

Adherence to the vegetarian diet may increase the risk of depression: a systematic review and meta-analysis of observational studies

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Context: Several epidemiological studies have investigated the association between a vegetarian diet and risk of depression, but because of inconsistency between studies, the exact association remains unclear. **Objective:** In this systematic review and meta-analysis, the relationship between vegetarian diets and risk of depression in observational studies was evaluated. **Data sources:** The Medline, Embase, Scopus, ISI Web of Science, and Cochrane Library databases were searched from inception through September 1, 2020. **Study selection:** Observational studies were included that examined mean levels of depression and risk for depression in vegetarians compared with nonvegetarians. **Data extraction:** Pooled effect sizes were estimated using the random-effects model and were reported as standardized mean differences or odds ratios (ORs) with their corresponding 95% CIs. Heterogeneity was tested using the I^2 statistic. **Results:** Combining 9 effect sizes in this meta-analysis illustrated that adherence to a vegetarian diet was associated with a 53% greater risk of depression compared with that of omnivores (95%CI, 1.14–2.07; $I^2 = 69.1\%$). Subgroup analysis of depression risk suggested that results depended on the type of vegetarian diet and country where the study was conducted. For studies that assessed a semivegetarian diet (OR, 1.86; 95%CI, 1.42–2.44; $I^2 = 35.7\%$) and those conducted in Europe and the United States (OR, 1.45; 95%CI, 1.06–1.98; $I^2 = 73.2\%$), there was a positive association between a vegetarian diet and depression, but in lacto-ovo vegetarians and Asian countries, a null association was found. Comparing mean depression scores showed no evidence of difference between vegetarians and nonvegetarians ($n = 16$; standardized mean difference, 0.10; 95%CI, -0.01 to 0.21 ; $I^2 = 79.1\%$). **Conclusion:** Vegetarian diet significantly increased depression risk; however, the findings were not robust, and more studies are required to investigate the vegetarian diet and depression association.

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INTRODUCTION

Depression affects more than 264 million people from all age groups worldwide¹ and imposes a remarkable economic burden.² According to a World Health Organization report, unipolar depressive disorders, accounting for 4.3% of total disability-adjusted life-years in 2004, were the third leading cause of depression burden, and it is projected that they will move up to first place by 2030.² The pathophysiology of depression is complex and has not been fully elucidated; however, it might be a result of an interaction among psychological,³ environmental,⁴ and biochemical factors.⁵ In this context, dietary intake may influence mental health by affecting various biochemical risk factors.⁶

Vegetarian diets are based mostly on plant-derived foods,⁷ but their definitions in different studies may vary. Vegetarian diets can be classified into several subtypes according to the eliminated foods. These subtypes include (1) the vegan diet, which contains no animal-source foods; (2) the lacto-ovo vegetarian diet, which may contain eggs and dairy products but eliminates meat; (3) the pescovegetarian diet, which contains fish and limits the consumption of other meats to less than once per month; and (4) the semivegetarian diet, which refers to diet in which meats and fish are occasionally consumed (ie, less than once a week).⁸ Well-planned vegetarian diets generally are of higher quality in comparison with nonvegetarian diets^{9,10} and, due to their high contents of magnesium and antioxidants, may influence mental health by affecting serum levels of inflammatory biomarkers¹¹ and neurotransmitter synthesis.¹² On the other hand, because of limited food choices, vegetarian diets might not meet daily recommended intakes for all nutrients (eg, iron and vitamin B₁₂)^{13,14} and, consequently, disrupt the function of the central nervous system.^{15,16}

Although the health benefits of plant-based diets have been well established,^{11,17–22} evidence of an association of these diets and depression is controversial. Whereas some studies indicated an inverse association,^{23,24} others reported a direct or a null association between a vegetarian diet and depression.^{25–27} Two recent published meta-analyses in this context also suggested a null association between a vegetarian diet and either depression risk²⁸ or depression mean scores.²⁹ Nevertheless, the limitations of these meta-analyses may cause misleading results. For example, plant-based diets and vegetarian diets identified by posteriori methods may not meet the exact definition of a vegetarian diet and therefore cannot be combined with vegetarian diets, in particular, when the primary aim of the study is examining the effects of a vegetarian diet. Furthermore, some eligible articles have not been

included in these studies,^{25,30,31} and the studies lacked some relevant subgroup analyses, such as the type of vegetarian diet, the mean age of participants, and the continent on which the study was conducted. These factors are relevant, owing to inherent varieties in different vegetarian diets, as well as the influence of diverse cultural and socioeconomic factors on the composition of vegetarian diets (either in food or nutrient patterns) of people from different nations. Besides, motivations to adhere to a vegetarian diet (eg, better health, ethical concerns, socioeconomic factors)³² may vary by age and potentially affect the associations.

Therefore, a comprehensive meta-analysis in this regard is warranted. Hence, we conducted a systematic review and meta-analysis to explore whether adherence to a vegetarian diet is associated with the risk and mean score of depression, and if so, what factors might be the potential sources of heterogeneity between studies.

METHODS

Search strategy

This study was performed according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement.³³ Databases, including PubMed/Medline, Embase, Scopus, ISI Web of Science, and the Cochrane Library, were searched up to September 1, 2020, to find relevant studies. Search strategies for each database were defined using the following keywords: (“Diet, Vegetarian” OR “vegetarian” OR “vegetarians” OR “Diets, Vegetarian” OR “Vegetarian Diets” OR “Vegetarian Diet” OR “Vegetarianism” OR “vegans” OR “vegans” OR “vegan”) AND (“depression” OR “depressive disorder” OR “Depressive Symptoms” OR “Depressive Symptom” OR “Depressive Disorders” OR “depressive” OR “Mood Disorders” OR “Mood Disorder” OR “Affective Disorder” OR “Mental Disorders” OR “Mental Disorder” OR “Psychiatric Diagnosis” OR “Behaviour Disorders”). No time and language restrictions were applied. The study protocol was not registered anywhere.

Titles and abstracts of all retrieved articles were screened by 2 independent reviewers (S.Fazelian and F.H.), and relevant articles were identified according to the inclusion and exclusion criteria. Studies were excluded if they (1) were not original research (eg, published as a review, letter to the editor, commentary), (2) reported results for mental health or eating disorders but not depression, (3) were randomized controlled trials, (4) assessed postpartum depression, or (5) were animal model studies. Studies were also excluded if they examined the associations for plant-based diets or

vegetarian diets identified by posteriori methods, because they could not necessarily meet the exact definition of a vegetarian diet.³⁴ Studies were included when they met all the PICOS criteria (Table 1). Accordingly, studies were eligible to be included if they (1) were conducted with humans, (2) compared the risk of depression in any type of vegetarian diet with omnivores, (3) had an observational design (ie, cohort, case-control, or cross-sectional), and (4) reported odds ratios (ORs), relative risks (RRs), or hazard ratios (HRs), along with 95% CIs, for depression or compared mean score of depression between vegetarians and nonvegetarians. Finally, the full texts of articles were assessed if needed.

