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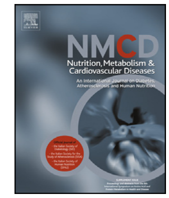

POSITION PAPER

Position paper on vegetarian diets from the working group of the Italian Society of Human Nutrition

C. Agnoli [a], L. Baroni [b], I. Bertini [c], S. Ciappellano [d], A. Fabbri [e], M. Papa [c], N. Pellegrini [f], R. Sbarbati [c], M.L. Scarino [g], V. Siani [c], S. Sieri [a,*]

[a] *Epidemiology and Prevention Unit, Fondazione IRCSS Istituto Nazionale dei Tumori, Milan, Italy*
[b] *Primary Treatment Unit, Northern Health and Social Security District 9, Treviso, Italy*
[c] *Independent Researcher, Italy*
[d] *Department of Food, Environmental and Nutritional Sciences, Division of Human Nutrition, University of Milan, Milan, Italy*
[e] *Nutrition Unit, Hygiene, Food and Nutrition Services, Department of Public Health, Local Health Unit, Reggio Emilia, Italy*
[f] *Department of Food and Drug, University of Parma, Parma, Italy*
[g] *Research Centre for Food and Nutrition, Council for Agricultural Research and Economics, Rome, Italy*

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Abstract *Background:* Interest in vegetarian diets is growing in Italy and elsewhere, as government agencies and health/nutrition organizations are emphasizing that regular consumption of plant foods may provide health benefits and help prevent certain diseases.
Methods and results: We conducted a Pubmed search, up to September, 2015, for studies on key nutrients (proteins, vitamin B12, iron, zinc, calcium, vitamin D, and n-3 fatty acids) in vegetarian diets. From 295 eligible publications the following emerged: Vegetarians should be encouraged to supplement their diets with a reliable source of vitamin B12 (vitamin-fortified foods or supplements). Since the plant protein digestibility is lower than that of animal proteins it may be appropriate for vegetarians to consume more proteins than recommended for the general population. Vegetarians should also be encouraged to habitually consume good sources of calcium, iron and zinc – particularly vegetables that are low in oxalate and phytate (e.g. Brassicaceae), nuts and seeds, and calcium-rich mineral water. Calcium, iron, and zinc bioavailability can be improved by soaking, germination, and sour-dough leavening that lower the phytate content of pulses and cereals. Vegetarians can ensure good n-3 fatty acid status by habitually consuming good sources of a-linolenic acid (walnuts, flaxseeds, chia seeds, and their oils) and limiting linoleic acid intake (corn and sunflower oils).
Conclusions: Well-planned vegetarian diets that include a wide variety of plant foods, and a reliable source of vitamin B12, provide adequate nutrient intake. Government agencies and health/nutrition organizations should provide more educational resources to help Italians consume nutritionally adequate vegetarian diets.

In response to increasing interest in eating vegetarian in Italy, in 2012 the Italian Society of Human Nutrition (SINU) set up a working group to assess the peer-reviewed literature on vegetarian diets so as to distil scientifically sound advice for the Italian public on how best to maximize the benefits and minimize the risks associated with the different types of vegetarian diet. The present position

* Corresponding author.
E-mail address: sabina.sieri@istitutotumori.mi.it (S. Sieri).

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paper summarizes the evidence pertaining to the availability of proteins, vitamin B12, iron, zinc, calcium, vitamin D, and n-3 fatty acids, in vegetarian diets and the nutritional status of these factors in vegetarians of all ages and lifestyles. These factors are key for vegetarians since they may not always be present in adequate amounts in some types of vegetarian diet. Based on the evidence, the paper makes recommendations intended for those who wish to follow a vegetarian diet.

Varieties of vegetarian diet

A vegetarian diet excludes consumption of all types of meat (pork, beef, mutton, lamb, poultry, game), meat products (sausages, salami, pâté, etc.), fish (including sushi), and molluscs and crustaceans, etc. Dairy products, eggs, and honey may be included, so that there are two main types of vegetarian diet:

(a) *Lacto-ovo-vegetarianism (LOV)*. This excludes meat but includes dairy products, eggs, and honey, together with a wide variety of plant foods. Subcategories are lacto-vegetarianism (LV) which excludes eggs, and ovo-vegetarianism (OV) which excludes dairy products. And
(b) *Veganism (VEG)*. This excludes meat, dairy products, eggs, and honey, but includes a wide variety of plant foods.

The nutritional profiles of LOV and VEG diets vary widely in relation to the types, quantities, and extent of processing of the plant foods consumed; for LOV, the variation is likely to be greatest, since animal products are also consumed.

However some people adhere to other plant-based diets that limit the foods consumed, and these must be clearly distinguished from LOV and VEG diets. They include:

Raw food diet: consisting exclusively of vegetables, including sprouted cereals and pulses, fresh and dried fruits, and seeds, as well as milk and eggs, all of which are mainly eaten raw.
Fruit diet: consisting exclusively of fresh and dried fruits, seeds, and some vegetables.
Macrobiotic diet: the strictly vegetarian version of this diet consists of cereals, pulses, vegetables, seaweed, and soy products; while dairy products, eggs, and some vegetables are avoided. Fish is consumed by some who adhere to a macrobiotic diet.

The publications reviewed in this paper mainly concern LOV and VEG diets as eaten in western and Asian countries. Consequently the recommendations mainly pertain to these diets, which are generally defined as “vegetarian”.

The nutritional adequacy of raw food, fruit and macrobiotic diets has been assessed by very few studies. What evidence is available on these diets is summarized. The claimed health benefits of these diets are not supported by the available evidence, and in many cases these diets may be nutritionally inadequate.

Methods

PubMed was searched for studies published up to September 2015. We used keywords (words or MeSH terms) within search strings incorporating various terms for vegetarian diet in combination with words relating to age, bioavailability, and nutritional status, in combination with the nutrients of interest (protein, vitamin B12, calcium, iron, zinc, and n-3 fatty acids). We confined ourselves to PubMed as preliminary searches on EMBASE revealed no additional studies. We also searched the reference lists of retrieved studies. We identified 815 publications: 150 on protein, 149 on vitamin B12, 291 on calcium and vitamin D, 59 on iron, 69 on zinc and 92 on n-3.

Review team members screened retrieved titles and abstracts and selected articles that seemed pertinent excluding those not in English or not concerned with humans. The full papers were read independently by two team members to select potentially eligible articles. Review team members then used a checklist (different for each study type: systematic review/meta-analysis, randomized controlled trial, cohort or case–control, or cross-sectional study) to arrive at an assessment of the scientific merit and relevance of each paper value. A total of 295 articles were considered eligible following this assessment.

Protein

Sources and bioavailability

There are concerns that a plant-based diet may not contain protein of adequate quality. Protein quality is determined by digestibility and amino acid content [1]. Purified or concentrated vegetable proteins (e.g. soy protein, gluten) have high digestibility (>95%) – similar to that of animal proteins. For some intact vegetable products, such as whole cereals and pulses, protein digestibility is lower (around 80–90%). Most other vegetable proteins have lower digestibility (50–80%) because of the presence of plant cell walls and anti-nutritional factors. Food processing and heat treatment also influence protein digestibility.

Foods of vegetable origin may contain high levels of antinutritional factors, which may be naturally-occurring (e.g. digestive enzyme inhibitors, tannins, phytate, glucosinolates, isothiocyanates), formed during processing (e.g. D-amino acids, lysinoalanine), or due to genetic modification (e.g. lectins) [2]. Pulses, cereals, potatoes, and tomatoes in particular contain inhibitors of digestive proteolytic enzymes [3]. Soybeans are the most concentrated source of trypsin inhibitors, whereas peas and processed soybean products contain considerably lower levels [2]. Because they are usually proteins, enzyme inhibitors can be inactivated by heat treatment, including extrusion [2], or removed by other processing procedures [3]. Tannins (water-soluble polyphenols) present, for example, in some peas and beans, can complex with proteins reducing digestibility [2]. Phytate, as acid in seeds, grains and nuts, or salts in other plant tissues, can reduce carboxypeptidase and aminopeptidase activity by chelating cofactors, or by interacting with the enzyme or its substrate [2]. Germination of seeds and grains produces enzymes that reduce polyphenol and phytate levels in the sprouts to thereby improve protein digestibility. Fermentation can also render the proteins of pulses and cereals more digestible [4–6].

Nutritional status of vegetarians at different ages

Consistent data indicate that the protein needs of vegetarians are easily met when the diet includes a variety of plant foods, and calorie intake is adequate [4–6]. A 2003 meta-analysis of nitrogen balance studies found that protein requirements (mg N/kg/day) in healthy adults were not influenced by the source (animal, vegetable, mixed) provided that vegetarians consumed either soy protein or a variety of other vegetable proteins [7]. However, while soy protein can meet protein needs as efficiently as animal protein, proteins from other plant sources (mainly pulses and cereals) are less well digested. Furthermore, when lysine tends to be the limiting essential amino acid – as in diets based mainly on cereals (especially wheat) – small quantities of other vegetable proteins, such as those from pulses or oily seeds, are required to obtain sufficient lysine and other essential amino acids.

Pregnancy and breastfeeding

Inadequate maternal protein intake during pregnancy reduces infant birthweight [8]. The few studies that investigated birthweight in infants born of vegetarian women [9–11] indicate that average birthweights of infants born to mothers on VEG or LOV diets do not differ significantly from the average of infants born to omnivorous (OMN) mothers [10,11]. By contrast, the birthweight of infants born to mothers on a macrobiotic diet was significantly lower than expected, and was attributed to lower maternal weight gain during gestation [10]. The milk of vegetarian mothers is nutritionally adequate, and infants breastfed by well-nourished vegetarian women grow normally [12,13]. However milk from women on a macrobiotic diet has a significantly lower protein content than milk from OMN [14].

Although infants of vegetarian mothers grow normally during the first six months [15,16], their growth rate is at the lower end of normal – interpreted as due to a propensity of vegetarian mothers to breastfeed for longer [17,18].

Studies on infants fed soy-isolate milk formula, irrespective of whether methionine supplemented, indicate no significant differences in growth compared to infants fed conventional cow milk formula [19]; furthermore, blood markers of protein metabolism are similar [19,20]. In a 2001 study [21] no differences were found in average height or weight between young adults fed soy-based formula and those fed cow milk for several months during childhood.

Preschool children (6 months to 3 years)

From the limited data available, it would seem that children who follow a LOV diet have similar growth to OMN children [12]. The growth of non-macrobiotic VEG preschool children is also in the normal range [16,17,22], although they seem to have an initially smaller stature and tend to be leaner than OMN children [16,17]. By contrast, preschool children on a macrobiotic diet were reported to have significantly lower growth than those on other vegetarian diets [23,24].

Children (4–10 years)

LOV children have similar growth to OMN children [25–27]. Non-macrobiotic VEG children tend to grow at standard rates [25,28], while macrobiotic children grow more slowly [27]. The average protein intake of vegetarian children meets recommendations [22,29–31], although they consume less protein than OMN children [18,22,29,31].

One study found that serum albumin levels were above the normal range in both vegetarian and OMN children [22]. Since plant proteins are less digestible and contain fewer essential amino acids than animal proteins, it may be advisable for VEG children to consume more protein. Messina and Mangels [32] suggested that protein intake should be increased by 30–35% in VEG children under 2 years, and by 20–30% in 2–6-year-olds [32].

Adolescents (11–18 years)

The available studies indicate that the growth of LOV children and adolescents is comparable to that of their OMN peers [8,25,33,34]. However adolescents on a macrobiotic diet have lower growth than reference [25,30,34–36]. As regards protein intake, this was lower in VEG [37] and LOV [33,38] than OMN in some studies, while in others protein intake was adequate [8,30,34,39].

Like younger VEG children, VEG adolescents may require more protein than their LOV or OMN counterparts because of the lower digestibility and poorer amino acid composition of plant proteins. Thus, Messina and Mangels [32] suggested that active VEG teenagers should obtain 7–10% of their calories from protein, and sedentary teenagers should obtain 10–13% of calories from protein.

Adults

Several studies have examined the adequacy of protein intake by adult vegetarians [40–49]. Protein intake in VEG and LOV adults is generally lower than in OMN, but meets requirements. Serum albumin was normal in one study on groups of vegetarians, indicating normal protein nutritional status [41]. Kniskern and Johnston [45] examined food intake over 4 consecutive days in a convenience sample of young adult vegetarian women, finding that animal protein accounted for only 21% of dietary protein, which is below the dietary reference intake (DRI) of animal protein (45–50% of total) considered adequate. The authors suggested that protein DRI for such women should be increased from 0.8 to 1.0 g/kg bodyweight/day to account for the reduced bioavailability of plant proteins.

