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Effect of vegetarian diets on zinc status: a systematic review and meta-analysis of studies in humans

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Abstract

Plant-based diets contain less saturated fat and cholesterol and more folate, fibre and phytochemicals than omnivorous diets, but some micronutrients, especially zinc, are poorly bioavailable. The findings of studies exploring the zinc intake and zinc status in populations that habitually consume vegetarian diets are inconsistent. This study aims to investigate the effects of plant-based diets on dietary zinc intake and status in humans using systematic review and meta-analysis techniques. Thirty-four studies were included in the systematic review. Of these, 26 studies (reporting 48 comparisons) compared males and/or females consuming vegetarian diets with non-vegetarian groups and were included in meta-analyses. Dietary zinc intakes and serum zinc concentrations were significantly lower (-0.88 ± 0.15 mg day^{-1}, $P < 0.001$ and -0.93 ± 0.27 μmol L^{-1}, $P = 0.001$ respectively; mean ± standard error) in populations that followed habitual vegetarian diets compared with non-vegetarians. Secondary analyses showed greater impact of vegetarian diets on the zinc intake and status of females, vegetarians from developing countries and vegans. Populations that habitually consume vegetarian diets have low zinc intakes and status. Not all vegetarian categories impact zinc status to the same extent, but a lack of consistency in defining vegetarian diets for research purposes makes dietary assessment difficult. Dietary practices that increase zinc bioavailability, the consumption of foods fortified with zinc or low-dose supplementation are strategies that should be considered for improving the zinc status of vegetarians with low zinc intakes or serum zinc concentrations at the lower end of the reference range.

Supporting information may be found in the online version of this article.

Keywords: vegetarian; dietary zinc intake; serum zinc concentration; zinc status

INTRODUCTION

A considerable body of information now exists exploring the nutritional content and health implications of vegetarian diets. In summarising the available scientific evidence, the American Dietetic Association and Dietitians of Canada affirmed that 'appropriately planned vegetarian diets are healthful, nutritionally adequate and may provide health benefits in the prevention and treatment of certain diseases'.[1] Vegetarian diets are reported to contain less saturated fatty acids and cholesterol and more folate, fibre and phytochemicals than omnivorous diets.[1,2] On the other hand, studies have shown that some micronutrients, including zinc,[3] are less bioavailable and present in lower amounts when obtained from plant-derived compared with animal food sources.

The importance of zinc in numerous biological processes suggests that it warrants special attention when evaluating the nutritional adequacy of vegetarian diets. The many roles of zinc include enzyme action, stabilisation of cell membranes, regulation of gene expression and cell signalling.[4] In zinc deficiency a diverse range of symptoms is reported, including growth retardation, impaired immunity and endocrine dysfunction.[5] Genomic analysis suggests a link between zinc and chronic diseases,[6,7] and zinc deficiency is reported to contribute significantly to the global burden of disease.[8] Although severe zinc deficiency is relatively rare in developed countries, based on population estimates of dietary zinc intake, mild deficiency states are believed to be highly prevalent.[9]

Studies that explore the zinc status of populations that consume plant-based diets are of varied quality and design and inconsistent in their findings. The aim of the present paper is to undertake a systematic review and meta-analysis of the association between habitual vegetarian diets and dietary zinc intake and status in humans.

METHODS

Search strategy

A literature search was conducted of Medline, PubMed, Web of Science and Scopus electronic databases up to June 2012 using the search strategy ('zinc' OR 'Zn') AND ('plant-based' OR 'vegetarian*' OR 'vegan*'). Studies were restricted to human investigations

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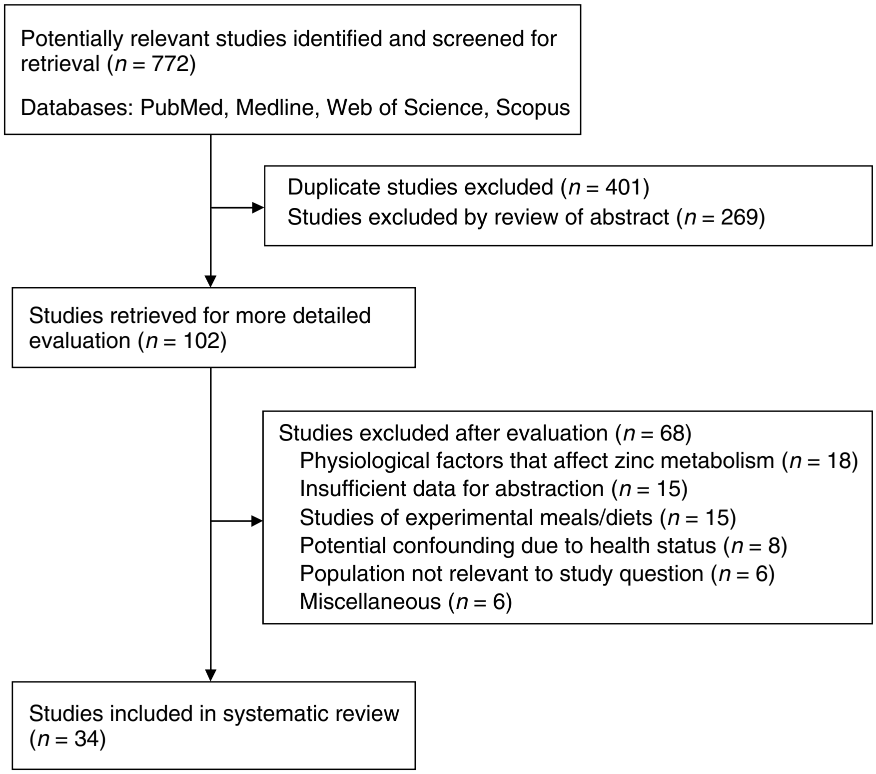