Data extraction

Two independent reviewers (S.Fazelian and F.H.) extracted the following information from the eligible articles: first author, publication year and country, study population, study design, sample size, sex and the average age of participants, duration of follow-up for cohort studies, types of vegetarian diets, instruments used to assess depression, and confounders adjusted for and effect sizes for association between vegetarian diet and depression risk. If there were different multivariate-adjusted models for the association between a vegetarian diet and depression, the model with the most adjustment was extracted.

The main types of vegetarian diets in this meta-analysis were considered as follows: vegan, lacto-ovo vegetarian, semivegetarian, and pesco-vegetarian diets. Vegan was defined as the elimination of any food from animal sources; lacto-ovo vegetarian was defined as the elimination of any food from animal sources, except for milk and egg; pesco-vegetarian and semivegetarian diets were defined as the elimination of meats and poultry, but not seafood, and elimination of red meat, respectively.⁸

Quality assessment

Two reviewers (S.Fazelian and F.H.) independently assessed the studies for their quality using the Newcastle Ottawa Scale (NOS).³⁵ The NOS is a validated questionnaire for observational and nonrandomized studies to evaluate the quality of studies based on the following items: population selection, comparability, and outcome. The NOS consists of 8 questions in 3 main domains: selection, comparability, and outcome. Cohort studies may receive a score ranging from 0 to 9, and cross-sectional studies are scored from 0 to 10 using this scale. In our meta-analysis, studies were classified as of high or low quality when their NOS score was >7 and <7, respectively.³⁶ All relevant studies were

enrolled in statistical analysis regardless of the quality score of the study.

Statistical analysis

Original articles that examined the risk of depression in any type of vegetarian diet compared with omnivores were included in this meta-analysis. To pool the association between a vegetarian diet and depression, risk estimates were extracted from each study and then calculated using the average of the natural logarithm ORs. For means, effect size was calculated via Hedges' *g* using the differences between means of depression (vegetarians vs omnivores) divided by their corresponding standard deviation.³⁷ The random-effects model based on the inverse-variance method was used to estimate the pooled effect size.^{38,39} To evaluate the heterogeneity between studies, the I^2 statistic was used. $I^2 > 50\%$ was considered as substantial heterogeneity,³⁹ and the potential sources of heterogeneity were explored using subgroup analysis. Subgroup analysis was performed on the basis of the type of vegetarian diet (semivegetarian, vegan, and lacto-ovo vegetarian), geographic location (Asia vs the United States and Europe), sex (male, female, and both sexes), age (< 50 years vs \geq 50 years), and study quality score (\leq 7 vs > 7). Egger and Begg regression tests and funnel plots were used to assess publication bias. Sensitivity analysis was done by removing any specific study to examine its effect on the overall estimate. The statistical significance level was defined as $P < 0.05$, and all statistical analyses were performed using Stata, version 11 (StataCorp, College Station, TX).

RESULTS

Search results

Figure 1 is the flow diagram for the databases search and study selection. Using the described search strategies, 921 studies were identified. After the removal of duplicates, 838 articles remained and were screened on the basis of their titles and abstracts, which resulted in the exclusion of 803 articles. Seven studies in which the association was investigated of plant-based diets or vegetarian diets identified by posteriori methods were excluded.^{40–46} After reviewing the full text of articles, 16 studies were identified that could be included in the present systematic review.^{23–27,30,31,47–55} Of these, 3 studies did not have enough information for meta-analysis and so only are summarized in the review,^{47,54,55} and 13 articles were included in the meta-analysis.^{23–27,30,31,48–53} Among these 13 studies, 6 reported the risk of depression in vegetarians compared with nonvegetarians,^{23,25–27,30,51} and 8 studies

Table 1 PICOS criteria for inclusion and exclusion of studies

Condition	Description
Participant	Human
Intervention	All types of vegetarian diets (including vegan, lacto-ovo vegetarian, semivegetarian, and pesco-vegetarian)
Comparison	Risk or mean score of depression between vegetarians and nonvegetarians
Outcome	Depression
Study designs	Cohort and cross-sectional