Elderly

Few studies on the nutritional status of vegetarian elderly are available. Protein intake was lower in vegetarian than

OMN women [50,51], but higher than recommended. In vegetarian men, protein intake was lower than in OMN men, although sufficient to meet requirements [50]. Two studies [52,53] that compared protein intake in elderly Chinese vegetarian and OMN females found that energy from protein was lower in vegetarians and did not always meet the DRI; however, serum markers of protein nutritional status do not seem to differ between vegetarian and OMN elderly [50,52,54].

Recommendations

Since the digestibility and essential amino acid content of plant proteins is lower than that of animal proteins, it may be appropriate for vegetarians to consume more protein than recommended for the general population. This increase can be easily achieved, even in the elderly, pregnant/breast-feeding women, and children, by consumption of a wide variety of plant foods.

Vitamin B12

Sources and bioavailability

Vitamin B12 is reliably present in foods of animal origin but only in small amounts. Some algae contain vitamin B12, however, bioavailability varies with algal species and can be very low [55]. Furthermore some algae contain considerable quantities of inactive vitamin B12 analogues, that can interfere with the absorption of active forms of B12 [55]. Until foods like tempeh are consistently shown to improve vitamin B12 status, they should not be relied upon as a source of vitamin B12.

Vitamin B12 requires intrinsic factor for absorption. Under physiological conditions intrinsic factor-dependent absorption is saturated with 1.5–2.5 μg of the vitamin per meal. Beyond this amount, the bioavailability of B12 decreases markedly.

Unlike the food-bound form, which must be released from its binding proteins, crystalline forms of vitamin B12 from supplements and fortified foods are in the free form, and can combine directly with haptocorrin for protection and subsequently with intrinsic factor for absorption [56]. Vitamin B12 in supplements is usually highly effective in correcting vitamin B12 deficiency [57–59].

The bioavailability of vitamin B12 in a LOV diet depends on the quantities and types of animal foods (dairy products, eggs) consumed, as well as on the consumption of fortified foods (e.g. breakfast cereals) and supplements. For VEG the only reliable sources of vitamin B12 are fortified foods and supplements.

Nutritional status of vegetarians at different ages

Vitamin B12 deficiency develops slowly, as the liver stores sufficient quantities to last several years. If storage is limited or requirements are high (e.g. in infants breastfed by VEG mothers not taking supplements), clinical symptoms may develop earlier. Folate intake is high in vegetarians, so the typical haematological alterations of vitamin B12 deficiency may not appear; however high folate cannot prevent the deleterious effects of B12 deficiency on the nervous system. Since plasma B12 includes variable amounts of the metabolically inactive form complexed with circulating haptocorrin [60], B12 status is optimally assessed in vegetarians using the markers homocysteine, holotranscobalamin II and methylmalonic acid [61]. Increased methylmalonic acid levels may be present in persons with serum vitamin B12 in the commonly accepted normal range (>156 pmol/L) but not exceeding 360 pmol/L (488 pg/mL) [62], so a reference limit of 360 pmol/L for serum vitamin B12 has been proposed [63] and should be adopted if holotranscobalamin II levels are not available.

Pregnancy and breastfeeding

One study found that vitamin B12 levels in a sample of pregnant LOV women were significantly lower than those of OMN controls: high plasma homocysteine plus low serum vitamin B12 was present in 25% of the LOV women in at least one trimester [64].

Preschool children (6 months to 3 years)

In a review of about a hundred case reports of B12-deficient children from various countries it was found that two thirds were born to vegetarian mothers, and a quarter were born to mothers with pernicious anaemia [65]. Vitamin B12 status seems to have been evaluated in only two cohorts of macrobiotic children. In a Dutch cohort, macrobiotic children had significantly lower "true" cobalamin levels than controls [23,66]. In a Norwegian cohort 85.4% had high serum levels (>0.43 mmol/L) of methylmalonic acid [67].

Children and adolescents (4–18 years)

All available studies indicate low B12 status in macrobiotic persons of this age group [68–70]. By contrast, most available studies on non-macrobiotic vegetarians (LOV + VEG, LOV) indicate that B12 (and when evaluated, homocysteine) levels are within normal range [30,31,71–73]. A small study on 6 LOV Asians who had migrated to Auckland found that half had asymptomatic B12 deficiency [74].

Adults and elderly

Numerous studies on vitamin B12 status in adult vegetarians have been conducted worldwide; many included elderly people, thus results of studies which included both adults and elderly are presented together.

A number of studies on vegetarians (LOV, LV, LOV + VEG) found that mean B12 plasma levels were in the normal range or did not differ from those of OMN [62,75–77].

Twenty-three studies specifically on LOV found compromised vitamin B12 status – as low serum B12 [43,52,78–94], high serum methylmalonic acid [62,77,80,82–84], high homocysteine [43,78,80,82–84,86–89,91,94], or low holotranscobalamin II [80,82–84]. One study [95] reported normal homocysteine levels in vegetarians, which were however higher than in OMN. Another study [76] found that serum B12 levels in vegetarians were not significantly lower than those in OMN. Finally, a study that examined serum B12, methylmalonic acid, homocysteine and holotranscobalamin II found that LOV had lower B12 status than OMN, but differences were not significant in the LOV subgroup taking B12 supplements [83].

Sixteen studies on VEG found compromised B12 status as low serum B12 [77,78,81,83,85,88,91,96–100], high serum methylmalonic acid [62,77,80,82–84,99], high homocysteine [76,77,80,82–84,88,91,100] and low holo-transcobalamin II [80,82–84,99]. Two of these studies included VEG on vitamin B12 supplements [78,83]. Another study that included VEG supplement users found that mean serum B12 and methylmalonic acid levels did not differ between VEG and OMN, nevertheless 10 of the 25 recruited VEG had vitamin B12 deficit as indicated by macrocytosis, circulating vitamin B12 concentrations $<$ 150 pmol/L, or serum methylmalonic acid $>$ 376 nmol/L [101]. In a prospective study on 20 adult OMN followed for 5 years while on a VEG diet, B12 levels were reduced only in those who did not take supplements [102].

The only available study on macrobiotic adults (who occasionally consumed animal products) reported that 51% had low serum B12, and 30% had high urinary methylmalonic acid [69].

Two studies evaluated B12 in VEG who mainly [103] or entirely [104] ate uncooked food. High urinary methylmalonic acid ($\geq$4.0 μg/mg creatinine) was present in 47% [103] and serum low B12 ($<$200 pmol/L) was present in 57% [104]. A study on raw foodists found increased homocysteine levels due to B12 deficiency in all participants (mixed, LOV and VEG), but LOV and VEG had lower serum B12 and higher total plasma homocysteine than mixed raw foodists [105].

A meta-analysis of 17 studies that compared homocysteine and B12 levels in vegetarians (3230 LOV/LV/VEG) with those in OMN [106] found that VEG had the highest mean homocysteine values, and lowest mean B12 levels, while levels in LOV were intermediate between those of VEG and OMN. In only two of these studies were mean plasma levels of homocysteine and B12 similar to those in OMN [73,101].

Recommendations

The vitamin B12 status of vegetarians should be monitored regularly. All vegetarians should be encouraged to include a reliable source of vitamin B12 in their diet (vitamin-fortified foods or supplement). Persons taking B12 tablets should be encouraged to chew them slowly or allow them to dissolve under the tongue to optimise absorption. For children, droplet formulations are suitable. In view of data [107,108] indicating that B12 absorption is often less than 50% [60], the European Food Safety Authority recommends that vitamin B12 absorption should be assumed to be 40% [109] when formulating recommended daily intakes, which should thus be 4 μg/day or greater. We therefore propose that, for preserving normal B12 levels in vegetarians, intake should adhere to the recommendations in Table 1. If B12 deficiency is discovered, supplementation with crystalline cobalamin should begin immediately at doses above 4 μg/day.

Calcium

Sources and bioavailability

Several plant foods, particularly leafy vegetables pulses, and nuts, contain good quantities of calcium, however the bioavailability of this mineral is inversely proportional to the amounts of oxalate and phytate in the diet [110,111] which are abundant in spinach, Swiss chard, and beet leaves. Dietary fibre seems not to impair calcium absorption, since in one study more calcium was absorbed from kale than cow milk [112].

Regardless of solubility, the calcium from calcium salts used to fortify foods is absorbed with similar efficiency to the calcium in cow milk [113] except that the absorption from calcium citrate malate is slightly higher [111]. The tricalcium phosphate used to fortify soy milk is absorbed with only about 75% of the efficiency of cow milk calcium [114]. The calcium from the calcium chloride and calcium sulphate used to produce tofu has similar bioavailability to the calcium from milk [115]. The bioavailability of calcium from mineral water is similar to or better than that from milk [116]. Calcium absorption from water is improved when water is consumed with food [117].

Because sodium and calcium share proximal renal tubule transport systems, high sodium intake promotes calcium excretion [111].

Nutritional status of vegetarians at different ages

Calcium status has been assessed in vegetarians by various methods: dietary calcium intake, serum calcium, ionized serum calcium, bone mineral density (BMD), and bone mineral content (BMC). In physiological conditions,

Table 1 Recommended dietary supplement values for preserving normal B12 levels in persons becoming vegetarians.

Age	LARN[a] (PRI)[c] (μg/day)	EFSA[b] (AI)[d] (μg/day)	Daily multi-dose	Daily single-dose (μg/day)
6–12 months	0.7	1.5	1 μg × 2	5
1–3 years	0.9	1.5	1 μg × 2	5
4–6 years	1.1	1.5	2 μg × 2	25
7–10 years	1.6	2.5	2 μg × 2	25
11–14 years	2.2	3.5	2 μg × 3	50
15–64 years	2.4	4.0	2 μg × 3	50
65+ years	2.4	4.0	2 μg × 3	50
Pregnancy	2.6	4.5	2 μg × 3	50
Breastfeeding	2.8	5.0	2 μg × 3	50

[a] LARN is an Italian acronym meaning Reference Levels of Nutrient and Energy Intake for the Italian Population.
[b] European Food Safety Authority.
[c] Population reference intake.
[d] Adequate intake.

serum calcium is maintained within narrow limits (2.25–2.60 mmol/L total serum calcium or 1.1–1.4 mmol/L ionized form) irrespective of calcium intake, with mobilization from bone if necessary. BMD and BMC are sensitive to changes in calcium intake over the long-term (>1 year) [118] and are not now used to assess calcium status.

Pregnancy and breastfeeding

A study [119,120] on breastfeeding women found that calcium intake was lower and 1,25-dihydroxy vitamin D blood levels significantly higher in macrobiotic women than OMN controls, while blood parathyroid hormone levels were similar. The higher 1,25-dihydroxy vitamin D levels suggest a hormonal response, in macrobiotic women, to low dietary calcium and lactation, that may increase the efficiency of calcium absorption [119,120].

Preschool children (6 months to 3 years)

Only one study on this age group seems to be available: it followed a cohort of macrobiotic children from birth [121,122]. At 10–20 months calcium intake and vitamin D in blood were significantly lower in the macrobiotic infants than OMN controls. At the same time (examination in August–November) subclinical or clinical rickets was present in 17% and 28%, respectively, of macrobiotic infants compared to 0% in controls. At follow-up of a subsample of 25 macrobiotic infants in March–April, physical symptoms of rickets were present in 55% of macrobiotic infants [121,122].

Children and adolescents (4–18 years)

Of several studies [22,29–31,123,124] on non-macrobiotic vegetarians, only one, on Chinese vegetarian children [30], found that calcium intake and BMD were similar to those in OMN children. The other studies found that vegetarian children had lower calcium intake than OMN [22,31]. In a large cohort of macrobiotic adolescents evaluated at various times from 1985 [125], calcium intake and BMC/BMD, but not 1,25-dihdroxyvitamin D, were significantly lower than in OMN controls [68,125]. The lower BMC and BMD were unrelated to calcium intake [125]. In a later examination of the same cohort, most of whom had switched to a vegetarian or even OMN diet, low BMD and BMC were associated with B12 deficiency (low serum vitamin B12 or high methylmalonic acid) [68].