Figure 1. QUOROM (PRISMA)[10] flow diagram of study selection.

published in English. Reference lists of retrieved studies were inspected for additional relevant articles. The PRISMA flow chart describing the studies identified from the search strategy is depicted in Fig. 1.[10]

Study selection

The title, abstract and descriptors of each study identified in the search were screened to determine the study's eligibility for full review. The full report was retrieved if the study potentially or definitely investigated zinc intake and/or status in a vegetarian population. Two investigators (SS and MF) independently reviewed each full report to determine if the depicted study met the inclusion criteria.

Data extraction

Data from all selected studies were abstracted by two investigators (SS and MF), and any differences were resolved by discussion. The data extraction worksheet included descriptive information such as the study authors, year of publication, country of study and number, gender and dietary patterns (vegan (VN), lacto-vegetarian (V-L), ovo-vegetarian (V-O), ovo-lacto-vegetarian (V-OL), vegetarian undefined (VU), low meat (LoM), non-vegetarian (NV)) of participants. Vegetarian populations were defined as LoM if study participants were described as consuming limited amounts of meat, fish or poultry. If more than one dietary pattern was included in a diet group and unable to be treated separately, the least restrictive definition was used (for example, a group that included VN, V-L and V-OL would be defined as V-OL). The methodology of each study was assessed using questions adapted from the STROBE checklist,[11] and data were extracted that related to zinc intake and/or zinc status outcomes. Units were converted to SI measures where applicable, and measures of variability were recorded as standard error (SE).

Statistical analyses

Separate and 'combined' meta-analyses of dietary zinc intake and serum zinc concentration were carried out on those studies with a control group using the Comprehensive Meta-Analysis package, version 2 (Biostat, Englewood, NJ, USA; www.meta-analysis.com). Results for dietary zinc intake (mg day^{-1}) and serum zinc concentration (μmol L^{-1}), analysed separately, were generated using vegetarian (VN, V-L, V-OL, VU or LoM) minus control group (NV) values and are summarised in the form of forest plots. Secondary analyses were conducted after grouping the studies by vegetarian status, gender and according to whether the study was conducted in a developed (World Bank Income Group 1) or developing (World Bank Income Group 2, 3, 4) country. Results are expressed as mean difference $\pm$ SE, with the standard error of difference calculated using the independence of vegetarian and control groups. In the combined analyses, results were expressed as the standardised mean difference to account for differences in the scales for measuring zinc intake and serum zinc. Where both the dietary zinc intake and serum zinc concentration are reported in the same study, dietary zinc intake was chosen as the preferred measure to be included in the combined analyses. The random effects model was utilised rather than the fixed effects approach, as differences in study design among included studies precluded the assumption of a common effect size. Sensitivity analyses were performed to determine the impact of studies with large numbers. Funnel plots of SE by mean were generated for each outcome to assess publication bias. Smaller, less precise studies appear at the bottom of a funnel plot and will have more variable effect size, while larger, more precise studies will have less varied effect size,

