-3 polyunsaturated fatty acids: results from the EPIC-Norfolk cohort. *American Journal of Clinical Nutrition* 92, 1040–1051.
- Wells, A.M., Haub, M.D., Fluckey, J., Williams, D.K., Chernoff, R., Campbell, W.W., 2003. Comparisons of vegetarian and beef-containing diets on hematological indexes and iron stores during a period of resistive training in older men. *Journal of the American Dietetic Association* 103, 594–601.
- West, A.L., Miles, E.A., Lillycrop, K.A., Han, L., Napier, J.A., Calder, P.C., Burdge, G.C., 2020. Dietary supplementation with seed oil from transgenic *Camelina sativa* induces similar increments in plasma and erythrocyte DHA and EPA to fish oil in healthy humans. *British Journal of Nutrition* 124, 922–930.
- Willett, W., Rockström, J., Loken, B., Springmann, M., Lang, T., Vermeulen, S., Garnett, T., Tilman, D., DeClerck, F., Wood, A., et al., 2019. Food in the Anthropocene: the EAT-Lancet Commission on healthy diets from sustainable food systems. *Lancet (north American Edition)* 393, 447–492.
- Wood, J.D., Giromini, C., Givens, D.I., 2024. Animal-derived foods: consumption, composition and effects on health and the environment: an overview. *Frontiers in Animal Science* 5, 1332694.
- World Cancer Research Fund (2023). Limit red and processed meat. Retrieved on 20 December 2023 from: <https://www.wcrf.org/diet-activity-and-cancer/cancer-prevention-recommendations/limit-red-and-processed-meat/#:~:text=There%20is%20strong%20evidence%20that,iron%2C%20zinc%20and%20vitamin%20B12.>
- World Cancer Research Fund/American Institute for Cancer Research (2018). Diet, nutrition, physical activity, and cancer: a global perspective. Continuous Update Project Expert Report 2018. Retrieved on 20 December 2023 from: [www.dietandcancerreport.org](http://www.dietandcancerreport.org).
- Wu, K., Spiegelman, D., Hou, T., Albanes, D., Allen, N.E., Berndt, S.I., van den Brandt, P.A., Giles, G.G., Giovannucci, E., Goldbohm, R.A., et al., 2016. Associations between unprocessed red and processed meat, poultry, seafood and egg intake and the risk of prostate cancer: a pooled analysis of 15 prospective cohort studies. *International Journal of Cancer* 138, 2368–2382.
- Wu, L., Sun, D., 2016. Meta-analysis of milk composition and the risk of cognitive disorders. *Nutrients* 8, 824.
- Yakar, S., Werner, H., Rosen, C.J., 2018. 40 Years of IGF1. Insulin-like growth factors: actions on the skeleton. *Journal of Molecular Endocrinology* 61, T115–T137.
- Zaoui, M., Louadj, L., Ferrand, N., Nehme, R., Sabbah, M., Abdennebi-Najar, L., 2024. Carcinogenic effect of low doses of polycyclic and heterocyclic aromatic hydrocarbons and amines and lack of protection by inulin supplementation. *Food and Chemical Toxicology* 185, 114454.
- Zeraatkar, D., Johnston, B.C., Bartoszko, J., Cheung, K., Bala, M.M., Valli, C., Rabassa, M., Sit, D., Milio, K., Sadeghirad, B., et al., 2019. Effect of lower versus higher red meat intake on cardiometabolic and cancer outcomes: a systematic review of randomized trials. *Annals of Internal Medicine* 171, 721–731.
- Zha, H., Yu, L., Tang, Y., Sun, L., Yuan, Q., 2023. Effect of iodine nutrition status on thyroid function and pregnancy outcomes. *Biological Trace Element Research* 201, 5143–5151.
- Zhang, Y., Chen, J., Qiu, J., Li, Y., Wang, J., Jiao, J., 2016. Intakes of fish and polyunsaturated fatty acids and mild-to-severe cognitive impairment risks: a dose-response meta-analysis of 21 cohort studies. *American Journal of Clinical Nutrition* 103, 330–340.
- Zhang, H., Greenwood, D.C., Risch, H.A., Bunce, D., Hardie, L.J., Cade, J.E., 2021. Meat consumption and risk of incident dementia: cohort study of 493,888 UK Biobank participants. *American Journal of Clinical Nutrition* 114, 175–184.
- Zhao, H., Wang, M., Peng, X., Zhong, L., Liu, X., Shi, Y., Li, Y., Chen, Y., Tang, S., 2023. Fish consumption in multiple health outcomes: an umbrella review of meta-analyses of observational and clinical studies. *Annals of Translational Medicine* 11, 152.
- Zhou, L., Bai, X., Huang, J., Tan, Y., Yang, Q., 2023. Vitamin B12 supplementation improves cognitive function in middle aged and elderly patients with cognitive impairment. *Nutrición Hospitalaria* 40, 724–731.