Adults

Numerous studies on calcium have been conducted on adult vegetarians worldwide. Most [22,47,126–133] found that calcium intake in vegetarians (LOV, LV, LOV + VEG) did not differ from that in OMN. However in two studies [134,135], calcium intake was higher in vegetarians, and in another [136] calcium intake was lower, but did not correlate with BMD. No significant difference in risk of fracture between vegetarians and OMN was reported after 5.2 years of follow up in one study [127]. Other studies have reported no difference in BMD between vegetarians and OMN [89,130,132,133]. However, a study on Taiwanese vegetarian women found that long-term VEG were at increased risk of lumbar spine fracture and femoral neck osteopenia compared to other long-term vegetarians. These differences were attributed to lower protein intake in VEG; calcium intake did not differ [136].

A prospective year-long study on pre-menopausal women found that vegetarian women tended to have lower (but stable) BMD than non-vegetarians over the year [137,138]; furthermore BMD at recruitment correlated significantly with vitamin B12 intake [137,138]. A study on 122 Germans (35 OMN, 23 VEG and 54 LV/LOV) and 73 Indian immigrants to Oman (54 OMN, 19 LV/LOV) [84] found increased bone turnover (as measured by alkaline phosphatase, osteocalcin, pro-collagen type I N-terminal peptide and C-terminal telopeptides of collagen I) in vegetarians (LOV + VEG). Multiple regression analysis showed a significant association between increased bone turnover and vitamin B12 status that was independent of vitamin D status [84]. Finally, in a study on Indian and Iranian post-menopausal women, a pure vegetarian diet was a risk factor for osteoporosis among Indian women only, but this was not significant after adjustment for weight and height [139]. From the studies reviewed above we conclude that in adult vegetarians, at-risk bone status correlates with long duration vegetarianism, low protein intake [136], and low vitamin B12 status [84,89,138].

All studies [126–129,136,140–145] found lower calcium intake in VEG than controls. A study that compared meat eaters, fish eaters, vegetarians and VEG found a higher fracture rate in VEG apparently related to markedly lower mean calcium intake [127]. A study on VEG Buddhist nuns found lower calcium intake, but no differences in BMD, fracture incidence, or frequency of osteoporosis compared to non-VEG [140,141]. Another study [130] found no difference in BMD (measured in lumbar spine and femoral neck) between VEG, LOV and OMN.

A study that compared 17 macrobiotic adults with VEG and LOV, found significantly lower calcium intake in the macrobiotic women than the other vegetarian groups [47]. A study on 18 raw foodists in comparison with those eating typical American diets [146] found that the raw foodists had significantly lower BMC and BMD than controls, with no differences in blood markers of bone turnover (C-telopeptide of type I collagen and bone-specific alkaline phosphatase).

Elderly

Elderly persons were included with adults in most of the studies reported above. We identified 2 studies conducted specifically on elderly women [53,147]. The first [53] on elderly Chinese female VEG, LV and OMN found that among the women vegetarian for over 30 years (36 VEG; 40 LV) mean calcium intake was significantly lower than in OMN, and was also significantly lower in VEG than LV. BMD at the femoral neck, but not at the spine, was lower in vegetarians than OMN. The second [147] was a prospective study on elderly white women (49 LOV, 140 OMN). The rate of loss of bone density over the five-year period, at each measurement site, was independent of calcium intake and was similar in both groups.

Intervention studies

Changes in nutritional status were evaluated during intervention studies with plant-based diets in healthy persons (Complete Health Improvement Project) [148] or low-fat VEG diets (about 10% of total energy) in diabetic [149] and in prostate cancer patients [150]. During the intervention period, reduced calcium and vitamin D intake [148] and lower vitamin D blood levels were observed [148]. A short-term study evaluated calcium balance in women who received a VEG diet during the first 10 days, and a LV diet during the following 10 days: calcium balance remained positive regardless of intake. This finding indicates that the lower calcium intake of the VEG diet was compensated for by reduced calcium excretion in faeces. The two diets were not associated with differences in calcium balance, apparent absorption, or bone calcium resorption (assessed by a urine marker) [151].

Recommendations

Vegetarians should be urged to make sure they adopt a diet that ensures their calcium intake is in line with Italian recommendations [60]. VEG especially should be urged to regularly consume foods that are good sources of calcium (vegetables low in oxalate and phytate, soy products, calcium-rich mineral water, and various nuts and seeds).

Iron

Sources and bioavailability

The bioavailability of iron in LOV, VEG and also OMN diets varies markedly. The main source of dietary iron in Italian OMN is cereals and cereal products (31.3%), followed by meat and meat products (16.9%), fresh and processed vegetables (13.5%), fruit (7.3%), pulses (3.2%), and potatoes and other tubers (3%) [152]. Thus Italian OMN obtain close to 60% of their iron from plant sources.

The typical Italian LOV and VEG diet may contain as much or more iron than an OMN diet, however iron bioavailability is lower [153,154] with only 5–12% absorbed, compared to 14–18% from OMN diets [155]. Non-haem iron provides 100% the iron of VEG and LOV diets, but only 85–90% of iron in OMN diets [155]. Much of the iron in soybeans is bound to ferritin and 22–34% of this is absorbed – a bioavailability comparable to that of haem iron (15–35%) [156–159].

Ascorbic acid, which chelates and reduces Fe^{3+}, is the most important facilitator of non-haem iron absorption. Thus the bioavailability of iron in a vegetarian diet can be enhanced by consuming ascorbic acid (citrus fruits, strawberries, kiwi, etc.) during a meal containing iron [160]. Other organic acids in fruits and vegetables (citric, malic, lactic and tartaric acids), as well as carotenes and retinol, also enhance non-haem iron absorption [161–163].

Soaking pulses and cereal grains activates endogenous phytases that reduce the number of phosphates bound to inositol hexaphosphate (phytate) progressively weakening its ability to sequester iron. Use of the sour-dough method to leaven dough also activates phytases in the flour, again reducing the ability of phytate to sequester iron.

Limited data indicate that the absorption of non-haem iron can increase over the long term in response low iron bioavailability [160] which might explain why the prevalence of iron deficiency is similar in LOV, VEG and OMN [153].

Nutritional status of vegetarians at different ages

The main tests on plasma or serum used to investigate iron nutritional status [60] are haemoglobin (to detect anaemia), transferrin saturation (measure of circulating iron), soluble transferrin receptor (more stable marker of iron levels in inflammation) and ferritin (indicator of iron storage). Since ferritin is also an inflammation marker, reactive protein C should also be determined.

Breastfeeding women and preschool children (6 months to 3 years)

The milk of LOV and VEG women is similar in composition to milk from non-vegetarian women [12] and is not deficient in minerals or vitamins when the maternal LOV/VEG diet is well-balanced [164]. When the children of vegetarian mothers are weaned their iron status should be monitored, and iron-rich foods should be eaten together with food containing ascorbic acid or other fruit acids so as to improve iron absorption [164].

The incidence of iron deficiency anaemia during weaning is not higher in LOV/VEG children than OMN children, and serum ferritin levels (and growth) are usually within normal ranges in LOV/VEG children [158].

Children (4–10 years)

LOV and VEG children have lower iron intakes than OMN children but their serum iron levels are within the normal range [72] and do not differ significantly from those of OMN children [161]. Pre-school and school-age VEG have adequate iron intake and anaemia has not been documented [17,165]. However, the Institute of Medicine [166], suggests that LOV/VEG children should consume 1.8 times more iron than OMN children, to ensure their nutritional needs are met. Macrobiotic children also often have low iron status [161].

Adolescents (11–18 years)

The development of LOV and VEG teenagers is similar to that of non-vegetarian teenagers [12]. Slovak LOV and LV children aged 11–14 years had lower serum iron and haemoglobin than OMN but levels were within the normal range [167]. However to meet iron needs in this period of rapid growth, LOV/VEG teenagers should consider iron supplementation [168]. In a Swedish study [123] the iron intake of adolescent (16–20 years) VEG (at least 6 months) of both sexes was compared with that of OMN. Iron intake in VEG and OMN males was similar. VEG females consumed more iron than OMN females and the population reference intake (PRI); in all cases iron intake was within the recommended range. However serum iron markers were lower than normal in VEG and OMN females but normal in VEG and OMN males, indicating that menstrual blood loss was responsible for the lower iron levels and that diet had no influence.

Adults
Even after many years on a LOV or VEG diet, serum iron levels in adults do not usually differ significantly from those in OMN [161]. Mean iron intake in LOV/VEG men can in fact be higher than in OMN men, and also higher than the PRI [169]. Nevertheless serum ferritin and haemoglobin are significantly lower in LOV and VEG males than OMN controls [101,134,135,170]. LOV/VEG women also have a similar iron intake to OMN controls [171] and after many years on a vegetarian diet their iron status is adequate [134,171,172]. Nevertheless, the risk of iron anaemia is reported to be about 40% in pre-menopausal women after one year on a VEG diet [100,101]. Haddad et al. [101] found that pre-menopausal VEG and OMN women had similar risks of developing iron anaemia. Studies on young females [170,173] also show that iron deficiency anaemia is present at similar levels in LOV and VEG (at least two years) and OMN. Thus menstrual iron loss rather than diet appears as the main cause of iron deficiency anaemia. In postmenopausal women, high blood ferritin has been found to be a risk factor for cardiovascular diseases [174], so LOV and VEG diets may be protective against these conditions.

Nevertheless iron and vitamin B12 status can both be compromised in adult LOV, LV, and occasional meat eaters; in such cases macrocytosis due to B12 deficiency can be masked by low iron status [77].

Elderly
A study that investigated the adequacy of LOV and VEG diets in elderly persons [134] found that mean daily mineral intake, iron included, and iron serum markers were within normal ranges [134] and did not differ significantly from OMN controls. In older men (59–78 years) undergoing 12 weeks of resistance training designed to maintain muscle mass, serum iron remained within normal limits throughout the training period, irrespective of whether they ate a beef-containing or vegetarian diet [175]. These findings suggest that a vegetarian diet is suitable for elderly persons [134,175].

Recommendations

Vegetarians should be advised increase iron intake above the PRI suggested for OMN, by eating a variety of iron-rich plant foods. Iron bioavailability can be increased by:

1. Eating ascorbic acid-rich foods together with iron-rich foods.
2. Using food preparation methods such as grinding, soaking and germination, and using the sour-dough method to leaven bread (or buy sour-dough bread). These processes lower the phytic acid content of cereals and legumes and thus reduce iron sequestration.
3. Using iron-fortified foods (e.g. breakfast cereals).

Iron supplementation is only recommended if iron status has been shown to be low by appropriate blood tests.

Zinc

Sources and bioavailability

According to the US Department of Agriculture (reported in Hunt [176]) over half the zinc in OMN diets (56%) comes from animal origin foods. Similarly, a 2013 Italian food survey [152] reported that 54.9% of the dietary zinc of Italians comes from animal products (24.8% meat and meat products, 21% milk and milk products, 6.9% fish, seafood and their products, 2.2% eggs), and 40.7% from plant foods (21.5% cereals and cereal products, 9.8% vegetables, 5.5% potatoes and other tubers, 2.8% fruits, 1.1% pulses), with sweet products, water and non-alcoholic beverages providing minimal amounts.

Good zinc sources for VEG and LOV are whole grains, cereals, pulses, nuts and seeds [177]. However, these foods are also rich in phytate which is a strong zinc chelating agent that severely limits intestinal absorption. Oxalate and some dietary fibres also decrease zinc absorption [178,179].

Zinc absorption from VEG/LOV diets is 15–26%, while that from typical OMN diets is 33–35% [178,180]. The consumption of small quantities of animal proteins considerably enhances zinc absorption [181], perhaps due to the release of amino acids during digestion which keep zinc in solution (prevent its chelation) [179]. Sulphur amino acids, cysteine-containing peptides, hydroxy acids (present in fruits) and other organic acids present in fermented food may all increase zinc absorption [181,182]. As with iron, procedures that activate the endogenous phytases present in cereals and pulses, like milling, sprouting, soaking, and sour-dough leavening, increase the bioavailability of zinc [153,183].

Nutritional status of vegetarians at different ages

Because of zinc's protein biochemical roles, various signs of zinc deficiency may manifest that also depend on the severity of the deficiency; for the same reason it is difficult to identify reliable biomarkers of zinc status [184,185]. Markers considered useful for assessing zinc nutritional status are plasma levels [186], serum levels [187] and urinary excretion [186].