Table 1. Reasons for study exclusion

Reason for exclusion	References
Insufficient data for abstraction	Agte, 2005a; Bhattacharya, 1985; Bindra, 1986; Brants, 1990; Chiplonkar, 2007; Dabek, 1994; Ellis, 1987; Fairweather-Tait, 1988; Gibson, 1983; Hunt, 1988; Khokar, 1994; Kies, 1988; Rohrig, 1998; Swerts, 1993; Wells, 2003
Physiological factors that affect zinc metabolism	Abraham, 1985; Abu-Assal, 1984; Bates, 1993; Campbell-Brown, 1985; Chiplonkar, 2010; Donovan, 1995; Donovan, 1996; Gibson, 1989; Gibson, 1991; Gibson, 1993; Huddle, 1998; King, 1981; Sharma, 2002; Taylor, 2004; Thane, 2000; Tupe, 2010; Ward, 1988; Wyatt, 2000
Potential confounding due to health status	Bakan, 1993; Brewer, 1993; Chiplonkar, 2004; Haugen, 1993; Hogg-Kollars, 2011; Rauma, 1993; Srikumar, 1992a; Tannhauser, 2001
Population not relevant to study question	Barr, 1994; Benemariya, 1993; Chen, 1992; Gibson, 2001; Thurnham, 1985; Wein, 1995
Studies of experimental meals/diets	Agte, 1994; Agte, 2005b; Chiplonkar, 2005; Freeland-Graves, 1980; Ganapathy, 1981; Hunt, 1998; Hunt, 2001; Johansson, 1994; Johnson, 1992; Kristensen, 2006; O'Connor, 2011; Rosado, 1992; Rosado, 2005; Srikumar, 1992b; Turner-McGrievy, 2004
Miscellaneous	Abdulla, 1981; Abdulla, 1984; Berglund, 1994; Garg, 2005; Karanja, 1999; Pushpanjali, 1995

closer to the 'true' value. For instance, an absence of studies in one area of the plot (e.g. small studies that have not found significant results) is evidence of publication bias.

RESULTS

Study characteristics

Many studies[12–79] were excluded from further evaluation, and the primary reasons for their exclusion are provided in Table 1. Thirty-four studies[80–113] qualified for inclusion in the present systematic review, all of which were observational in design. The included studies reported on one or more of the following outcome measures: zinc intake (24 studies), serum zinc (18 studies), hair zinc (three studies), red blood cell (RBC) zinc (two studies) and urinary zinc (one study). Nine studies reported on both zinc intake and at least one biomarker of zinc status (see Online Supplementary Table in 'Supporting information'). Excluding the largest study[83] ($n = 55\,319$), the average number of subjects per study was 100.

Of the 34 included studies, 26 studies[80,82,83,85–89,92–98,100–102,105–110,112,113] compared males and/or females consuming vegetarian dietary patterns with NV control groups, allowing meta-analyses to be conducted of the dietary zinc intake (35 comparisons) and serum zinc concentration (23 comparisons) (Online Supplementary Table). The eight studies without NV control groups[81,84,90,91,99,103,104,111] compared males and females within one dietary pattern, compared one vegetarian group with another or had no control group.

Dietary zinc intake

In a meta-analysis of all studies that compared the dietary zinc intake of vegetarian groups with NV controls (18 studies, 35 comparisons), the zinc intake of vegetarians was found to be lower than that of NV (-0.88 ± 0.15 mg day^{-1}, $P < 0.001$; Fig. 2).

In secondary analyses (Table 2), there was no significant difference in the zinc intake of V-OL (ten studies, 16 comparisons) compared with NV controls (-0.28 ± 0.25 mg day^{-1}, $P = 0.271$), while VN (eight studies, ten comparisons), LoM (three studies, four comparisons), VU (three studies, three comparisons) and V-L (two studies, two comparisons) groups were found to have a lower zinc intake than controls. Vegetarians had a lower dietary zinc intake than controls in both male and female populations; when categorised by country type, the difference in dietary zinc intake of vegetarians was greater in developing compared with developed countries (-1.90 ± 0.87 mg day^{-1}, $P < 0.05$ and -0.80 ± 0.16 mg day^{-1}, $P < 0.001$ respectively; Table 2).

In sensitivity analyses, the lower zinc intakes of vegetarians overall (Fig. 2) and when categorised by vegetarian status, gender or country type (Table 2) were no longer significant after removal of the largest study[83] comparing the dietary zinc intake of vegetarian groups with NV controls ($n = 55\,319$; four comparisons). No other impact of individual or particular groups of studies was observed. There was no evidence of publication bias in the funnel plots of SE by mean.

Serum zinc concentration

Of those studies that compared the serum zinc concentration of vegetarian groups with NV controls (13 studies, 23 comparisons), values were lower in the vegetarian populations (-0.93 ± 0.27 µmol L^{-1}, $P = 0.001$; Fig. 3).

In secondary analyses (Table 2), the VN (four studies, six comparisons) and VU (three studies, four comparisons) categories had lower serum zinc compared with controls (-1.17 ± 0.45 µmol L^{-1}, $P < 0.01$ and -1.78 ± 0.45 µmol L^{-1}, $P < 0.001$ respectively), as did female vegetarians (-1.40 ± 0.56 µmol L^{-1}, $P = 0.01$) and vegetarian populations from developing countries (-0.76 ± 0.27 µmol L^{-1}, $P < 0.01$).

For serum zinc concentrations, there was no impact of individual or particular groups of studies on effect sizes in sensitivity analyses and there was no evidence of publication bias in the funnel plots of SE by mean.