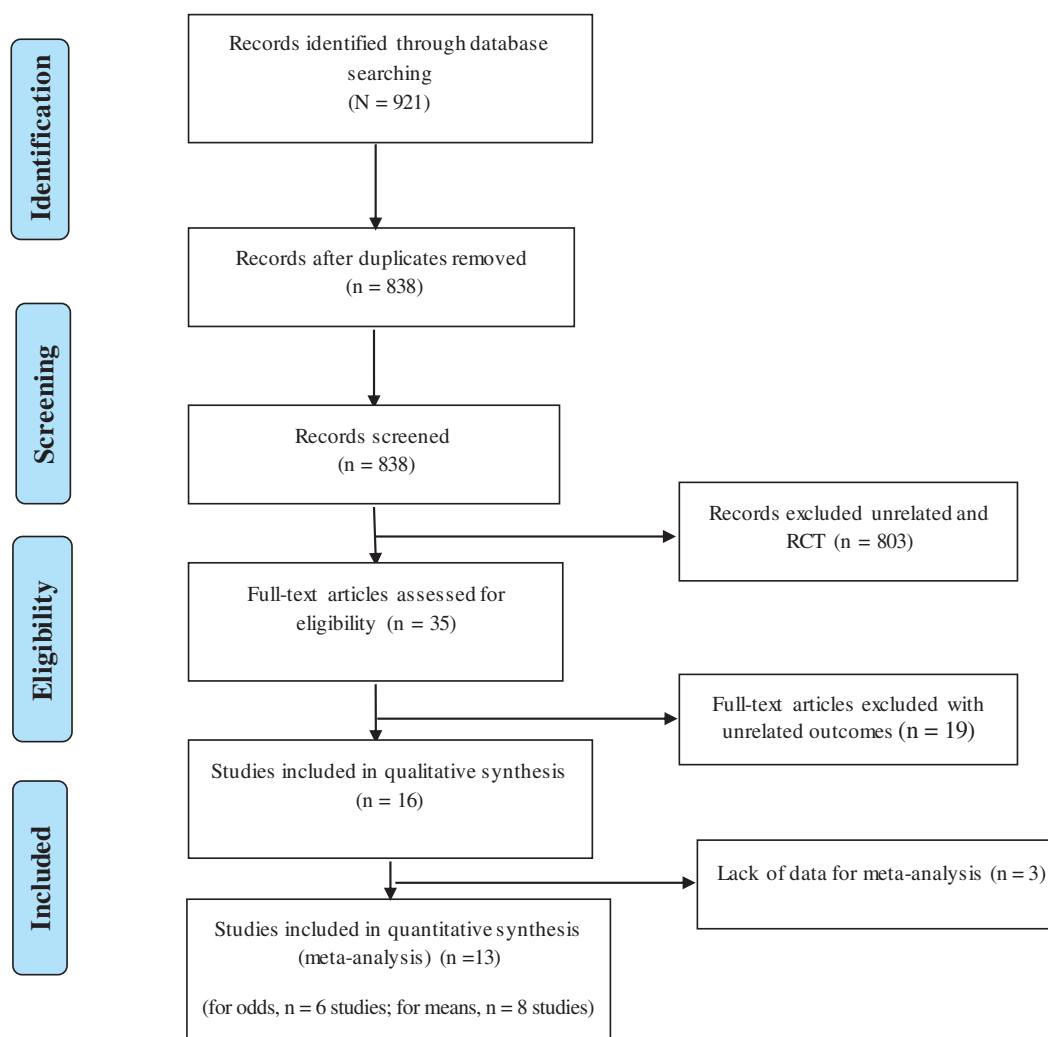


Figure 1 Flow diagram of database searches and study selection

compared the mean score of depression between vegetarians and omnivores.^{24,25,31,48–50,52,53}

Findings from systematic review

Fifteen cross-sectional studies,^{23–27,30,31,47–54} and 1 study with both cross-sectional and cohort data⁵⁵ were eligible to be included in the present systematic review. Thirteen of these studies were included in the meta-analysis and their characteristics are summarized in

Table 2.^{23–27,30,31,48–53} All studies were published between 1998 and 2020. Of these studies, 1 was conducted in Asia (China),²⁵ 8 studies were conducted in Europe (Finland, France, Swiss, England, Spain, and Germany),^{26,27,30,31,50–52,54} 5 studies were from the United States,^{23,24,48,49,53} and 1 study was conducted in Australia.⁴⁷ One study was a multinational study.⁵⁵ Participants in all the included studies were older than 13 years. Eight studies used a food frequency questionnaire to assess the dietary intakes of participants,^{23–}

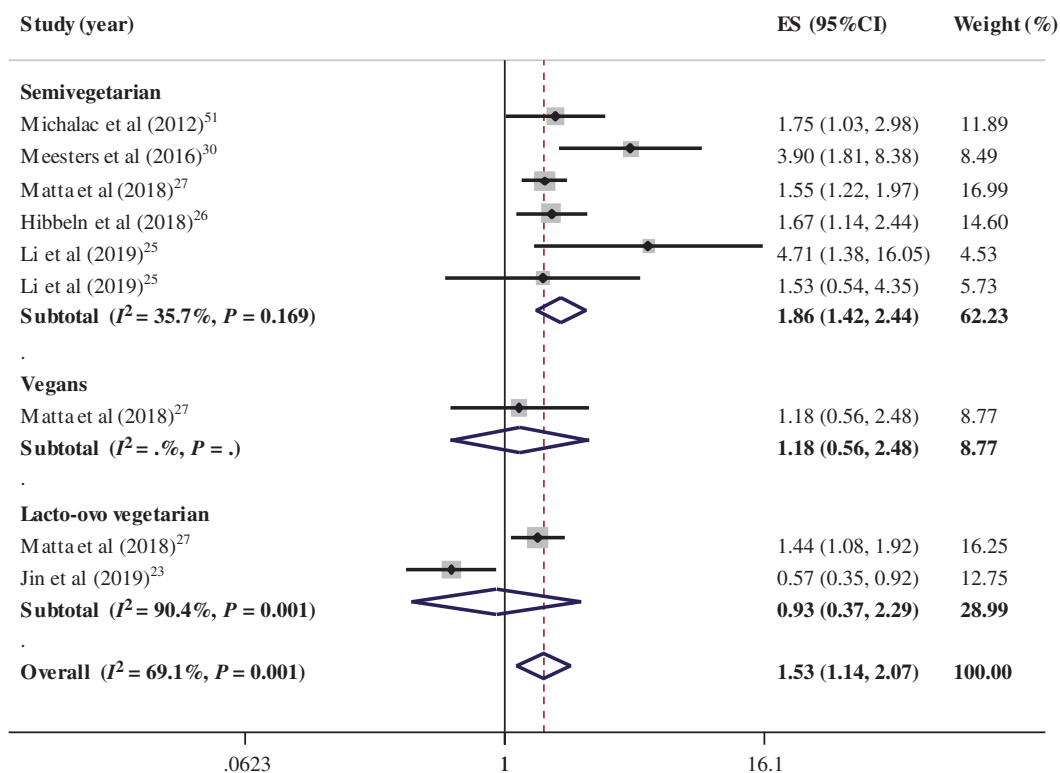


Figure 2 Forest plot of the association between vegetarian diet and risk of depression, based on type of vegetarian diet Abbreviation: ES, Effect Size

^{27,30,48,53} and 8 studies used brief questions about the regular consumption of food groups.^{31,47,49–52,54,55} One study was conducted with male participants only,²⁶ 3 with female participants only,^{31,47,50} and the rest were conducted with men and women.^{23–25,27,30,48,49,51–55}

The most common type of vegetarian diet evaluated by the included studies was the semivegetarian diet,^{24–26,30,31,47,49–51,53–55} followed by the lacto-ovo vegetarian diet.^{23,27,48–50,52,53} The vegan diet was assessed in 4 studies.^{27,48,52,53} Two effect sizes on the risk of depression in vegans and female vegetarians^{25,27} and 5 effect sizes on the mean depression score^{31,48,53} revealed no significant relationship, whereas 6 and 8 effect sizes indicated either higher risk^{25–27,30,51} or higher scores^{25,49,50,53} of depression, respectively, in vegetarians compared with nonvegetarians. One study found a lower risk²³ and 3 effect sizes showed a lower mean score^{24,52} for depression in vegetarians. One study suggested that vegetarian women had poorer mental health than did nonvegetarian women,⁴⁷ and authors of another report suggested no association between vegetarianism and mental health in the United States, Russia, or Germany, but a positive link in China.⁵⁵ A recent cross-sectional study also indicated that semivegetarians, but not lacto-ovo vegetarians, who had strong orthorexic tendencies had greater depressive symptoms compared with omnivores, but in those with lower and medium

tendencies to orthorexia, no significant difference was found.⁵⁴ Five studies used the Centre for Epidemiologic Studies Depression questionnaire for depression assessment,^{23,27,49,50,52} 4 studies used the Depression Anxiety Stress Scale,^{24,48,53,55} 1 study used the Hospital Anxiety and Depression Scale,³¹ and 1 study used the Edinburgh Postnatal Depression Scale.²⁶ The *Diagnostic and Statistical Manual of Mental Disorders*, the Geriatric Depression Scale, the Munich Composite International Diagnostic Interview, the Medical Outcomes Study Short-Form Health Survey, the Patient Health Questionnaire–9, and self-report measurement were other questionnaires that were used in the included studies.^{25,30,47,51,54} Quality scores ranged from 6 to 9.