Breastfeeding women and preschool children (6 months to 3 years)
If breast-feeding LOV/VEG mothers have adequate zinc intake, the zinc nutritional status of their infants does not differ from that of breast-fed infants of OMN mothers [164]. When breast-feeding is not possible or insufficient [188], adequate zinc intake for LOV infants can be provided by modified cow milk formula, and soy or rice preparations [20,189]. Pre-term birth, low birthweight, and certain

diseases may indicate need for infant iron and zinc supplementation [190]. LOV and OMN women had similar zinc intake during pregnancy [191] although intake was below the PRI. Plasma zinc levels were lower in these women than in non-pregnant women, suggesting that zinc nutritional status is influenced more by pregnancy than by LOV/OMN diet [191]. Nevertheless those on a VEG diet have lower zinc intake [192] and lower zinc plasma levels [101] than those on a LOV diet.

Children (4–10 years)
The zinc intake of pre-school LOV [31,178] or VEG [193] children is similar to that of age-matched OMN. Nevertheless low zinc serum levels have been found in children on low meat/high calcium diets, who also show deficient growth and loss of taste [194,195].

Adolescents (11–18 years)
Teenagers have high zinc requirements, and those on LOV and VEG diets may have inadequate zinc status [196,197]. Thus, Canadian adolescent girls were found to have a mean zinc intake of 7 mg/day – lower than the PRI of 9 mg/day [166]. Serious zinc deficiency in children and teenagers can interfere with bone growth, and sexual and behavioural development [198].

Adults
Mean daily zinc intakes of a population of Canadian 7th Day Adventists on a LOV diet [171] were similar to those of OMN controls and higher than the PRI (9 mg/day); mean zinc serum was within the normal range. In Flemish adults of both sexes on LOV diet for at least a year, mean daily zinc intake was higher than in OMN controls [134]. These findings suggest that people on a long-term LOV or VEG diet have adequate zinc nutritional status and that they adapt to low zinc bioavailability better over the long term than the short term [178]. The adaptation may occur by increasing absorption [178].

The zinc intake of middle-aged Japanese men on LOV or semi-LOV diets was lower than that advised by the Japanese National Health and Nutrition Survey although within the Japanese PRI range [135]. Brazilian (Sao Paolo) men and women who had been vegetarians for at least 5 years had low zinc levels in erythrocytes [199]. In a small group of Swedish men and women who changed from an OMN to an LV diet and pursued it for 12 months, zinc intake did not change but plasma levels had lowered at 3 months, although they remained in the normal range [200]. No further zinc plasma decrease occurred in the following 6–12 months, and excretion, in urine and faeces decreased [200].

Elderly
A LOV diet was compared with an OMN diet in institutionalized elderly persons [50]. Mean daily zinc intake was similar and within the normal range in both groups. However serum zinc was lower than reference in both groups, suggesting that the PRI for zinc in elderly people might be set too low. Since elderly LOV and OMN have similar nutritional status for zinc and similar health, it can be concluded that a balanced LOV diet is suitable for the elderly [12].

Recommendations

Vegetarians should be encouraged to consume more dietary zinc than the PRI suggested for OMN, especially when the dietary phytate:zinc ratio is high.

Zinc absorption can be improved by adopting food preparation methods (soaking, germination fermentation, sour-dough leavening of bread) that reduce phytate levels in zinc rich foods.

Zinc-fortified foods (e.g. breakfast cereals) can also be used.

Zinc-rich foods should be eaten together with foods that contain organic acids such as fruit, and vegetables of Brassicaceae family.

N-3 fatty acids

Sources and bioavailability

The only n-3 fatty acid present in useful amounts in plant foods is α-linolenic acid (ALA, 18:3 n-3). Its main sources are flaxseeds, hemp seeds, chia seeds, walnuts and their oils, and some seaweeds [201]. For eicosapentaenoic acid (EPA, 20:5 n-3) and docosahexaenoic acid (DHA, 22:6 n-3), vegetable sources are extremely limited, the main one being certain seaweeds [201–203].

ALA is an essential fatty acid, while EPA and DHA can be synthesized from ALA. However ALA elongation to EPA and DHA is limited, and influenced by diet: high dietary linoleic acid [204]; inadequate intakes of energy, protein, pyridoxine, biotin, calcium, copper, magnesium, and zinc [205,206]; and excessive intakes of trans fatty acids [201] and alcohol, can all impair EPA and DHA synthesis [207].

Nutritional status of vegetarians at different ages

Pregnancy and breastfeeding
Infants born to vegetarian mothers had low DHA in plasma and umbilical artery phospholipids, but birthweight and head circumference were normal [208]. Breast milk from vegetarian mothers was reported as higher in ALA but lower in DHA than milk from OMN mothers [209]. Vegetarian mothers had lower dietary intakes of EPA, docosapentaenoic acid (DPA, 22:5 n-3), and DHA, higher dietary n-6:n-3 ratio, and higher erythrocyte DPA than OMN mothers [210].

Children (4–10 years)
A study on 20 children reared on a VEG diet found that the dietary n-6:n-3 ratio was very high at 44:1, and that ALA provided 0.2% of the total energy intake [211].

Adolescents (11–18 years)

In a study that compared plasma fatty acid profile in vegetarian (VEG, LOV, and pescovegetarian) and OMN children, all vegetarians had higher ALA than OMN children. VEG had highest ALA levels and highest n-6:n-3 ratio, but lowest EPA, DHA and n-3. Pescovegetarians had highest EPA and DHA and lowest n-6:n-3 ratio [212].

Adults and elderly

Numerous studies on the n-3 fatty acid status of adult vegetarians are available. Findings of studies that did not distinguish VEG from LOV [208,213–227] and studies that did distinguish VEG from LOV [228–233] are reported.

Findings on ALA intake and blood levels are contrasting: some studies [213,219,224,229,230,232,233] found higher levels in vegetarians than OMN; others [215,217,221,222,231] found lower levels; others again found no difference [208,225].

In all studies [208,213,215,217,219,221,222,225,229–233] except one [224], EPA and DHA intake and status were lower in vegetarians. DPA intake was also lower in vegetarians [229,231], while findings on DPA status varied: lower in vegetarians [218,221,230,232], higher in vegetarians [217,229,233], no difference [225].

Vegetarians had lower n-3 intake than OMN who ate a lot of meat, but higher n-3 intake than OMN who ate a moderate amount of meat [231]; total n-3 blood levels were always lower in vegetarians than OMN [217,218,221,222,225,229,230]. Long chain n-3 intake [231] and status [229] were lower in vegetarians than OMN. The n-6:n-3 ratio of ingested food was higher in vegetarians in two studies [229,231] but lower in another [213]. The n-6:n-3 ratio in blood was always higher in vegetarians [215,217,218,222,229,230].

In one study dietary intake and status of EPA, DHA, DPA, total n-3, long-chain n-3, and n-6:n-3 ratio were all lower in vegetarians than OMN who usually eat fish, but higher than in OMN who do not eat fish [233].

Results on ALA intake and status in VEG are mixed. Some studies reported higher levels in VEG than other dietary groups [229,230,233–235]; others [231,233] reported lower levels; and others again reported no differences [33,229,232,234].

Most studies found higher EPA, DHA, and DPA intake and status in VEG than other dietary groups [229–234]. However, one study [235] found higher EPA and DPA, but lower DHA in VEG, than OMN.

Most studies reported lower total n-3 and long chain n-3 intake and status in VEG than other dietary groups [230,232,233]. However one study [229] reported higher total n-3 intake in VEG and another [233] reported that VEG women had higher total n-3 plasma levels. VEG had also a higher n-6:n-3 ratio in blood [229,230].

Recommendations

Vegetarians can improve their n-3 nutritional status by regularly consuming good sources of ALA (e.g. walnuts, flaxseeds, chia seeds and their oils) and limiting intake of sources of linoleic acid (e.g. corn and sunflower oils). To enhance the conversion of ALA to EPA and DHA, vegetarians should be advised to ensure their diet contains sufficient proteins, pyridoxine, biotin, calcium, copper, magnesium, and zinc (i.e. to eat a varied diet). They should also be advised to reduce intake of n-6 fatty acids and trans fatty acids, by limiting consumption of processed and deep-fried foods, and alcohol.

Pregnant and breastfeeding women and children < 2 years, with increased requirement for long chain n-3 fatty acids, and those who convert ALA poorly to long chain n-3 (the elderly, people with diabetes or other chronic diseases) should be advised to consume an algae-based supplement of known nutrient content.

Table 2 summarizes dietary recommendations for each of the nutrients considered.

Athletes

The available evidence indicates that a vegetarian diet has neither a beneficial nor a detrimental effect on physical fitness [196], aerobic endurance during running [236,237], lung function, aerobic and anaerobic performance, arm and leg circumferences, hand grip, back strength, and haemoglobin and total serum protein [238]. Varied and well-planned vegetarian diets are compatible with successful athletic performance [196].

However, no long-term studies have assessed the protein intake of vegetarian and OMN athletes in relation to performance. One review [239] concluded (not based on the findings of specific studies) that the protein intake of a LOV diet was adequate for athletes, but that a VEG diet could contain insufficient energy and protein for an athlete with high energy expenditure. Other position papers and reviews [240–242] made recommendations for vegetarian athletes based on the protein requirements of OMN athletes corrected for the reduced digestibility of plant proteins. Thus, the daily protein requirement for athletes who

Table 2 Recommendations for those who wish to follow a vegetarian diet.

- Since the digestibility of plant proteins is lower than that of animal proteins, it may be appropriate for vegetarians to consume more proteins than recommended for the general population
- Vegetarians should be encouraged to supplement their diets with a reliable source of vitamin B12 (vitamin-fortified foods or supplements)
- Vegetarians should be encouraged to regularly consume foods that are good sources of calcium
- Vegetarians should be encouraged to increase their iron intake above the population reference intake suggested for omnivores, by eating a variety of iron-rich plant foods that are low in phytate and oxalate
- Vegetarians should be encouraged to consume more dietary zinc than the population reference intake suggested for omnivores, especially when the dietary phytate:zinc ratio is high
- Vegetarians can improve their n-3 nutritional status by regularly consuming good sources of alpha-linolenic acid and limiting intake of sources of linoleic acid

practice aerobic sports was considered to be 1.2–1.4 g/kg bodyweight/day, while for strength sports 1.6–1.7 g/kg bodyweight/day was suggested; vegetarian athletes were advised to increase their protein intake by 10% to 1.3–1.8 g/kg bodyweight/day for aerobic and strength sports, respectively.

Despite the lower bioavailability of some trace elements, including zinc, in vegetarian diets most studies have found no difference in trace element status between athletes and non-athletes [196]. However, since body glycogen stores are optimized by consumption of plant carbohydrate, the high phytate content of the diet may reduce iron and zinc bioavailability [196,243]. Lower ferritin levels have been found in semi-vegetarian female runners [237] and LOV athletes of both sexes [244,245] compared to OMN controls, but this did not significantly affect their endurance during long distance running.

It has been suggested [246] that zinc supplementation can be advantageous in athletes because urinary zinc excretion may increase with intense training [247]. To avoid zinc supplementation, LOV and VEG athletes can increase zinc intake by consuming high zinc foods (beans, whole grains, nuts, pumpkin seeds and hemp seeds) [246]. Although all these foods contain phytate, they provide sufficient bioavailable zinc.

Conclusions

Interest in and appreciation of vegetarian diets are growing in Italy and elsewhere. The evidence reviewed in this paper makes it clear that well-planned vegetarian diets that include a wide variety of plant foods, and a reliable source of vitamin B12, provide adequate nutrient intake. For Italians, a healthy and nutritionally adequate vegetarian diet can be obtained by choosing from among the large variety of plant foods traditionally consumed in Italy (cereals, pulses, vegetables, fruits, seeds, nuts, olive oil). Consuming foods from other cultures (e.g. soy products) and processed foods (e.g. seitan, wheat meat, extruded soy) is a matter of personal choice: such foods are not necessary to ensure the nutritional adequacy of a vegetarian diet. We urge government agencies and health and nutrition organizations to provide more educational resources to help Italians consume a nutritionally adequate vegetarian diet.