Combined analyses

In the overall combined analysis of dietary zinc intake and serum zinc concentration, expressed as standardised mean differences and favouring zinc intake data where available and serum zinc where not, vegetarians had significantly lower zinc status compared with NV controls (-0.33 ± 0.05 units, $P < 0.001$; Fig. 4). The result remained significant (-0.28 ± 0.10 units, $P = 0.004$) after removal of the largest study[83] ($n = 55\,319$; four comparisons). No other impact of individual or particular groups of studies was observed. There was no evidence of publication bias in the funnel plots of SE by mean.

When grouped according to gender, the difference between measures of zinc status in vegetarians compared with controls was greater in females (-0.40 ± 0.08 units, $P < 0.001$) compared with males (-0.29 ± 0.08 units, $P < 0.001$), while not reaching

Model	Study name	Difference in means	Standard error	p-Value
	Alexander et al., 1994 (c,g)	-0.80	0.66	0.226
	Ball et al., 2000 (b,g)	-1.60	0.57	0.005
	Ball et al., 2000 (a,g)	-1.60	0.85	0.061
	Ball et al., 2000 (a,d)	-0.80	1.07	0.453
	Davey et al., 2003 (b,f)	-1.49	0.03	0.000
	Davey et al., 2003 (b,d)	-1.94	0.06	0.000
	Davey et al., 2003 (a,f)	-1.34	0.05	0.000
	Davey et al., 2003 (a,d)	-1.79	0.09	0.000
	Deriemaeker et al., 2011 (b,f)	1.00	1.96	0.610
	Deriemaeker et al., 2011 (a,f)	1.40	1.59	0.378
	Deriemaeker et al., 2010 (b,f)	4.70	0.45	0.000
	Deriemaeker et al., 2010 (a,f)	4.50	0.79	0.000
	Faber et al., 1986 (b,f)	-2.30	0.68	0.001
	Faber et al., 1986 (a,f)	-5.10	1.50	0.001
	Freeland-Graves et al., 1980 (c,e)	-1.40	2.48	0.572
	Freeland-Graves et al., 1980 (c,f)	-1.50	1.52	0.324
	Freeland-Graves et al., 1980 (c,d)	-4.80	3.09	0.121
	Haddad et al., 1999 (b,d)	-3.20	1.32	0.015
	Haddad et al., 1999 (a,d)	2.10	1.59	0.187
	Janelle et al., 1995 (b,f)	-2.80	0.93	0.003
	Janelle et al., 1995 (b,e)	-2.90	1.11	0.009
	Janelle et al., 1995 (b,d)	-2.60	1.47	0.076
	Kelsay et al., 1988 (b,f)	-0.18	1.46	0.902
	Kelsay et al., 1988 (a,f)	1.14	1.54	0.460
	Kim et al., 2007 (b,h)	-1.71	0.39	0.000
	Levin et al., 1986 (b,f)	-0.60	0.86	0.485
	Levin et al., 1986 (a,f)	0.50	1.01	0.621
	Li et al., 2000 (a,f)	-2.30	0.60	0.000
	Li et al., 2000 (a,d)	-1.20	0.87	0.170
	Nieman et al., 1989 (b,f)	-0.01	0.73	0.989
	Pohit et al., 1985 (a,h)	0.73	2.25	0.746
	Raghunath et al., 2006 (c,h)	-0.80	0.22	0.000
	Rauma et al., 1995 (b,d)	1.00	1.00	0.317
	Wilson et al., 1999 (a,g)	-0.70	0.96	0.467
	Wilson et al., 1999 (a,d)	-0.10	1.07	0.925
Fixed		-1.50	0.02	0.000
Random		-0.88	0.15	0.000

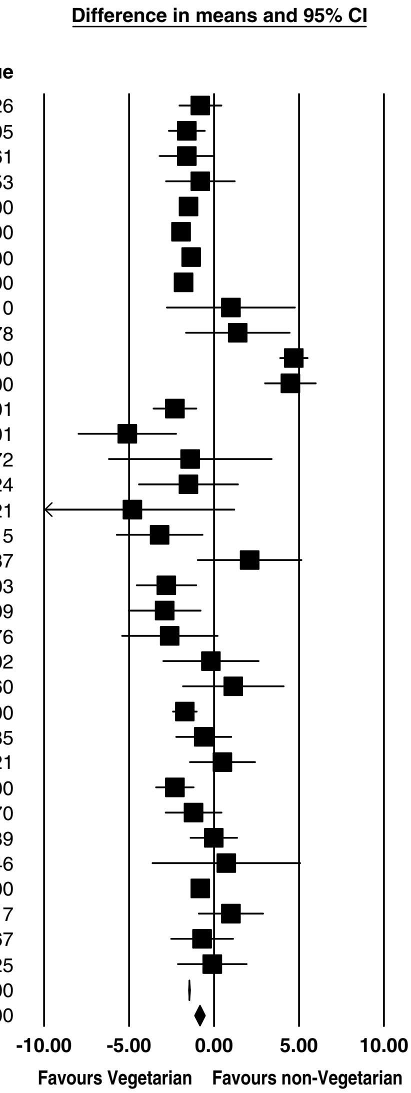

Figure 2. Overall ungrouped analysis of dietary zinc intake (mg day^{-1}) in vegetarians compared with NV controls: a, male; b, female; c, male & female; d, vegan (VN); e, lacto-vegetarian (V-L); f, ovo-lacto-vegetarian (V-OL); g, low meat (LoM); h, vegetarian undefined (VU). Upon removal of the largest study[83] (four comparisons, $n = 55\,319$), the result was no longer significant (-0.63 ± 0.42 mg day^{-1}, $P = 0.14$). There was no evidence of publication bias in the funnel plots of SE by mean.