Findings from meta-analysis

In total, 9 effect sizes extracted from 6 studies^{23,25–27,30,51} were included in the statistical analysis based on the ORs with 95% CIs. In comparison with omnivores, those who adhered to a vegetarian-based dietary pattern had 53% greater odds for depression (95%CI, 1.14–2.07; $P = 0.005$; $I^2 = 69.1\%$). In subgroup analysis according to the type of vegetarian diet, only the semi-vegetarian diet was positively associated with the odds of depression with a low heterogeneity (OR, 1.86; 95%CI, 1.42–

Table 2 Summary of characteristics of observational studies evaluating the relation between vegetarian diets and depression

Reference, country; study design	No. of participants, sex, and age (years)	Dietary assessment	Diet type	Depression assessment	Adjustment for confounders	Main findings	NOS score
Li et al. (2019) ²⁵ China; cross-sectional	1051 elderly men and women; ≥ 60 y	FFQ	Meat-based vs vegetable-based	GDS	Sex, education, occupation, marital status, residence, living alone, religion, annual family income, self-rated health, and drinking	A vegetable-based diet in the total sample size, and male sex, but not female, was associated with higher risk of depression.	8
Matta et al. (2018) ²⁷ France; cross-sectional	90 380 men and women; 18–69 y	24-item FFQ	Lacto-ovo vegetarian, vegan, pescovegetarian, and omnivore	CESD	Age, sex, education, income, fruits, vegetables, legumes, grains consumption, smoking, alcohol, and physical activity	Pesco-vegetarian and lacto-ovo vegetarian diets were associated with a higher risk of depression.	8
Meesters et al. (2017) ³⁰ Finland; cross-sectional	4905 men and women; mean age of 39 y	FFQ	Vegetarianism vs general population	DSM	Sex	In the total sample and women, but not men, vegetarianism diet was associated with greater risk of SAD.	7
Jin et al. (2019) ²³ United States; cross-sectional	892 women and men; 40–83 y	FFQ	Vegetarian vs nonvegetarian	CESD	Age, sex, education, occupation, marital status, income, smoking, BMI, physical activity, alcohol, cultural beliefs, and antidepressant use	Vegetable-based diet was inversely associated with the risk of depression.	8
Schreiner et al. (2019) ³¹ Switzerland; cross-sectional	1254 women; median age, 28–29 y	Brief questions about regular diet	Vegetarian vs nonvegetarian	HADS	–	Depression incidence was not significantly different between vegetarians and nonvegetarians.	6
Hibbeln et al. (2018) ²⁶ United Kingdom; cross-sectional	9668 adult males	FFQ	Vegetarian diet vs omnivore	EPDS	Housing tenure, number of children in the household, age, religion, family history of depression, child psychiatric contact, education, ethnicity, oily-fish consumption, alcohol and tobacco consumption,	Vegetarians had higher depression scores on average than nonvegetarians.	8

(continued)

Table 2 Continued

Reference, country; study design	No. of participants, sex, and age (years)	Dietary assessment	Diet type	Depression assessment	Adjustment for confounders	Main findings	NOS score
Beezhold et al. (2010) ²⁴ United States; cross-sectional	138 men and women; mean age, 40–45 y	FFQ	Vegetarian diet vs nonvegetarian	DASS	– marital and employment status.	Vegans reported less depression than did omnivores.	8
Forestell et al. (2018) ⁴⁹ United States; cross-sectional	6450 men and women; 16–47 y	General Eating Habits Scale	Vegetarian, semivegetarian, and omnivore	CESD	–	Vegetarians and semivegetarians were more neurotic and depressed than omnivores.	7
Lindeman et al. (2002) ⁵⁰ Finland; cross-sectional	2226 women; 13–74 y	Brief questions about the consumption of food groups in regular	Omnivore, semivegetarian, and vegetarian	CESD	–	Vegetarian and semivegetarian women were more depressed than omnivores.	6
Beezhold et al. (2015) ⁴⁸ United States; cross-sectional	342 men and women; 25–60 y	FFQ	Vegan, vegetarian, and omnivore	DASS	Age	Depression score was not significantly different among 3 groups.	7
Michalak et al. (2012) ⁵¹ Germany; cross-sectional	4181 men and women; 18–65 y	Brief questions about the consumption of food groups in regular	Completely vegetarian, predominantly vegetarian, and omnivore	M-CIDI	–	Vegetarians indicated elevated prevalence rates for depressive disorders.	6
Timko et al. (2012) ⁵³ United States; cross-sectional	486 181 men and women; mean, 24.9 y	FFQ	Vegan, lacto-ovo vegetarian, and semivegetarian vs omnivore	DASS	–	No significant difference in the mean score of depression was observed among groups.	7
Rodríguez Jiménez et al. (1998) ⁵² Spain; cross-sectional	80 men and women; 25–70 y	FFQ	Vegan and lacto-ovo vegetarian vs omnivore	CESD	–	Omnivores had greater mean depression scores compared those of vegetarians.	7

Abbreviations: BMI, body mass index; CESD, Center for Epidemiologic Studies Depression; dash (–) No adjustment; DASS, Depression Anxiety Stress Scale; DSM, *Diagnostic and Statistical Manual of Mental Disorders*; EPDS, Edinburgh Postnatal Depression Scale; FFQ, food frequency questionnaire; GDS, Geriatric Depression Scale; HADS, Hospital Anxiety and Depression Scale; MCS, Mental Component Summary; M-CIDI, Munich Composite International Diagnostic Interview; SAD, seasonal affective disorder.