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References

[1] WHO/FAO. Protein and amino acid requirements in human nutrition. Report of a joint WHO/FAO/UNU expert consultation. WHO; 2013. Report No: 935. Geneva.
[2] Gilani GS, Wu XC, Cockell KA. Impact of antinutritional factors in food proteins on the digestibility of protein and the bioavailability of amino acids and on protein quality. Br J Nutr 2012;108(Suppl. 2):S315–32.
[3] Friedman M, Brandon DL. Nutritional and health benefits of soy proteins. J Agric Food Chem 2001;49:1069–86.
[4] Inoue G, Fujita Y, Niiyama Y. Studies on protein requirements of young men fed egg protein and rice protein with excess and maintenance energy intakes. J Nutr 1973;103:1673–87.
[5] Istfan N, Murray E, Janghorbani M, Young VR. An evaluation of the nutritional value of a soy protein concentrate in young adult men using the short-term N-balance method. J Nutr 1983;113:2516–23.
[6] Young VR, Puig M, Queiroz E, Scrimshaw NS, Rand WM. Evaluation of the protein quality of an isolated soy protein in young men: relative nitrogen requirements and effect of methionine supplementation. Am J Clin Nutr 1984;39:16–24.
[7] Rand WM, Pellett PL, Young VR. Meta-analysis of nitrogen balance studies for estimating protein requirements in healthy adults. Am J Clin Nutr 2003;77:109–27.
[8] Cooper R, Allen A, Goldberg R, Trevisan M, Van Horn L, Liu K, et al. Seventh-day adventist adolescents – life-style patterns and cardiovascular risk factors. West J Med 1984;140:471–7.
[9] Shull MW, Reed RB, Valadian I, Palombo R, Thorne H, Dwyer JT. Velocities of growth in vegetarian preschool children. Pediatrics 1977;60:410–7.
[10] Thomas J, Ellis FR. The health of vegans during pregnancy. Proc Nutr Soc 1977;36:46A.
[11] Ward RJ, Abraham R, McFadyen IR, Haines AD, North WR, Patel M, et al. Assessment of trace metal intake and status in a Gujerati pregnant Asian population and their influence on the outcome of pregnancy. Br J Obstet Gynaecol 1988;95:676–82.
[12] Craig WJ, Mangels AR. Position of the American Dietetic association: vegetarian diets. J Am Diet Assoc 2009;109:1266–82.
[13] Finley DA, Lonnerdal B, Dewey KG, Grivetti LE. Breast milk composition: fat content and fatty acid composition in vegetarians and non-vegetarians. Am J Clin Nutr 1985;41:787–800.
[14] Dagnelie PC, van Staveren WA, Roos AH, Tuinstra LG, Burema J. Nutrients and contaminants in human milk from mothers on macrobiotic and omnivorous diets. Eur J Clin Nutr 1992;46:355–66.
[15] Dwyer JT, Palombo R, Valadian I, Reed RB. Preschoolers on alternate life-style diets. Associations between size and dietary indexes with diets limited in types of animal foods. J Am Diet Assoc 1978;72:264–70.
[16] O’Connor H, Munas Z, Griffin H, Rooney K, Cheng HL, Steinbeck K. Nutritional adequacy of energy restricted diets for young obese women. Asia Pac J Clin Nutr 2011;20:206–11.
[17] Sanders TA. Growth and development of British vegan children. Am J Clin Nutr 1988;48:822–5.
[18] van Staveren WA, Dhuyvetter JH, Bons A, Zeelen M, Hautvast JG. Food consumption and height/weight status of Dutch preschool children on alternative diets. J Am Diet Assoc 1985;85:1579–84.
[19] Fomon SJ, Thomas LN, Filer Jr LJ, Anderson TA, Bergmann KE. Requirements for protein and essential amino acids in early infancy. Studies with a soy-isolate formula. Acta Paediatr Scand 1973;62:33–45.
[20] Lasekan JB, Ostrom KM, Jacobs JR, Blatter MM, Ndife LI, Gooch III WM, et al. Growth of newborn, term infants fed soy formulas for 1 year. Clin Pediatr (Phila) 1999;38:563–71.
[21] Strom BL, Schinnar R, Ziegler EE, Barnhart KT, Sammel MD, Macones GA, et al. Exposure to soy-based formula in infancy and endocrinological and reproductive outcomes in young adulthood. JAMA 2001;286:807–14.
[22] Yen CE, Yen CH, Huang MC, Cheng CH, Huang YC. Dietary intake and nutritional status of vegetarian and omnivorous preschool children and their parents in Taiwan. Nutr Res 2008;28:430–6.
[23] Dagnelie PC, van Staveren WA. Macrobiotic nutrition and child health: results of a population-based, mixed-longitudinal cohort study in The Netherlands. Am J Clin Nutr 1994;59:1187S–96S.
[24] Dwyer JT, Andrew EM, Berkey C, Valadian I, Reed RB. Growth in “new” vegetarian preschool children using the Jenss-Bayley curve fitting technique. Am J Clin Nutr 1983;37:815–27.
[25] Hebbelinck M, Clarys P, De Malsche MA. Growth, development, and physical fitness of Flemish vegetarian children, adolescents, and young adults. Am J Clin Nutr 1999;70:579S–85S.
[26] Sabate J, Lindsted KD, Harris RD, Johnston PK. Anthropometric parameters of schoolchildren with different life-styles. Am J Dis Child 1990;144:1159–63.

[27] Van Dusseldorp M, Arts IC, Bergsma JS, De Jong N, Dagnelie PC, van Staveren WA. Catch-up growth in children fed a macrobiotic diet in early childhood. J Nutr 1996;126:2977–83.
[28] O'Connell JM, Dibley MJ, Sierra J, Wallace B, Marks JS, Yip R. Growth of vegetarian children: the Farm study. Pediatrics 1989; 84:475–81.
[29] Ambroszkiewicz J, Klemarczyk W, Gajewska J, Chelchowska M, Laskowska-Klita T. Serum concentration of biochemical bone turnover markers in vegetarian children. Adv Med Sci 2007;52: 279–82.
[30] Leung SS, Lee RH, Sung RY, Luo HY, Kam CW, Yuen MP, et al. Growth and nutrition of Chinese vegetarian children in Hong Kong. J Paediatr Child Health 2001;37:247–53.
[31] Thane CW, Bates CJ. Dietary intakes and nutrient status of vegetarian preschool children from a British national survey. J Hum Nutr Diet 2000;13:149–62.
[32] Messina V, Mangels AR. Considerations in planning vegan diets: children. J Am Diet Assoc 2001;101:661–9.
[33] Persky VW, Chatterton RT, Van Horn LV, Grant MD, Langenberg P, Marvin J. Hormone levels in vegetarian and nonvegetarian teenage girls: potential implications for breast cancer risk. Cancer Res 1992;52:578–83.
[34] Nathan I, Hackett AF, Kirby S. A longitudinal study of the growth of matched pairs of vegetarian and omnivorous children, aged 7–11 years, in the north-west of England. Eur J Clin Nutr 1997; 51:20–5.
[35] Sabate J, Lindsted KD, Harris RD, Sanchez A. Attained height of lacto-ovo vegetarian children and adolescents. Eur J Clin Nutr 1991;45:51–8.
[36] Sanders TA. Vegetarian diets and children. Pediatr Clin North Am 1995;42:955–65.
[37] Larsson CL, Westerterp KR, Johansson GK. Validity of reported energy expenditure and energy and protein intakes in Swedish adolescent vegans and omnivores. Am J Clin Nutr 2002;75: 268–74.
[38] Houghton LA, Green TJ, Donovan UM, Gibson RS, Stephen AM, O'Connor DL. Association between dietary fiber intake and the folate status of a group of female adolescents. Am J Clin Nutr 1997;66:1414–21.
[39] Perry CL, McGuire MT, Neumark-Sztainer D, Story M. Adolescent vegetarians: how well do their dietary patterns meet the healthy people 2010 objectives? Arch Pediatr Adolesc Med 2002;156: 431–7.
[40] Andrich DE, Filion ME, Woods M, Dwyer JT, Gorbach SL, Goldin BR, et al. Relationship between essential amino acids and muscle mass, independent of habitual diets, in pre- and postmenopausal US women. Int J Food Sci Nutr 2011;62:719–24.
[41] Caso G, Scalfi L, Marra M, Covino A, Muscaritoli M, McNurlan MA, et al. Albumin synthesis is diminished in men consuming a predominantly vegetarian diet. J Nutr 2000;130:528–33.
[42] Delanghe J, De Slypere JP, De Buyzere M, Robbrecht J, Wieme R, Vermeulen A. Normal reference values for creatine, creatinine, and carnitine are lower in vegetarians. Clin Chem 1989;35:1802–3.
[43] Huang YC, Chang SJ, Chiu YT, Chang HH, Cheng CH. The status of plasma homocysteine and related B-vitamins in healthy young vegetarians and nonvegetarians. Eur J Nutr 2003;42:84–90.
[44] Ingenbleek Y, McCully KS. Vegetarianism produces subclinical malnutrition, hyperhomocysteinemia and atherogenesis. Nutrition 2012;28:148–53.
[45] Kniskern MA, Johnston CS. Protein dietary reference intakes may be inadequate for vegetarians if low amounts of animal protein are consumed. Nutrition 2011;27:727–30.
[46] Laidlaw SA, Shultz TD, Cecchino JT, Kopple JD. Plasma and urine taurine levels in vegans. Am J Clin Nutr 1988;47:660–3.
[47] Leblanc JC, Yoon H, Kombadjian A, Verger P. Nutritional intakes of vegetarian populations in France. Eur J Clin Nutr 2000;54:443–9.
[48] Sebekova K, Krajcovicova-Kudlackova M, Blazicek P, Parrak V, Schinzel R, Heidland A. Functional hyperhomocysteinemia in healthy vegetarians: no association with advanced glycation end products, markers of protein oxidation, or lipid peroxidation after correction with vitamin B(12). Clin Chem 2003;49:983–6.
[49] Turner-McGrievy GM, Barnard ND, Scialli AR, Lanou AJ. Effects of a low-fat vegan diet and a step II diet on macro- and micronutrient intakes in overweight postmenopausal women. Nutrition 2004;20:738–46.
[50] Deriemaeker P, Aerenhouts D, De Ridder D, Hebbelinck M, Clarys P. Health aspects, nutrition and physical characteristics in matched samples of institutionalized vegetarian and non-vegetarian elderly (>65 yrs). Nutr Metab (Lond) 2011;8:37.
[51] Tylavsky FA, Anderson JJ. Dietary factors in bone health of elderly lactoovovegetarian and omnivorous women. Am J Clin Nutr 1988;48:842–9.
[52] Woo J, Kwok T, Ho SC, Sham A, Lau E. Nutritional status of elderly Chinese vegetarians. Age Ageing 1998;27:455–61.
[53] Lau EM, Kwok T, Woo J, Ho SC. Bone mineral density in Chinese elderly female vegetarians, vegans, lacto-vegetarians and omnivores. Eur J Clin Nutr 1998;52:60–4.
[54] Brants HA, Lowik MR, Westenbrink S, Hulshof KF, Kistemaker C. Adequacy of a vegetarian diet at old age (Dutch Nutrition Surveillance System). J Am Coll Nutr 1990;9:292–302.
[55] Watanabe F, Yabuta Y, Tanioka Y, Bito T. Biologically active vitamin B12 compounds in foods for preventing deficiency among vegetarians and elderly subjects. J Agric Food Chem 2013;61:6769–75.
[56] Carmel R. Malabsorption of food cobalamin. Baillieres Clin Haematol 1995;8:639–55.
[57] Allen LH. How common is vitamin B-12 deficiency? Am J Clin Nutr 2009;89:693S–6S.
[58] Campbell AK, Miller JW, Green R, Haan MN, Allen LH. Plasma vitamin B-12 concentrations in an elderly latino population are predicted by serum gastrin concentrations and crystalline vitamin B-12 intake. J Nutr 2003;133:2770–6.
[59] Blacher J, Czernichow S, Raphael M, Roussel C, Chadefaux-Vekemans B, Morineau G, et al. Very low oral doses of vitamin B-12 increase serum concentrations in elderly subjects with food-bound vitamin B-12 malabsorption. J Nutr 2007;137:373–8.
[60] SINU. Intake levels of reference of nutrients and energy-IV revision. Italian Society of Human Nutrition; 2014.
[61] Mangels R, Messina V, Messina M. The dietitian's guide to vegetarian diets. Ontario, Canada: Jones and Bartlett Learning; 2011. p. 181.
[62] Herrmann W, Schorr H, Purschwitz K, Rassoul F, Richter V. Total homocysteine, vitamin B(12), and total antioxidant status in vegetarians. Clin Chem 2001;47:1094–101.
[63] Herrmann W, Geisel J. Vegetarian lifestyle and monitoring of vitamin B-12 status. Clin Chim Acta 2002;326:47–59.
[64] Koebnick C, Hoffmann I, Dagnelie PC, Heins UA, Wickramasinghe SN, Ratnayaka ID, et al. Long-term ovo-lacto vegetarian diet impairs vitamin B-12 status in pregnant women. J Nutr 2004;134: 3319–26.
[65] Mathey C, Di Marco JN, Poujol A, Cournelle MA, Brevaut V, Livet MO, et al. [Failure to thrive and psychomotor regression revealing vitamin B12 deficiency in 3 infants]. Arch Pediatr 2007;14:467–71.
[66] Dagnelie PC, van Staveren WA, Hautvast JG. Stunting and nutrient deficiencies in children on alternative diets. Acta Paediatr Scand Suppl 1991;374:111–8.
[67] Schneede J, Dagnelie PC, van Staveren WA, Vollset SE, Refsum H, Ueland PM. Methylmalonic acid and homocysteine in plasma as indicators of functional cobalamin deficiency in infants on macrobiotic diets. Pediatr Res 1994;36:194–201.
[68] Dhonukshe-Rutten RA, van Dusseldorp M, Schneede J, de Groot LC, van Staveren WA. Low bone mineral density and bone mineral content are associated with low cobalamin status in adolescents. Eur J Nutr 2005;44:341–7.
[69] Miller DR, Specker BL, Ho ML, Norman EJ. Vitamin B-12 status in a macrobiotic community. Am J Clin Nutr 1991;53:524–9.
[70] van Dusseldorp M, Schneede J, Refsum H, Ueland PM, Thomas CM, de Boer E, et al. Risk of persistent cobalamin deficiency in adolescents fed a macrobiotic diet in early life. Am J Clin Nutr 1999;69:664–71.
[71] Ambroszkiewicz J, Klemarczyk W, Chelchowska M, Gajewska J, Laskowska-Klita T. Serum homocysteine, folate, vitamin B12 and total antioxidant status in vegetarian children. Adv Med Sci 2006;51:265–8.
[72] Laskowska-Klita T, Chelchowska M, Ambroszkiewicz J, Gajewska J, Klemarczyk W. The effect of vegetarian diet on selected essential nutrients in children. Med Wieku Rozw 2011;15:318–25.
[73] Yen CE, Yen CH, Cheng CH, Huang YC. Vitamin B-12 status is not associated with plasma homocysteine in parents and their preschool children: lacto-ovo, lacto, and ovo vegetarians and omnivores. J Am Coll Nutr 2010;29:7–13.