significance in those studies with combined male and female populations (-0.21 ± 0.12 units, $P = 0.06$).

Other outcomes

Owing to insufficient numbers of comparisons, meta-analyses were unable to be conducted for other measures of zinc status. Of the two studies that compared hair zinc levels between vegetarians and NV controls, one reported no difference in hair zinc of male or female VN compared with NV[110] and the other reported no difference in hair zinc of female V-OL compared with controls.[113] One study[100] reported no difference in RBC zinc concentrations between LoM and NV controls.

DISCUSSION

The present meta-analysis found that dietary zinc intakes and serum zinc concentrations are lower in populations that follow habitual vegetarian diets compared with NV control groups. Combined analyses of the dietary zinc intake and serum zinc concentration support the possibility of a gender difference in zinc status, with the difference in values between vegetarians and non-vegetarians being wider in females than in males.

The recommended dietary intake (RDI) for zinc varies between countries, being 14 mg day^{-1} for men and 8 mg day^{-1} for women in Australia[114] and 9.5 mg day^{-1} for men and 7.0 mg day^{-1} for women in the UK.[115] In the present meta-analysis, vegetarians overall were found to consume 0.9 mg day^{-1} less dietary zinc than NV populations, which represents a difference of approximately 6–12% of the RDI. No significant difference was observed in the zinc intake of V-OL compared with NV, while the difference was greater in VN (-1.7 mg day^{-1}). Although the difference in dietary zinc intake between vegetarian and NV groups shown in the present meta-analysis is modest, it may be important for certain categories of vegetarians, such as those who are at the lower end of the range of adequate intakes and who do not take supplements, and vegetarian populations that consume large amounts of phytic acid (PA).

Table 2. Secondary analyses of differences in dietary zinc intake and serum zinc concentration in studies with non-vegetarian controls when grouped by vegetarian status, gender and country type

	Dietary zinc intake (mg day^{-1})				Serum zinc concentration (µmol L^{-1})			
Modulator	*n* (studies, comparisons)	Mean difference[b]	SE	*P* value	*n* (studies, comparisons)	Mean difference[b]	SE	*P* value
Vegetarian status								
VN	8, 10	−1.65	0.19	0.000[c]	4, 6	−1.17	0.45	0.009
V-L	2, 2	−2.65	1.02	0.009	1, 1	−1.23	0.94	0.191
V-OL	10, 16	−0.28	0.25	0.271[d]	6, 9	−0.75	0.42	0.077
LoM	3, 4	−1.24	0.36	0.001	2, 3	0.11	0.81	0.893
VU	3, 3	−1.13	0.42	0.007	3, 4	−1.78	0.45	0.000
Gender								
M	11, 15	−0.71	0.28	0.011[e]	8, 9	−0.75	0.41	0.069
F	12, 15	−0.90	0.27	0.001[f]	8, 8	−1.40	0.56	0.012
M & F	3, 5	−0.83	0.20	0.000	4, 6	−0.20	0.33	0.542
Country type[a]								
Developed	15, 31	−0.80	0.16	0.000[g]	8, 14	−1.03	0.55	0.060
Developing	3, 4	−1.90	0.87	0.029	5, 9	−0.76	0.27	0.005

Abbreviations: F, female; LoM, low meat; M, male; V-L, lacto-vegetarian; VN, vegan; V-OL, ovo-lacto-vegetarian; VU, vegetarian undefined.
[a] Defined as developed (World Bank Income Group 1) or developing (World Bank Income Group 2, 3, 4).
[b] Minus signs (−) denote that vegetarians have lower values.
[c−g] In sensitivity analyses, exclusion of the largest study[83] resulted in changes to dietary intake results (mean ± SE) as follows: [c] −0.82 ± 0.62, $P = 0.185$; [d] −0.08 ± 0.90, $P = 0.925$; [e] −0.16 ± 0.70, $P = 0.823$; [f] −0.84 ± 0.82, $P = 0.305$; [g] −0.44 ± 0.51, $P = 0.388$.