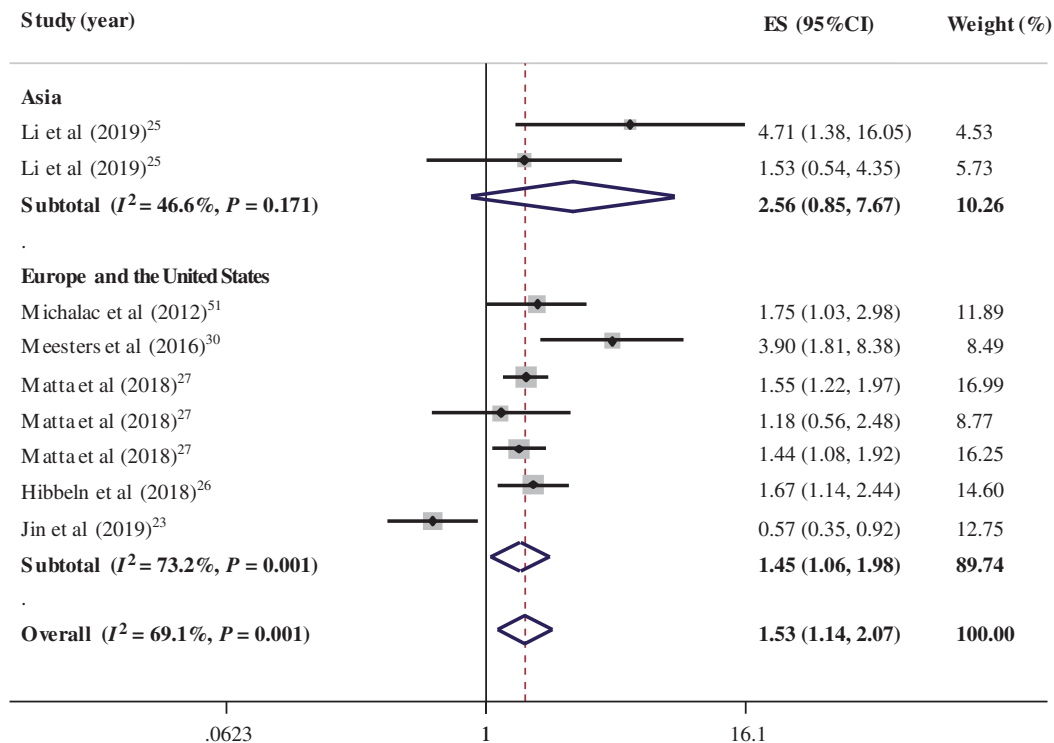


Figure 3 Forest plot of the association between vegetarian diet and risk of depression, based on country where the study was conducted

2.44; $P < 0.0001$; $I^2 = 35.7\%$), while veganism (OR, 1.18; 95%CI, 0.56–2.48; $P = 0.662$) and lacto-ovo vegetarianism (OR, 0.93; 95%CI, 0.37–2.29; $P = 0.867$; $I^2 = 90.4\%$) were not related to the chance of depression in comparison with omnivores (Figure 2^{23,25–27,30,51}).

The association between a vegetarian diet and depression odds stratified on the basis of the country where the study was conducted is shown in Figure 3.^{23,25–27,30,51} Overall, compared with omnivores, the pooled OR for depression in vegetarians was significantly higher only in the United States and European countries (OR, 1.45; 95%CI 1.06–1.98; $P = 0.019$; $I^2 = 73.2\%$), whereas in China, no association was observed (OR, 2.56; 95%CI, 0.85–7.67; $P = 0.093$; $I^2 = 46.6\%$). Subgroup analysis based on sex and study quality led to a tendency toward greater risk in both sexes, male participants, and high-quality studies (Table 3). In subgroup analysis based on age, a vegetarian diet was associated with a greater risk of depression only in younger individuals (OR, 1.53; 95%CI, 1.14–2.07; $P < 0.0001$; $I^2 = 0.0\%$) (Table 3).

Given that some studies examined the association of plant-based diets or some vegetarian dietary patterns identified by posteriori methods, their effects on the relationship underwent additional investigation. After combining the studies that were included in the main analysis, the significance disappeared (OR, 1.03; 95%CI, 0.86–1.23; $P = 0.769$; $I^2 = 80.7\%$). In a subgroup

analysis based on this factor, significant heterogeneity was found between subgroups ($P < 0.0001$) as was an inverse significant association in the subgroup of plant-based diets (OR, 0.79; 95%CI, 0.68–0.92; $P = 0.002$; $I^2 = 59.1\%$) (data not shown).

In total, combining 16 effect sizes from 8 studies^{24,25,31,48–50,52,53} indicated that the mean score of depression was not significantly different between vegetarians and omnivores (standardized mean difference [SMD], 0.10; 95%CI, –0.01 to 0.21; $P = 0.08$; $I^2 = 79.1\%$). Subgroup analysis based on the type of vegetarian diet indicated the results were not related to the vegetarian type (Figure 4^{24,25,31,48–50,52,53}). In subgroup analysis by sex, in studies that separately assessed male^{49,50} and female participants,⁴⁹ a vegetarian diet was associated with greater scores of depression compared with omnivores (men: $n = 4$ studies, SMD, 0.38, 95%CI, 0.21–0.55, $I^2 = 52.1\%$; and women: $n = 2$ studies, SMD, 0.1, 95%CI, 0.04–0.17; $I^2 = 0.0\%$). However, in studies in which both men and women were assessed,^{24,25,31,48,52,53} the mean difference did not statistically differ between vegetarians and nonvegetarians ($n = 10$ studies; SMD, –0.07; 95%CI, –0.25 to 0.12; $I^2 = 81.0\%$). In studies deemed of low quality,^{31,48–50,52,53} adherence to a vegetarian diet was associated with significantly higher mean depression scores ($n = 14$ studies; SMD, 0.14; 95%CI, 0.03–0.25; $I^2 = 73.6\%$), whereas in studies deemed of high quality,^{24,25} no significant

Table 3 Subgroup analysis for the association between vegetarian diet and depression risk

	Effect size	I^2 (%)	Odds ratio	95%CI	P_{Between}
Sex					0.446
Both	6	77.0	1.42	0.98–2.06	
Male	2	860.1	2.36	0.91–6.17	
Female	1	–	1.53	0.54–4.35	
Study quality score					0.040
≥8	7	868.1	1.36	0.99–1.87	
≤7	2	64.8	2.49	1.14–5.42	
Age, years					0.741
< 50	5	0.0%	1.53	1.31–2.79	
≥ 50	4	87.1	1.90	0.61–5.94	

Abbreviations: dash (–), not estimated.

association was observed ($n = 2$ studies; SMD, -0.22 ; 95%CI, -1.09 to 0.65 ; $I^2 = 95.5\%$). Because of homogeneity in terms of the country where the study was conducted, their effects could not be explored. Additional analysis, including a study examining a plant-based diet in relation to mean depression score,⁴⁰ could not affect the main results (SMD, 0.06 ; 95%CI, -0.06 to 0.18 ; $I^2 = 83.4\%$).