[74] Rush EC, Chhichhia P, Hinckson E, Nabiryo C. Dietary patterns and vitamin B(12) status of migrant Indian preadolescent girls. Eur J Clin Nutr 2009;63:585–7.
[75] Herrmann W. The importance of hyperhomocysteinemia as a risk factor for diseases: an overview. Clin Chem Lab Med 2001;39: 666–74.
[76] Majchrzak D, Singer I, Manner M, Rust P, Genser D, Wagner KH, et al. B-vitamin status and concentrations of homocysteine in Austrian omnivores, vegetarians and vegans. Ann Nutr Metab 2006;50:485–91.
[77] Obeid R, Geisel J, Schorr H, Hubner U, Herrmann W. The impact of vegetarianism on some haematological parameters. Eur J Haematol 2002;69:275–9.
[78] Bissoli L, Di Francesco V, Ballarin A, Mandragona R, Trespidi R, Brocco G, et al. Effect of vegetarian diet on homocysteine levels. Ann Nutr Metab 2002;46:73–9.
[79] Gammon CS, von Hurst PR, Coad J, Kruger R, Stonehouse W. Vegetarianism, vitamin B12 status, and insulin resistance in a group of predominantly overweight/obese South Asian women. Nutrition 2012;28:20–4.
[80] Geisel J, Schorr H, Bodis M, Isber S, Hubner U, Knapp JP, et al. The vegetarian lifestyle and DNA methylation. Clin Chem Lab Med 2005;43:1164–9.
[81] Gilsing AM, Crowe FL, Lloyd-Wright Z, Sanders TA, Appleby PN, Allen NE, et al. Serum concentrations of vitamin B12 and folate in British male omnivores, vegetarians and vegans: results from a cross-sectional analysis of the EPIC-Oxford cohort study. Eur J Clin Nutr 2010;64:933–9.
[82] Herrmann W, Obeid R, Schorr H, Geisel J. Functional vitamin B12 deficiency and determination of holotranscobalamin in populations at risk. Clin Chem Lab Med 2003;41:1478–88.
[83] Herrmann W, Schorr H, Obeid R, Geisel J. Vitamin B-12 status, particularly holotranscobalamin II and methylmalonic acid. Am J Clin Nutr 2003;78:131–6.
[84] Herrmann W, Obeid R, Schorr H, Hubner U, Geisel J, Sand-Hill M, et al. Enhanced bone metabolism in vegetarians – the role of vitamin B12 deficiency. Clin Chem Lab Med 2009;47:1381–7.
[85] Hokin BD, Butler T. Cyanocobalamin (vitamin B-12) status in Seventh-day Adventist ministers in Australia. Am J Clin Nutr 1999;70:576S–8S.
[86] Hung CJ, Huang PC, Lu SC, Li YH, Huang HB, Lin BF, et al. Plasma homocysteine levels in Taiwanese vegetarians are higher than those of omnivores. J Nutr 2002;132:152–8.
[87] Karabudak E, Kiziltan G, Cigerim N. A comparison of some of the cardiovascular risk factors in vegetarian and omnivorous Turkish females. J Hum Nutr Diet 2008;21:13–22.
[88] Krajcovicova-Kudlackova M, Blazicek P, Kopcova J, Bederova A, Babinska K. Homocysteine levels in vegetarians versus omnivores. Ann Nutr Metab 2000;44:135–8.
[89] Krivosikova Z, Krajcovicova-Kudlackova M, Spustova V, Stefikova K, Valachovicova M, Blazicek P, et al. The association between high plasma homocysteine levels and lower bone mineral density in Slovak women: the impact of vegetarian diet. Eur J Nutr 2010;49:147–53.
[90] Kwok T, Cheng G, Woo J, Lai WK, Pang CP. Independent effect of vitamin B12 deficiency on hematological status in older Chinese vegetarian women. Am J Hematol 2002;70:186–90.
[91] Mann NJ, Li D, Sinclair AJ, Dudman NP, Guo XW, Elsworth GR, et al. The effect of diet on plasma homocysteine concentrations in healthy male subjects. Eur J Clin Nutr 1999;53:895–9.
[92] Reddy S, Sanders TA. Haematological studies on pre-menopausal Indian and Caucasian vegetarians compared with Caucasian omnivores. Br J Nutr 1990;64:331–8.
[93] Refsum H, Yajnik CS, Gadkari M, Schneede J, Vollset SE, Orning L, et al. Hyperhomocysteinemia and elevated methylmalonic acid indicate a high prevalence of cobalamin deficiency in Asian Indians. Am J Clin Nutr 2001;74:233–41.
[94] Su TC, Jeng JS, Wang JD, Torng PL, Chang SJ, Chen CF, et al. Homocysteine, circulating vascular cell adhesion molecule and carotid atherosclerosis in postmenopausal vegetarian women and omnivores. Atherosclerosis 2006;184:356–62.
[95] Chen CW, Lin YL, Lin TK, Lin CT, Chen BC, Lin CL. Total cardiovascular risk profile of Taiwanese vegetarians. Eur J Clin Nutr 2008;62:138–44.
[96] Bar-Sella P, Rakover Y, Ratner D. Vitamin B12 and folate levels in long-term vegans. Isr J Med Sci 1990;26:309–12.
[97] Crane M, Sample C, Patchett S, Register D. Vitamin B12 in total vegetarians (vegans). J Nutr Med 1994;4:419–30.
[98] Crane M, Sample C, Register D, Lukens R, Gregory R. Cobalamin (CBL) studies on two total vegetarian (vegan) families. Veg Nutr 1998;23:87–92.
[99] Herrmann W, Obeid R, Schorr H, Geisel J. The usefulness of holotranscobalamin in predicting vitamin B12 status in different clinical settings. Curr Drug Metab 2005;6:47–53.
[100] Waldmann A, Koschizke JW, Leitzmann C, Hahn A. Homocysteine and cobalamin status in German vegans. Public Health Nutr 2004;7:467–72.
[101] Haddad EH, Berk LS, Kettering JD, Hubbard RW, Peters WR. Dietary intake and biochemical, hematologic, and immune status of vegans compared with nonvegetarians. Am J Clin Nutr 1999;70: 586S–93S.
[102] Madry E, Lisowska A, Grebowiec P, Walkowiak J. The impact of vegan diet on B-12 status in healthy omnivores: five-year prospective study. Acta Sci Pol Technol Aliment 2012;11:209–12.
[103] Donaldson MS. Metabolic vitamin B12 status on a mostly raw vegan diet with follow-up using. Ann Nutr Metab 2000;44: 229–34.
[104] Rauma AL, Torronen R, Hanninen O, Mykkanen H. Vitamin B-12 status of long-term adherents of a strict uncooked vegan diet ("living food diet") is compromised. J Nutr 1995;125:2511–5.
[105] Koebnick C, Garcia AL, Dagnelie PC, Strassner C, Lindemans J, Katz N, et al. Long-term consumption of a raw food diet is associated with favorable serum LDL cholesterol and triglycerides but also with elevated plasma homocysteine and low serum HDL cholesterol in humans. J Nutr 2005;135:2372–8.
[106] Obersby D, Chappell DC, Dunnett A, Tsiami AA. Plasma total homocysteine status of vegetarians compared with omnivores: a systematic review and meta-analysis. Br J Nutr 2013;109: 785–94.
[107] Roman VB, Ribas BL, Ngo J, Gurinovic M, Novakovic R, Cavelaars A, et al. Projected prevalence of inadequate nutrient intakes in Europe. Ann Nutr Metab 2011;59:84–95.
[108] Doets EL, In 't Veld PHV, Szczecinska A, Dhonukshe-Rutten RA, Cavelaars AE, van 't Veer P, et al. Systematic review on daily vitamin B12 losses and bioavailability for deriving recommendations on vitamin B12 intake with the factorial approach. Ann Nutr Metab 2013;62:311–22.
[109] EFSA. Scientific opinion on dietary reference values for cobalamin (vitamin B12). EFSA J 2015;13:4150.
[110] Weaver CM, Plawecki KL. Dietary calcium: adequacy of a vegetarian diet. Am J Clin Nutr 1994;59:1238S–41S.
[111] Weaver CM, Proulx WR, Heaney R. Choices for achieving adequate dietary calcium with a vegetarian diet. Am J Clin Nutr 1999;70:543S–8S.
[112] Heaney RP, Weaver CM. Calcium absorption from kale. Am J Clin Nutr 1990;51:656–7.
[113] Heaney RP, Recker RR, Weaver CM. Absorbability of calcium sources: the limited role of solubility. Calcif Tissue Int 1990;46: 300–4.
[114] Heaney RP, Dowell MS, Rafferty K, Bierman J. Bioavailability of the calcium in fortified soy imitation milk, with some observations on method. Am J Clin Nutr 2000;71:1166–9.
[115] Weaver CM, Heaney RP, Connor L, Martin BR, Smith DL, Nielsen S. Bioavailability of calcium from tofu as compared with milk in premenopausal women. J Agric Food Chem 2002;50:3874–6.
[116] Heaney RP. Absorbability and utility of calcium in mineral waters. Am J Clin Nutr 2006;84:371–4.
[117] Van Dokkum W, De La Guéronnière V, Schaafsma G, Bouley C, Luten J, Latge C. Bioavailability of calcium of fresh cheeses, enteral food and mineral water. A study with stable calcium isotopes in young adult women. Br J Nutr 1996;75:893–903.
[118] Gibson RS. Principles of nutritional assessment. Oxford University Press; 2005.
[119] Specker BL, Tsang RC, Ho M, Miller D. Effect of vegetarian diet on serum 1,25-dihydroxyvitamin D concentrations during lactation. Obstet Gynecol 1987;70:870–4.
[120] Specker BL. Nutritional concerns of lactating women consuming vegetarian diets. Am J Clin Nutr 1994;59:1182S–6S.