PA is abundant in diets that include unrefined cereals, pulses and whole grains as staples,[116] as are common in lower-income countries. PA forms poorly soluble complexes with zinc in the gastrointestinal tract, resulting in reduced zinc absorption or reabsorption,[117,118] and the World Health Organization estimates zinc bioavailability based on the molar ratio of PA to zinc in the diet.[119] Although it has been suggested that the requirement for dietary zinc may be as much as 50% greater for some vegetarians,[120] the PA content of different vegetarian diets is not always known.

In the present meta-analysis, the serum zinc concentration was 0.9 µmol L^{-1} lower in vegetarians compared with NV populations. As with dietary zinc intake, no significant difference was observed in the serum zinc levels of V-OL compared with NV, while the difference was greater in VN (−1.2 µmol L^{-1}). The difference in the serum zinc concentration may be important for vegetarian populations at the lower end of the reference range (10–18 µmol L^{-1}). Serum or plasma zinc is the most widely accepted measure of zinc status,[5,121] and the lower serum zinc concentrations in populations that follow habitual vegetarian diets may reflect the lower zinc intake or bioavailability of vegetarian diets. In an 8 week cross-over intervention study comparing controlled V-OL and NV diets, participants demonstrated a 14% reduction in zinc intake and a 21% reduction in absorptive efficiency after the V-OL diet and a 5% reduction in plasma zinc within the normal range, but zinc balance was maintained.[51] The effectiveness of homeostatic mechanisms in maintaining plasma zinc concentrations within defined limits, even in the presence of dietary zinc restriction,[122] renders it an insensitive marker of zinc status. The development of a specific and reliable zinc biomarker is necessary to clarify the relationship between dietary zinc intake and zinc status.

Limitations of the existing literature on vegetarian nutrition relate to the lack of specificity in definitions ascribed to vegetarian populations for research purposes.[123,124] 'Plant-based' or 'vegetarian' diets encompass a spectrum of dietary patterns (Table 3). In strict terms, an individual is considered a vegetarian if they abstain from eating all flesh foods (meat, poultry, fish); those who follow a total vegetarian or 'vegan' diet consume only plant-derived foods, excluding all foods of animal origin, including eggs and dairy products. In categorising populations for the meta-analysis, it was observed in numerous cases that the term 'vegetarian' was not defined. In other instances, participants were included in particular vegetarian categories despite not strictly meeting classic criteria (for example, individuals who consumed limited amounts of animal flesh were described as V-OL) or grouped together despite restricting animal products to varied degrees (for example, VN were included with V-OL). The limited statistical power of many studies, especially those investigating VN diets, restricted the exploration of the effects of subgroup modulators such as vegetarian status, gender and country type. Similarly, studies that did not include an NV comparison group were unable to be included in the meta-analysis.

Other limitations of study design and reporting are not unique to researchers studying vegetarian diets but apply to nutrition research more broadly. Detailed dietary intakes, supplement use and other lifestyle-related practices need to be ascertained and reported using appropriate methodologies. Inclusion criteria and participant characteristics (including the age and health status of participants) were not always stated, and in a number of cases dietary information was collected but no zinc intake data was presented. More generally, details of laboratory protocols (including sample preparation and instrumentation) were not always defined.

Strengths of the present meta-analysis include the use of the random effects model of meta-analysis, which allows for heterogeneity among studies, and the carrying out of sensitivity analyses and assessments of publication bias. In sensitivity analyses, one study[83] was found to have an impact on effect size in the investigations of dietary zinc intake in vegetarians compared with controls. The study explored the baseline characteristics of the