Publication bias and sensitivity analysis

In spite of slight asymmetry in the funnel plots (Figure 5), there was no evidence of publication bias according to Egger and Begg regression tests either for studies that assessed the risk of depression (Egger test, $P = 0.590$; Begg test, $P = 0.466$) or for studies that assessed the mean difference (Egger test, $P = 0.425$; Begg test, $P = 0.392$). In sensitivity analysis, the removal of no study could considerably change the odds of

depression in vegetarians. Because the method of Li et al²⁵ method to determine vegetarian individuals was less precise, 2 effect sizes extracted from their study were also excluded. This led to a slight decrease in the pooled effect size either in the semivegetarian subgroup (OR, 1.79 ; 95%CI, 1.36 – 2.36 ; $P < 0.0001$; $I^2 = 41.2\%$) or overall (OR, 1.45 ; 95%CI, 1.06 – 1.98 ; $P = 0.019$; $I^2 = 73.2\%$), though the significance remained unchanged. Excluding the study by Beezhold et al²⁴ or the study by Rodríguez Jiménez⁵² led to a significant increase in the mean level of depression scores in vegetarians compared with nonvegetarians.

DISCUSSION

The pooled effect size of existing investigations examining the association between vegetarian diets and depression risk illustrated scarce reports in this regard. Comparing the mean score of depression between

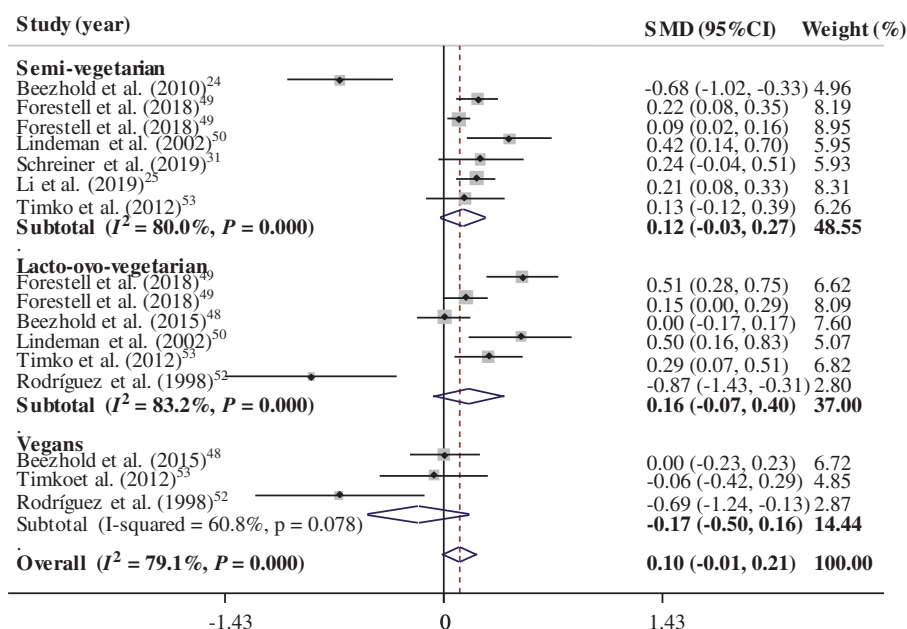


Figure 4 Forest plot comparing the mean of depression score between vegetarians and nonvegetarians based on type of vegetarian diet. Abbreviation: SMD, standardized mean difference

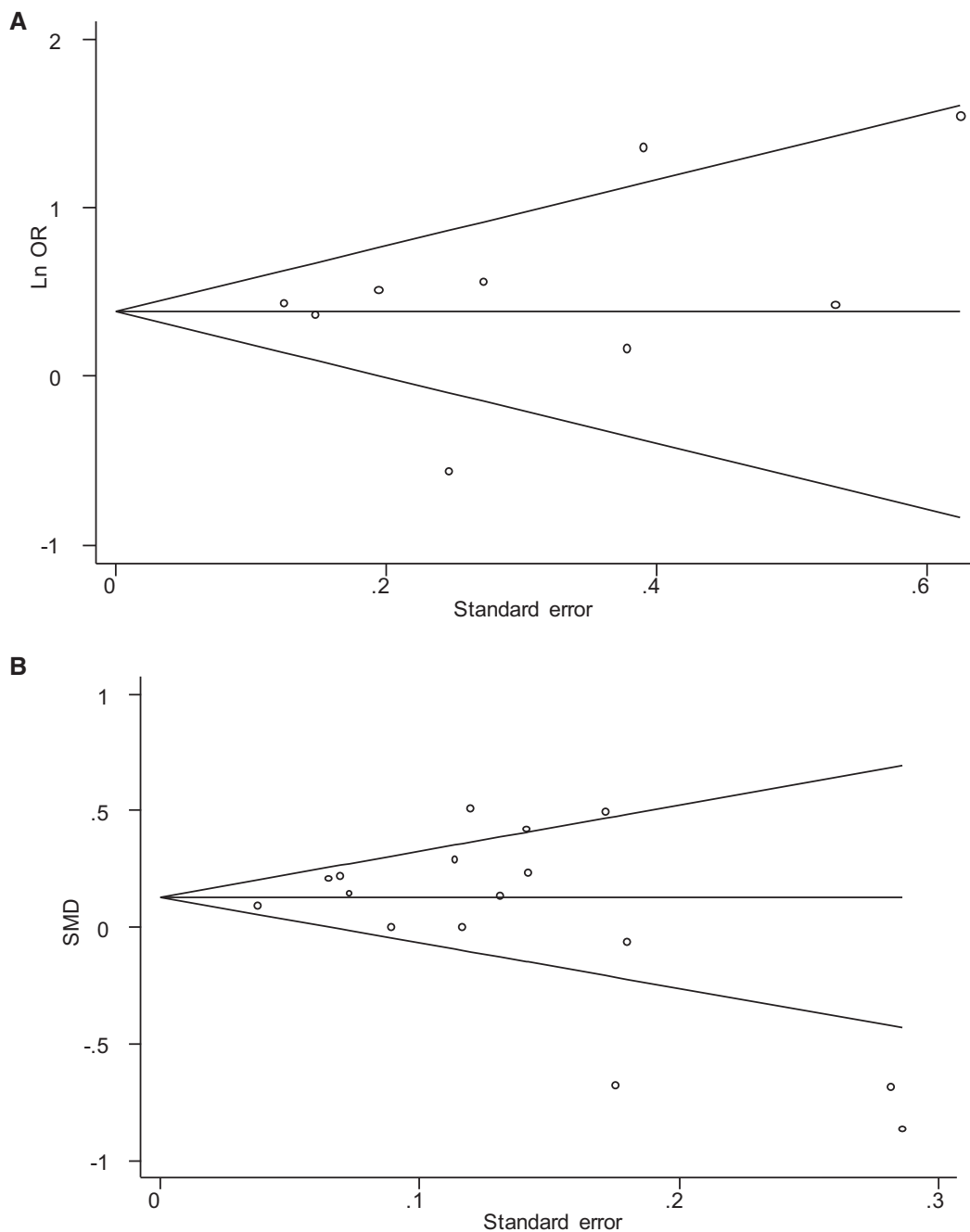


Figure 5 Funnel plots for the studies of the vegetarian diet in relation to depression risk (A) and depression mean score (B).
Abbreviations: OR, odds ratio; SMD, standardized mean difference

vegetarians and nonvegetarians suggested no difference, whereas in studies that evaluated the odds of depression, adherence to a vegetarian-based dietary pattern was associated with increased odds of depression. This association was dependent on the type of vegetarian diet, the country where the study was conducted, the quality of studies, and the mean age of participants.