[121] Dagnelie PC, Vergote FJ, van Staveren WA, van den BH, Dingjan PG, Hautvast JG. High prevalence of rickets in infants on macrobiotic diets. Am J Clin Nutr 1990;51:202–8.
[122] Dagnelie PC, van Dusseldorp M, van Staveren WA, Hautvast JG. Effects of macrobiotic diets on linear growth in infants and children until 10 years of age. Eur J Clin Nutr 1994;48(Suppl. 1):S103–11.
[123] Larsson CL, Johansson GK. Dietary intake and nutritional status of young vegans and omnivores in Sweden. Am J Clin Nutr 2002;76: 100–6.
[124] Donovan UM, Gibson RS. Dietary intakes of adolescent females consuming vegetarian, semi-vegetarian, and omnivorous diets. J Adolesc Health 1996;18:292–300.
[125] Parsons TJ, van Dusseldorp M, van der Vliet M, van de Werken K, Schaafsma G, van Staveren WA. Reduced bone mass in Dutch adolescents fed a macrobiotic diet in early life. J Bone Min Res 1997;12:1486–94.
[126] Lamberg-Allardt C, Karkkainen M, Seppanen R, Bistrom H. Low serum 25-hydroxyvitamin D concentrations and secondary hyperparathyroidism in middle-aged white strict vegetarians. Am J Clin Nutr 1993;58:684–9.
[127] Appleby P, Roddam A, Allen N, Key T. Comparative fracture risk in vegetarians and nonvegetarians in EPIC-Oxford. Eur J Clin Nutr 2007;61:1400–6.
[128] Davey GK, Spencer EA, Appleby PN, Allen NE, Knox KH, Key TJ. EPIC-Oxford: lifestyle characteristics and nutrient intakes in a cohort of 33 883 meat-eaters and 31 546 non meat-eaters in the UK. Public Health Nutr 2003;6:259–69.
[129] Janelle KC, Barr SI. Nutrient intakes and eating behavior scores of vegetarian and nonvegetarian women. J Am Diet Assoc 1995;95: 180–6.
[130] Outila TA, Lamberg-Allardt CJ. Ergocalciferol supplementation may positively affect lumbar spine bone mineral density of vegans. J Am Diet Assoc 2000;100:629.
[131] Cade JE, Burley VJ, Greenwood DC. The UK women's cohort study: comparison of vegetarians, fish-eaters and meat-eaters. Public Health Nutr 2004;7:871–8.
[132] Lloyd T, Schaeffer JM, Walker MA, Demers LM. Urinary hormonal concentrations and spinal bone densities of premenopausal vegetarian and nonvegetarian women. Am J Clin Nutr 1991;54: 1005–10.
[133] Tesar R, Notelovitz M, Shim E, Kauwell G, Brown J. Axial and peripheral bone density and nutrient intakes of postmenopausal vegetarian and omnivorous women. Am J Clin Nutr 1992;56: 699–704.
[134] Deriemaeker P, Alewaeters K, Hebbelinck M, Lefevre J, Philippaerts R, Clarys P. Nutritional status of Flemish vegetarians compared with non-vegetarians: a matched samples study. Nutrients 2010;2:770–80.
[135] Nakamoto K, Watanabe S, Kudo H, Tanaka A. Nutritional characteristics of middle-aged Japanese vegetarians. J Atheroscler Thromb 2008;15:122–9.
[136] Chiu JF, Lan SJ, Yang CY, Wang PW, Yao WJ, Su LH, et al. Long-term vegetarian diet and bone mineral density in postmenopausal Taiwanese women. Calcif Tissue Int 1997;60:245–9.
[137] Barr SI, Rideout CA. Nutritional considerations for vegetarian athletes. Nutrition 2004;20:696–703.
[138] Barr SI, Prior JC, Janelle KC, Lentle BC. Spinal bone mineral density in premenopausal vegetarian and nonvegetarian women: cross-sectional and prospective comparisons. J Am Diet Assoc 1998; 98:760–5.
[139] Keramat A, Patwardhan B, Larijani B, Chopra A, Mithal A, Chakravarty D, et al. The assessment of osteoporosis risk factors in Iranian women compared with Indian women. BMC Musculoskelet Disord 2008;9:28.
[140] Ho-Pham LT, Nguyen PL, Le TT, Doan TA, Tran NT, Le TA, et al. Veganism, bone mineral density, and body composition: a study in Buddhist nuns. Osteoporos Int 2009;20:2087–93.
[141] Ho-Pham LT, Vu BQ, Lai TQ, Nguyen ND, Nguyen TV. Vegetarianism, bone loss, fracture and vitamin D: a longitudinal study in Asian vegans and non-vegans. Eur J Clin Nutr 2012;66:75–82.
[142] Lightowler HJ, Davies GJ. Micronutrient intakes in a group of UK vegans and the contribution of self-selected dietary supplements. J R Soc Promot Health 2000;120:117–24.
[143] Outila TA, Karkkainen MU, Seppanen RH, Lamberg-Allardt CJ. 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. J Am Diet Assoc 2000;100:434–41.
[144] Strohle A, Waldmann A, Koschizke J, Leitzmann C, Hahn A. Diet-dependent net endogenous acid load of vegan diets in relation to food groups and bone health-related nutrients: results from the German Vegan Study. Ann Nutr Metab 2011;59:117–26.
[145] Waldmann A, Koschizke JW, Leitzmann C, Hahn A. Dietary intakes and lifestyle factors of a vegan population in Germany: results from the German Vegan Study. Eur J Clin Nutr 2003;57:947–55.
[146] Fontana L, Shew JL, Holloszy JO, Villareal DT. Low bone mass in subjects on a long-term raw vegetarian diet. Arch Intern Med 2005;165:684–9.
[147] Reed JA, Anderson JJ, Tylavsky FA, Gallagher Jr PN. Comparative changes in radial-bone density of elderly female lacto-ovovegetarians and omnivores. Am J Clin Nutr 1994;59: 1197S–202S.
[148] Merrill RM, Aldana SG. Consequences of a plant-based diet with low dairy consumption on intake of bone-relevant nutrients. J Womens Health (Larchmt) 2009;18:691–8.
[149] Turner-McGrievy GM, Barnard ND, Cohen J, Jenkins DJ, Gloede L, Green AA. Changes in nutrient intake and dietary quality among participants with type 2 diabetes following a low-fat vegan diet or a conventional diabetes diet for 22 weeks. J Am Diet Assoc 2008;108:1636–45.
[150] Dunn-Emke SR, Weidner G, Pettengill EB, Marlin RO, Chi C, Ornish DM. Nutrient adequacy of a very low-fat vegan diet. J Am Diet Assoc 2005;105:1442–6.
[151] Kohlenberg-Mueller K, Raschka L. Calcium balance in young adults on a vegan and lactovegetarian diet. J Bone Min Metab 2003;21:28–33.
[152] Sette S, Le Donne C, Piccinelli R, Mistura L, Ferrari M, Leclercq C. The Third National Food Consumption Survey, INRAN-SCAI 2005–06: major dietary sources of nutrients in Italy. Int J Food Sci Nutr 2013;64:1014–21.
[153] Craig WJ. Nutrition concerns and health effects of vegetarian diets. Nutr Clin Pract 2010;25:613–20.
[154] Hunt JR. Bioavailability of iron, zinc, and other trace minerals from vegetarian diets. Am J Clin Nutr 2003;78:633S–9S.
[155] Hurrell R, Egli I. Iron bioavailability and dietary reference values. Am J Clin Nutr 2010;91:1461S–7S.
[156] Lonnerdal B. Soybean ferritin: implications for iron status of vegetarians. Am J Clin Nutr 2009;89:1680S–5S.
[157] Lonnerdal B, Bryant A, Liu X, Theil EC. Iron absorption from soybean ferritin in nonanemic women. Am J Clin Nutr 2006;83: 103–7.
[158] Agarwal U. Rethinking red meat as a prevention strategy for iron deficiency. Infant, Child Adolesc Nutr 2013;5:231–5.
[159] Theil EC, Briat J. Plant ferritin and non-heme iron nutrition in humans. 2004. HarvestPlus technical monograph 1, Washington, DC and Cali.
[160] Hunt JR, Roughead ZK. Adaptation of iron absorption in men consuming diets with high or low iron bioavailability. Am J Clin Nutr 2000;71:94–102.
[161] Craig WJ. Iron status of vegetarians. Am J Clin Nutr 1994;59: 1233S–7S.
[162] Collings R, Harvey LJ, Hooper L, Hurst R, Brown TJ, Ansett J, et al. The absorption of iron from whole diets: a systematic review. Am J Clin Nutr 2013;98:65–81.
[163] Garcia-Casal MN, Layrisse M, Solano L, Baron MA, Arguello F, Llovera D, et al. Vitamin A and beta-carotene can improve nonheme iron absorption from rice, wheat and corn by humans. J Nutr 1998;128:646–50.
[164] Vegetarian weaning. Nutrition Standing Committee of the British Paediatric Association. Arch Dis Child 1988;63:1286–92.
[165] Fulton JR, Hutton CW, Stitt KR. Preschool vegetarian children. Dietary and anthropometric data. J Am Diet Assoc 1980;76: 360–5.
[166] Institute of Medicine. Dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. 2001. Washington, DC.
[167] Krajcovicova-Kudlackova M, Simoncic R, Bederova A, Grancicova E, Magalova T. Influence of vegetarian and mixed