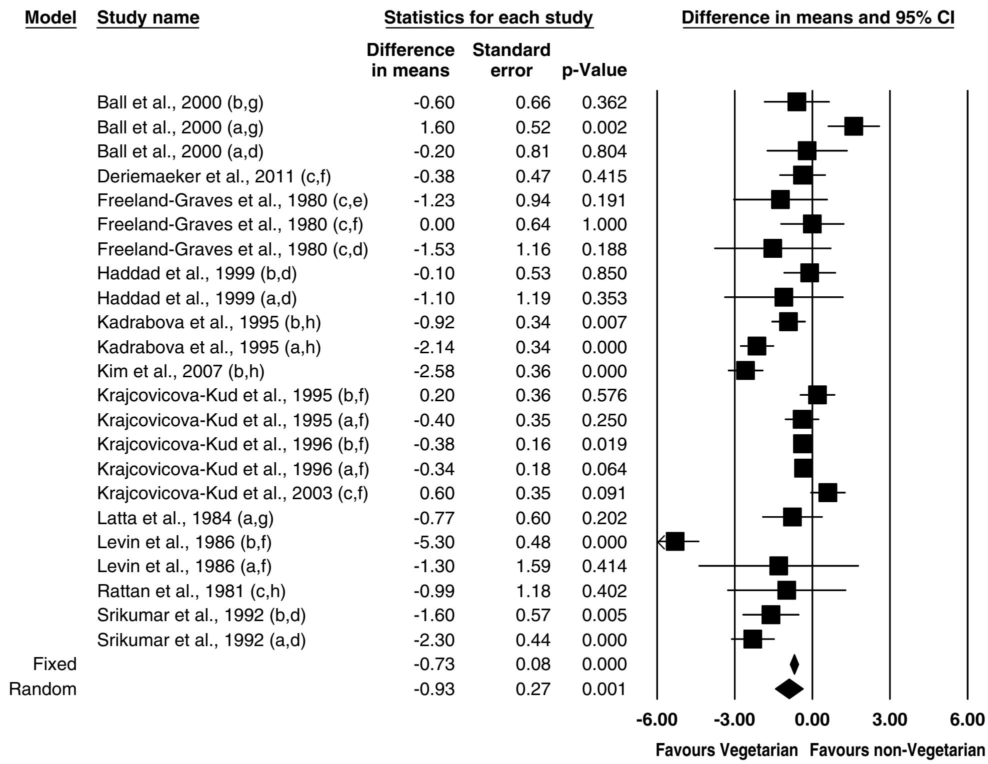

Figure 3. Overall ungrouped analysis of serum zinc concentration (μmol L^{-1}) in vegetarians compared with NV controls: a, male; b, female; c, male & female; d, vegan (VN); e, lacto-vegetarian (V-L); f, ovo-lacto-vegetarian (V-OL); g, low meat (LoM); h, vegetarian undefined (VU). No impact of individual or particular groups of studies on effect sizes was observed in sensitivity analyses. There was no evidence of publication bias in the funnel plots of SE by mean.

Table 3. Classification of vegetarian eating patterns

Type of vegetarian	Definition
Classic	
Ovo-lacto-/lacto-ovo-, ovo-, lacto-vegetarian	Diet is devoid of all flesh foods but includes egg (ovo) and/or dairy (lacto) products
Vegan	Diet excludes all animal products
Variant	
Macrobiotic diet	Dietary regimen that involves eating grains as a staple food supplemented with vegetables, beans and fruit, avoiding highly processed foods and most animal products
Raw vegan	Diet excludes all food of animal origin and all food cooked above 48 °C
Fruitarian	Diet consists primarily of fruit but may include nuts, seeds and vegetables that are harvested without harming the plant
New	
Meat reductionist	Diet includes only limited amounts of animal flesh
Semi-vegetarian	Seafood and poultry are the only animal flesh consumed
Pesco-vegetarian	Seafood/fish is the only animal flesh consumed
Pollo-vegetarian	Poultry is the only animal flesh consumed

participants in the EPIC-Oxford cohort and was of large numbers ($n = 55\,319$). The finding of a lower zinc intake in vegetarian compared with NV populations was no longer significant after removal of the four comparisons contributed by the study; however, the result of the combined analyses of the dietary zinc intake and serum zinc concentration remained significant. The assessment of the study's methodology did not highlight any quality or design issues that would undermine the reliability of the meta-analysis; nonetheless, its impact on effect size suggests the desirability of repeating the meta-analysis when further studies become available.

The present meta-analysis quantifies the differences in the dietary zinc intake and serum zinc concentration in vegetarian compared with NV populations and provides evidence that not all vegetarian categories impact zinc status to the same extent. Populations who habitually consume strict vegetarian diets have lower zinc intakes and status. Dietary practices that increase zinc bioavailability, the consumption of foods fortified with zinc or low-dose supplementation are strategies that should be considered for improving the zinc status of vegetarians with low zinc intakes or serum zinc concentrations at the lower end of the reference range. Future developments in zinc bioavailability and biomarker