To date, cumulative evidence has suggested beneficial effects of adhering to a vegetarian diet on various health outcomes, such as chronic inflammation¹¹ and diabetes mellitus.²² Given that there is a bidirectional

association between chronic disease, inflammation, and mental disorders,^{56–58} it is probable that adhering to a vegetarian diet can be associated with mental health. In support of this hypothesis, the favorable associations between the dietary inflammatory index, fruits, vegetables, plant-based dietary patterns, and the risk of depression and anxiety have been reported by several studies and meta-analyses.^{2,59–61} However, studies investigating vegetarian diets in relation to depression are scarce and have reported inconsistent findings. For example, although most studies showed a null association between

a vegetarian diet and depression,^{24,43} some others either found a direct association^{25,26,30,49,50} or even an inverse association.²³

Various factors may affect the relationship between a vegetarian diet and depression risk. For example, the length of time being on a vegetarian diet²⁶ and the reasons for adhering to a vegetarian diet by study population^{25,30,62} may influence the final results. In the Avon Longitudinal Study of Parents and Children, Hibbeln et al²⁶ illustrated that individuals who were vegetarians for a longer time tended to have higher scores of depression. Moreover, vegetarianism may be a result of various motives, including religion, health concerns, socioeconomic factors, and having particular viewpoints regarding the environment and killing of animals.^{25,30,62} Therefore, because of their potential consequences on or relation to mental status, such motives should be considered when examining and interpreting these associations. Nonetheless, most of the included studies in our meta-analysis did not take these factors into account and adjusted the roles of these factors.

According to the subgroup analysis, using different definitions of vegetarian diets and the country where the study was conducted may be potential sources of heterogeneity between studies. Some of the studies included in the present meta-analysis separately examined vegan and other vegetarian dietary patterns,^{27,43} but some studies combined vegans with vegetarians because only a few participants in the study were vegans.²⁶ In addition, the common vegetarian dietary pattern and environmental context or culture may play an important role in the mental health of vegetarians. For example, whereas lacto-ovo vegetarians are more common in Europe and North America,^{63,64} in China, the average intake of dairy products is less than that of Western vegetarians.^{65,66} It is worth mentioning that nutrient balance of the diet may be influenced by the type of vegetarian diet, the eliminated food items, and even the proportion of certain consumed foods. Because specific nutrient deficiencies can affect mental health, a combination of these studies may result in misleading findings and results should be interpreted cautiously. In addition, vegetarianism in Asia is more common; as a result, vegetarians may not be viewed as a social minority to the same degree, and they may experience less ostracism and more social support, which may improve their daily experiences.

Although vegetarian-based dietary patterns are rich in several nutrients, such as fiber, antioxidants, folate, and magnesium, and have anti-inflammatory properties,^{11,67} they may not be able to meet recommended dietary allowance for all nutrients, such as long-chain omega-3 fatty acids, cobalamin, and iron,^{13,67} and

thereby lead to adverse effects on mental health. Study results suggested that semi- and pesco-vegetarians, who consume fish and poultry besides other foods consumed in the lacto-ovo vegetarian diet, had a higher risk for depression, whereas no significant association was found for lacto-ovo vegetarians. The reason for this finding is unclear. However, it might be related to a higher score of dietary restraint in semivegetarians⁵³ and also the food choices of participants. Dietary restraint, which is the intentional restriction of food intake to reduce or keep body weight at a more desirable level,⁶⁸ can potentially cause nutrient imbalance or deficiency. A cross-sectional study⁴¹ elucidated that, in spite of a lack of association between a plant-based diet and depression in patients with type 2 diabetes, adhering to healthy and unhealthy plant-based diets was associated with a lower and higher risk of depression, respectively. Matta et al²⁷ consistently demonstrated an interaction between a vegetarian diet and depression risk according to the consumption of legumes. They showed that increasing the intake of legumes was associated with a dramatic decline in the risk of depression.²⁷ Another explanation might be the extent to which the foods are processed; researchers reported that in a prospective cohort, a higher proportion of processed foods was associated with a 21% increase in the risk of depressive symptoms.⁶⁹ Therefore, consuming a vegetarian diet excluding any animal-derived foods, compared with plant-based diets and fruit and vegetables, might not have additional benefits for mental health.

The exact reason for the higher risk for depression we found in younger adults in the present meta-analysis is not clear. However, the impetus to adhere to a vegetarian diet might play a role.⁷⁰ It has been illustrated that animal-motivated vegetarians exhibit more dietary restraint than do health-motivated vegetarians,³² which might adversely affect mental status.

Although plant-based diets have been generally considered vegetarian diets,³⁴ in contrast with an earlier meta-analysis,²⁸ we did not include plant-based diets, or vegetarian diets identified by posteriori methods, in the meta-analysis. Indeed, labelling identified dietary patterns by posteriori methods is subjective, and because these methods use a scoring system or factor loadings of foods, it is probable that meat or fish take a low factor loading. But, their consumption frequency should be more than once a week, which will not be in accordance with the definition of vegetarian diets.⁸ In support of this point, in the study by Hosseinzadeh et al,⁴⁴ the mean consumption of processed meat was 4.5 g/d in the top quintile of the lacto-ovo vegetarian dietary pattern; therefore, it is probable that the mean consumption of other meats is higher. However, there was no report in this regard in their article.⁴⁴

There are several limitations in our meta-analysis that need to be taken into account when interpreting the results. First, there were only a few studies in this area, and almost all the studies included in the present meta-analysis were cross-sectional; therefore, it was not possible to draw any causal relationships. Second, although maximally adjusted models of original articles were used in all analysis, residual and unmeasured confounding cannot be completely ruled out. Third, the duration of and reasons for adhering to a vegetarian diet, which can potentially influence the associations, were not determined in the most of studies. Fourth, using different, self-reported screening questionnaires, rather than diagnostic methods, to identify depressed individuals may cause heterogeneity and influence the accuracy of findings. Thus, these findings should be interpreted cautiously, and prospective studies are needed to confirm these results. Fifth, in spite of performing various subgroup analyses, between-studies heterogeneity could not be completely eliminated. It should be kept in mind that all vegetarian diets are not necessarily healthy, and differences in dietary restraint due to maladaptive behavior toward food may be another potential source of inconsistency.⁵³ However, because these differences were not explored in the original articles, it was not possible to do additional analysis based on it.