nutrition on selected haematological and biochemical parameters in children. Nahrung 1997;41:311–4.
[168] Donovan UM, Gibson RS. Iron and zinc status of young women aged 14 to 19 years consuming vegetarian and omnivorous diets. J Am Coll Nutr 1995;14:463–72.
[169] Wilson AK, Ball MJ. Nutrient intake and iron status of Australian male vegetarians. Eur J Clin Nutr 1999;53:189–94.
[170] Huang YC, Lin WJ, Cheng CH, Su KH. Nutrient intakes and iron status of healthy young vegetarians and non vegetarians. Nutr Res 1999;19:663–74.
[171] Anderson BM, Gibson RS, Sabry JH. The iron and zinc status of long-term vegetarian women. Am J Clin Nutr 1981;34:1042–8.
[172] Ball MJ, Bartlett MA. Dietary intake and iron status of Australian vegetarian women. Am J Clin Nutr 1999;70:353–8.
[173] Harvey LJ, Armah CN, Dainty JR, Foxall RJ, John LD, Langford NJ, et al. Impact of menstrual blood loss and diet on iron deficiency among women in the UK. Br J Nutr 2005;94:557–64.
[174] Hanson LN, Engelman HM, Alekel DL, Schalinske KL, Kohut ML, Reddy MB. Effects of soy isoflavones and phytate on homocysteine, C-reactive protein, and iron status in postmenopausal women. Am J Clin Nutr 2006;84:774–80.
[175] Wells AM, Haub MD, Fluckey J, Williams DK, Chernoff R, Campbell WW. Comparisons of vegetarian and beef-containing diets on hematological indexes and iron stores during a period of resistive training in older men. J Am Diet Assoc 2003;103:594–601.
[176] Hunt JR. Moving toward a plant-based diet: are iron and zinc at risk? Nutr Rev 2002;60:127–34.
[177] Venti CA, Johnston CS. Modified food guide pyramid for lacto-vegetarians and vegans. J Nutr 2002;132:1050–4.
[178] Gibson RS. Content and bioavailability of trace elements in vegetarian diets. Am J Clin Nutr 1994;59:1223S–32S.
[179] Lonnerdal B. Dietary factors influencing zinc absorption. J Nutr 2000;130:1378S–83S.
[180] Hunt JR, Matthys LA, Johnson LK. Zinc absorption, mineral balance, and blood lipids in women consuming controlled lactoovovegetarian and omnivorous diets for 8 wk. Am J Clin Nutr 1998;67:421–30.
[181] Sandstrom B, Arvidsson B, Cederblad A, Bjorn-Rasmussen E. Zinc absorption from composite meals. I. The significance of wheat extraction rate, zinc, calcium, and protein content in meals based on bread. Am J Clin Nutr 1980;33:739–45.
[182] Wegmuller R, Tay F, Zeder C, Brnic M, Hurrell RF. Zinc absorption by young adults from supplemental zinc citrate is comparable with that from zinc gluconate and higher than from zinc oxide. J Nutr 2014;144:132–6.
[183] Chiplonkar SA, Agte VV. Predicting bioavailable zinc from lower phytate forms, folic acid and their interactions with zinc in vegetarian meals. J Am Coll Nutr 2006;25:26–33.
[184] King JC. Zinc: an essential but elusive nutrient. Am J Clin Nutr 2011;94:679S–84S.
[185] Gibson RS, Hess SY, Hotz C, Brown KH. Indicators of zinc status at the population level: a review of the evidence. Br J Nutr 2008; 99(Suppl. 3):S14–23.
[186] Lowe NM, Fekete K, Decsi T. Methods of assessment of zinc status in humans: a systematic review. Am J Clin Nutr 2009;89: 2040S–51S.
[187] Roohani N, Hurrell R, Kelishadi R, Schulin R. Zinc and its importance for human health: an integrative review. J Res Med Sci 2013;18:144–57.
[188] Casey CE, Neville MC, Hambidge KM. Studies in human lactation: secretion of zinc, copper, and manganese in human milk. Am J Clin Nutr 1989;49:773–85.
[189] Breastfeeding and the use of human milk. Pediatrics 1997;100: 1035–9. American Academy of Pediatrics. Work group on breastfeeding.
[190] Allen LH. Zinc and micronutrient supplements for children. Am J Clin Nutr 1998;68:495S–8S.
[191] King JC, Stein T, Doyle M. Effect of vegetarianism on the zinc status of pregnant women. Am J Clin Nutr 1981;34:1049–55.
[192] Foster M, Chu A, Petocz P, Samman S. Effect of vegetarian diets on zinc status: a systematic review and meta-analysis of studies in humans. J Sci Food Agric 2013;93:2362–71.
[193] Sanders TA, Purves R. An anthropometric and dietary assessment of the nutritional status of vegan preschool children. J Hum Nutr 1981;35:349–57.
[194] Smit Vanderkooy PD, Gibson RS. Food consumption patterns of Canadian preschool children in relation to zinc and growth status. Am J Clin Nutr 1987;45:609–16.
[195] Cavan KR, Gibson RS, Grazioso CF, Isalgue AM, Ruz M, Solomons NW. Growth and body composition of periurban Guatemalan children in relation to zinc status: a cross-sectional study. Am J Clin Nutr 1993;57:334–43.
[196] Nieman DC. Physical fitness and vegetarian diets: is there a relation? Am J Clin Nutr 1999;70:570S–5S.
[197] Treuherts J. Possible inter-relationship between zinc and dietary fiber in a group of lacto-ovo vegetarian adolescents. J Plant Food 1982;4:89–93.
[198] Gibson RS, Yeudall F, Drost N, Mtitimuni B, Cullinan T. Dietary interventions to prevent zinc deficiency. Am J Clin Nutr 1998;68: 484S–7S.
[199] de Bortoli MC, Cozzolino SM. Zinc and selenium nutritional status in vegetarians. Biol Trace Elem Res 2009;127:228–33.
[200] Srikumar TS, Johansson GK, Ockerman PA, Gustafsson JA, Akesson B. Trace element status in healthy subjects switching from a mixed to a lactovegetarian diet for 12 mo. Am J Clin Nutr 1992;55:885–90.
[201] Davis BC, Kris-Etherton PM. Achieving optimal essential fatty acid status in vegetarians: current knowledge and practical implications. Am J Clin Nutr 2003;78:640S–6S.
[202] Gebauer SK, Psota TL, Harris WS, Kris-Etherton PM. n-3 fatty acid dietary recommendations and food sources to achieve essentiality and cardiovascular benefits. Am J Clin Nutr 2006;83: 1526S–35S.
[203] Sánchez-Machado DI, López-Cervantes J, López-Hernández J, Paseiro-Losada P. Fatty acids, total lipid, protein and ash contents of processed edible seaweeds. Food Chem 2004;85:439–44.
[204] Arterburn LM, Hall EB, Oken H. Distribution, interconversion, and dose response of n-3 fatty acids in humans. Am J Clin Nutr 2006; 83:1467S–76S.
[205] Horrobin DF. Nutritional and medical importance of gamma-linolenic acid. Prog Lipid Res 1992;31:163–94.
[206] Siguel EN, Lerman RH. Altered fatty acid metabolism in patients with angiographically documented coronary artery disease. Metabolism 1994;43:982–93.
[207] Nervi AM, Peluffo RO, Brenner RR, Leikin AI. Effect of ethanol administration on fatty acid desaturation. Lipids 1980;15:263–8.
[208] Reddy S, Sanders TA, Obeid O. The influence of maternal vegetarian diet on essential fatty acid status of the newborn. Eur J Clin Nutr 1994;48:358–68.
[209] Sanders TA, Reddy S. The influence of a vegetarian diet on the fatty acid composition of human milk and the essential fatty acid status of the infant. J Pediatr 1992;120:S71–7.
[210] Lakin V, Haggarty P, Abramovich DR, Ashton J, Moffat CF, McNeill G, et al. Dietary intake and tissue concentration of fatty acids in omnivore, vegetarian and diabetic pregnancy. Prostagl Leukot Essent Fat Acids 1998;59:209–20.
[211] Sanders TA, Manning J. The growth and development of vegan children. J Hum Nutr Diet 1992;5:11–21.
[212] Krajcovicova-Kudlackova M, Simoncic R, Bederova A, Klvanova J. Plasma fatty acid profile and alternative nutrition. Ann Nutr Metab 1997;41:365–70.
[213] Beezhold BL, Johnston CS, Daigle DR. Vegetarian diets are associated with healthy mood states: a cross-sectional study in seventh day adventist adults. Nutr J 2010;9:26.
[214] Conquer JA, Holub BJ. Supplementation with an algae source of docosahexaenoic acid increases (n-3) fatty acid status and alters selected risk factors for heart disease in vegetarian subjects. J Nutr 1996;126:3032–9.
[215] Conquer JA, Holub BJ. Dietary docosahexaenoic acid as a source of eicosapentaenoic acid in vegetarians and omnivores. Lipids 1997; 32:341–5.
[216] Geppert J, Kraft V, Demmelmair H, Koletzko B. Docosahexaenoic acid supplementation in vegetarians effectively increases omega-3 index: a randomized trial. Lipids 2005;40:807–14.
[217] Huang T, Yu X, Shou T, Wahlqvist ML, Li D. Associations of plasma phospholipid fatty acids with plasma homocysteine in Chinese vegetarians. Br J Nutr 2013;109:1688–94.
[218] Korpela R, Seppo L, Laakso J, Lilja J, Karjala K, Lahteenmaki T, et al. Dietary habits affect the susceptibility of low-density lipoprotein to oxidation. Eur J Clin Nutr 1999;53:802–7.

[219] Lee HY, Woo J, Chen ZY, Leung SF, Peng XH. Serum fatty acid, lipid profile and dietary intake of Hong Kong Chinese omnivores and vegetarians. Eur J Clin Nutr 2000;54:768–73.
[220] Li D, Sinclair A, Wilson A, Nakkote S, Kelly F, Abedin L, et al. Effect of dietary alpha-linolenic acid on thrombotic risk factors in vegetarian men. Am J Clin Nutr 1999;69:872–82.
[221] Li D, Ball M, Bartlett M, Sinclair A. Lipoprotein(a), essential fatty acid status and lipoprotein lipids in female Australian vegetarians. Clin Sci (Lond) 1999;97:175–81.
[222] Manjari V, Suresh Y, Sailaja Devi MM, Das UN. Oxidant stress, anti-oxidants and essential fatty acids in South Indian vegetarians and non-vegetarians. Prostagl Leukot Essent Fat Acids 2001; 64:53–9.
[223] Mezzano D, Munoz X, Martinez C, Cuevas A, Panes O, Aranda E, et al. Vegetarians and cardiovascular risk factors: hemostasis, inflammatory markers and plasma homocysteine. Thromb Haemost 1999;81:913–7.
[224] Phinney SD, Odin RS, Johnson SB, Holman RT. Reduced arachidonate in serum phospholipids and cholesteryl esters associated with vegetarian diets in humans. Am J Clin Nutr 1990;51: 385–92.
[225] Ryan L, Symgton AM. Algal-oil supplements are a viable alternative to fish-oil supplements in terms of docosahexaenoic acid (22:6n-3, DHA). J Funct Foods 2015;19:852–8.
[226] Wu WH, Lu SC, Wang TF, Jou HJ, Wang TA. Effects of docosahexaenoic acid supplementation on blood lipids, estrogen metabolism, and in vivo oxidative stress in postmenopausal vegetarian women. Eur J Clin Nutr 2006;60:386–92.
[227] Yep YL, Li D, Mann NJ, Bode O, Sinclair AJ. Bread enriched with microencapsulated tuna oil increases plasma docosahexaenoic acid and total omega-3 fatty acids in humans. Asia Pac J Clin Nutr 2002;11:285–91.
[228] Fokkema MR, van Rieke HM, Bauermann OJ, Smit EN, Muskiet FA. Short-term carnitine supplementation does not augment LCPomega3 status of vegans and lacto-ovo-vegetarians. J Am Coll Nutr 2005;24:58–64.
[229] Kornsteiner M, Singer I, Elmadfa I. Very low n-3 long-chain polyunsaturated fatty acid status in Austrian vegetarians and vegans. Ann Nutr Metab 2008;52:37–47.
[230] Li D, Sinclair A, Mann N, Turner A, Ball M, Kelly F, et al. The association of diet and thrombotic risk factors in healthy male vegetarians and meat-eaters. Eur J Clin Nutr 1999;53:612–9.
[231] Mann N, Pirotta Y, O'Connell S, Li D, Kelly F, Sinclair A. Fatty acid composition of habitual omnivore and vegetarian diets. Lipids 2006;41:637–46.
[232] Rosell MS, Lloyd-Wright Z, Appleby PN, Sanders TA, Allen NE, Key TJ. Long-chain n-3 polyunsaturated fatty acids in plasma in British meat-eating, vegetarian, and vegan men. Am J Clin Nutr 2005;82:327–34.
[233] Welch AA, Shakya-Shrestha S, Lentjes MA, Wareham NJ, Khaw KT. 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 product-precursor ratio [corrected] of alpha-linolenic acid to long-chain n-3 polyunsaturated fatty acids: results from the EPIC-Norfolk cohort. Am J Clin Nutr 2010;92:1040–51.
[234] Sanders TA, Roshanai F. Platelet phospholipid fatty acid composition and function in vegans compared with age- and sex-matched omnivore controls. Eur J Clin Nutr 1992;46:823–31.
[235] Sarter B, Kelsey KS, Schwartz TA, Harris WS. Blood docosahexaenoic acid and eicosapentaenoic acid in vegans: associations with age and gender and effects of an algal-derived omega-3 fatty acid supplement. Clin Nutr 2015;34:212–8.
[236] Williams MH. Nutritional aspects of human physical and athletic performance. Charles C. Thomas Publisher; 1985. p. 30.
[237] Snyder AC, Dvorak LL, Roepke JB. Influence of dietary iron source on measures of iron status among female runners. Med Sci Sports Exerc 1989;21:7–10.
[238] Hanne N, Dlin R, Rotstein A. Physical fitness, anthropometric and metabolic parameters in vegetarian athletes. J Sports Med Phys Fitness 1986;26:180–5.
[239] Fogelholm M. Dairy products, meat and sports performance. Sports Med 2003;33:615–31.
[240] Rodriguez NR, DiMarco NM, Langley S. Position of the American Dietetic Association, Dietitians of Canada, and the American College of Sports Medicine: nutrition and athletic performance. J Am Diet Assoc 2009;109:509–27.
[241] ADA. Position of Dietitians of Canada, the American Dietetic Association, and the American College of Sports Medicine: nutrition and athletic performance. Can J Diet Pract Res 2000;61:176–92.
[242] Venderley AM, Campbell WW. Vegetarian diets: nutritional considerations for athletes. Sports Med 2006;36:293–305.
[243] Ruud JS. Vegetarianism: implications for athletes. 1990. Omaha.
[244] Seiler D, Nagel D, Franz H, Hellstern P, Leitzmann C, Jung K. Effects of long-distance running on iron metabolism and hematological parameters. Int J Sports Med 1989;10:357–62.
[245] Richter EA, Kiens B, Raben A, Tvede N, Pedersen BK. Immune parameters in male athletes after a lacto-ovo vegetarian diet and a mixed Western diet. Med Sci Sports Exerc 1991;23:517–21.
[246] Fuhrman J, Ferreri DM. Fueling the vegetarian (vegan) athlete. Curr Sports Med Rep 2010;9:233–41.
[247] Clarkson PM, Haymes EM. Trace mineral requirements for athletes. Int J Sport Nutr 1994;4:104–19.