Model	Study name	Std diff in means	Standard error	p-Value
	Alexander et al., 1994 (c,g)	-0.242	0.201	0.228
	Ball et al., 2000 (b,g)	-0.693	0.255	0.007
	Ball et al., 2000 (a,g)	-0.481	0.260	0.064
	Ball et al., 2000 (a,d)	-0.281	0.376	0.455
	Davey et al., 2003 (b,f)	-0.604	0.011	0.000
	Davey et al., 2003 (b,d)	-0.763	0.026	0.000
	Davey et al., 2003 (a,f)	-0.504	0.019	0.000
	Davey et al., 2003 (a,d)	-0.655	0.035	0.000
	Deriemaeker et al., 2011 (b,f)	0.152	0.299	0.610
	Deriemaeker et al., 2011 (a,f)	0.471	0.542	0.385
	Deriemaeker et al., 2011 (c,f)	-0.213	0.261	0.415
	Deriemaeker et al., 2010 (b,f)	1.758	0.198	0.000
	Deriemaeker et al., 2010 (a,f)	1.354	0.265	0.000
	Faber et al., 1986 (b,f)	-1.251	0.402	0.002
	Faber et al., 1986 (a,f)	-1.408	0.461	0.002
	Freeland-Graves et al., 1980 (c,e)	-0.175	0.310	0.572
	Freeland-Graves et al., 1980 (c,f)	-0.202	0.205	0.326
	Freeland-Graves et al., 1980 (c,d)	-0.600	0.391	0.125
	Haddad et al., 1999 (b,d)	-0.989	0.432	0.022
	Haddad et al., 1999 (a,d)	0.590	0.457	0.196
	Janelle et al., 1995 (b,f)	-0.900	0.313	0.004
	Janelle et al., 1995 (b,e)	-0.872	0.350	0.013
	Janelle et al., 1995 (b,d)	-0.732	0.424	0.084
	Kadrabova et al., 1995 (b,h)	-0.809	0.314	0.010
	Kadrabova et al., 1995 (a,h)	-1.881	0.362	0.000
	Kelsay et al., 1988 (b,f)	-0.047	0.379	0.902
	Kelsay et al., 1988 (a,f)	0.296	0.402	0.463
	Kim et al., 2007 (b,h)	-0.709	0.167	0.000
	Krajcovicova-Kud et al., 1995 (b,f)	0.128	0.231	0.579
	Krajcovicova-Kud et al., 1995 (a,f)	-0.273	0.248	0.270
	Krajcovicova-Kud et al., 1996 (b,f)	-0.358	0.154	0.020
	Krajcovicova-Kud et al., 1996 (a,f)	-0.304	0.166	0.066
	Krajcovicova-Kud et al., 2003 (c,f)	0.230	0.138	0.097
	Latta et al., 1984 (a,g)	-0.377	0.291	0.195
	Levin et al., 1986 (b,f)	-0.153	0.219	0.486
	Levin et al., 1986 (a,f)	0.093	0.189	0.621
	Li et al., 2000 (a,f)	-0.767	0.207	0.000
	Li et al., 2000 (a,d)	-0.369	0.270	0.172
	Nieman et al., 1989 (b,f)	-0.005	0.332	0.989
	Pohit et al., 1985 (a,h)	0.173	0.536	0.746
	Raghunath et al., 2006 (c,h)	-0.500	0.137	0.000
	Rattan et al., 1981 (c,h)	-0.258	0.286	0.367
	Rauma et al., 1995 (b,d)	0.316	0.318	0.320
	Srikumar et al., 1992 (b,d)	-0.807	0.271	0.003
	Srikumar et al., 1992 (a,d)	-1.149	0.273	0.000
	Wilson et al., 1999 (a,g)	-0.186	0.257	0.468
	Wilson et al., 1999 (a,d)	-0.035	0.374	0.925
Fixed		-0.588	0.008	0.000
Random		-0.327	0.047	0.000

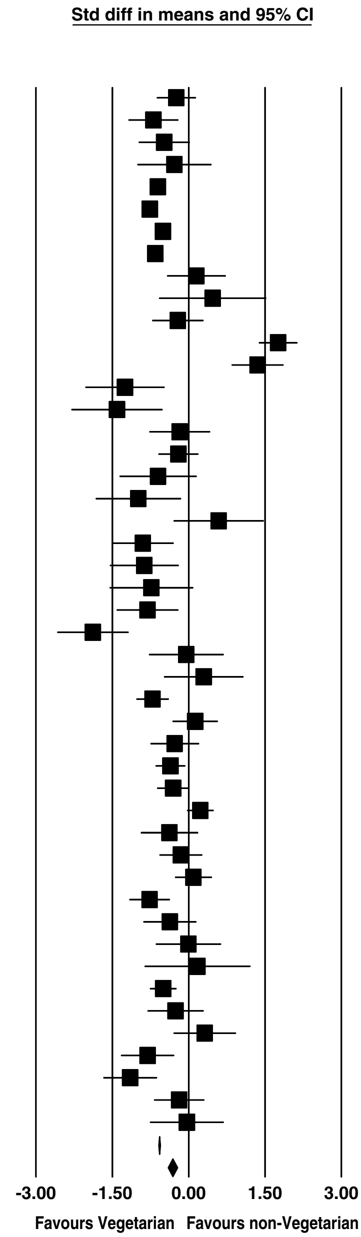

Figure 4. Overall ungrouped combined analysis of dietary zinc intake and serum zinc concentration in vegetarians compared with NV controls expressed as standardised difference in means: a, male; b, female; c, male & female; d, vegan (VN); e, lacto-vegetarian (V-L); f, ovo-lacto-vegetarian (V-OL); g, low meat (LoM); h, vegetarian undefined (VU). The result remained significant (-0.28 ± 0.10 units, $P = 0.004$) upon removal of the largest study[83] (four comparisons, $n = 55\,319$). There was no evidence of publication bias in the funnel plots of SE by mean.

research will allow the relationships between zinc intake, zinc status and health to be elucidated further.

SUPPORTING INFORMATION

Supporting information may be found in the online version of this article.

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