Finally, this study has its strengths. First, the associations were examined on the basis of various subgroup analyses, including the type of vegetarian diet and the country where the study was conducted. Second, a comprehensive literature review was conducted to find relevant articles and made no restriction for data and language.

CONCLUSION

In conclusion, this meta-analysis showed that a vegetarian diet compared with an omnivore diet was associated with an increased risk of depression, although the mean score for depression was not significantly different between vegetarians and omnivores. However, because of the scarce data in this regard and the lack of robustness in the findings, more investigations, particularly prospective cohorts, are warranted to confirm these results and risk for depression.

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REFERENCES

1. World Health Organization. Depression. January 2020. <https://www.who.int/en/news-room/fact-sheets/detail/depression>. Accessed August 2020.
2. World Health Organization. The global burden of disease: 2014. Available at: <https://apps.who.int/iris/handle/10665/43942>. Accessed August 2020.
3. Caspi A, Sugden K, Moffitt TE, et al. Influence of life stress on depression: moderation by a polymorphism in the 5-HTT gene. *Science*. 2003;301:386–389.
4. Lopresti AL, Hood SD, Drummond PD. A review of lifestyle factors that contribute to important pathways associated with major depression: diet, sleep and exercise. *J Affect Disord*. 2013;148:12–27.
5. Brown GW, Harris TO. Depression and the serotonin transporter 5-HTTLPR polymorphism: a review and a hypothesis concerning gene–environment interaction. *J Affect Disord*. 2008;111:1–12.
6. Molendijk M, Molero P, Sánchez-Pedreño FO, et al. Diet quality and depression risk: a systematic review and dose-response meta-analysis of prospective studies. *J Affect Disord*. 2018;226:346–354.
7. Dagnelie PC, Mariotti F. *Vegetarian Diets: Definitions and Pitfalls in Interpreting Literature on Health Effects of Vegetarianism. Vegetarian and Plant-Based Diets in Health and Disease Prevention*. Cambridge, MA: Academic Press; 2017:3–10.
8. Fraser GE. Vegetarian diets: what do we know of their effects on common chronic diseases? *Am J Clin Nutr*. 2009;89:1607S–1612S.
9. Rogerson D. Vegan diets: practical advice for athletes and exercisers. *J Int Soc Sports Nutr*. 2017;14:36.
10. Craig WJ, Mangels AR, American Dietetic Association. Position of the American Dietetic Association: vegetarian diets. *J Am Diet Assoc*. 2009;109:1266–1282.
11. Haghhighatdoost F, Bellissimo N, Totossi de Zepetnek JO, et al. Association of vegetarian diet with inflammatory biomarkers: a systematic review and meta-analysis of observational studies. *Public Health Nutr*. 2017;20:2713–2721.
12. Poleszak E. Modulation of antidepressant-like activity of magnesium by serotonergic system. *J Neural Transm (Vienna)*. 2007;114:1129–1134.
13. Haider LM, Schwingshackl L, Hoffmann G, et al. The effect of vegetarian diets on iron status in adults: a systematic review and meta-analysis. *Crit Rev Food Sci Nutr*. 2018;58:1359–1374.
14. Allès B, Baudry J, Méjean C, et al. Comparison of sociodemographic and nutritional characteristics between self-reported vegetarians, vegans, and meat-eaters from the NutriNet-Santé study. *Nutrients*. 2017;9:1023.
15. Allen LH. Causes of vitamin B12 and folate deficiency. *Food Nutr Bull*. 2008;29:S20–S34.
16. Rizzo G, Laganà AS, Rapisarda AMC, et al. Vitamin B12 among vegetarians: status, assessment and supplementation. *Nutrients*. 2016;8:767.
17. Neuhauser ML. The importance of healthy dietary patterns in chronic disease prevention. *Nutr Res*. 2019;70:3–6.
18. Onvani S, Haghhighatdoost F, Surkan P, et al. Adherence to the Healthy Eating Index and Alternative Healthy Eating Index dietary patterns and mortality from all causes, cardiovascular disease and cancer: a meta-analysis of observational studies. *J Hum Nutr Diet*. 2017;30:216–226.
19. Satija A, Hu FB. Plant-based diets and cardiovascular health. *Trends Cardiovasc Med*. 2018;28:437–441.
20. Chiang JK, Lin YL, Chen CL, et al. Reduced risk for metabolic syndrome and insulin resistance associated with ovo-lacto-vegetarian behavior in female Buddhists: a case-control study. *PLoS One*. 2013;8:E71799.
21. Dinu M, Abbate R, Gensini GF, et al. Vegetarian, vegan diets and multiple health outcomes: a systematic review with meta-analysis of observational studies. *Crit Rev Food Sci Nutr*. 2017;57:3640–3649.
22. Lee Y, Park K. Adherence to a vegetarian diet and diabetes risk: a systematic review and meta-analysis of observational studies. *Nutrients*. 2017;9: 603.
23. Jin Y, Kandula NR, Kanaya AM, et al. Vegetarian diet is inversely associated with prevalence of depression in middle-older aged South Asians in the United States. *Ethn Health*. 2019;1–8.

24. 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.
25. Li X, Cao H-j, Xie S-y, et al. Adhering to a vegetarian diet may create a greater risk of depressive symptoms in the elderly male Chinese population. *J Affect Disord*. 2019;243:182–187.
26. Hibbeln JR, Northstone K, Evans J, et al. Vegetarian diets and depressive symptoms among men. *J Affect Disord*. 2018;225:13–17.
27. Matta J, Czemichow S, Kesse-Guyot E, et al. Depressive symptoms and vegetarian diets: Results from the Constances Cohort. *Nutrients*. 2018;10:1695.
28. Askari M, Daneshzad E, Darooghegi MM, et al. L. Vegetarian diet and the risk of depression, anxiety, and stress symptoms: a systematic review and meta-analysis of observational studies. *Crit Rev Food Sci Nutr*. 2020;1–11.
29. Iguacel I, Huybrechts I, Moreno LA, et al. Vegetarianism and veganism compared with mental health and cognitive outcomes: a systematic review and meta-analysis. *Nutr Rev*. 2020;nuaa030.
30. Meesters AN, Maukonen M, Partonen T, et al. Is there a relationship between vegetarianism and seasonal affective disorder? A pilot study. *Neuropsychobiology*. 2016;74:202–206.
31. Schreiner P, Yilmaz B, Rossel J-B, et al.; Swiss IBD Cohort Study Group. Vegetarian or gluten-free diets in patients with inflammatory bowel disease are associated with lower psychological well-being and a different gut microbiota, but no beneficial effects on the course of the disease. *United European Gastroenterol J*. 2019;7:767–781.
32. Rosenfeld DL. Why some choose the vegetarian option: are all ethical motivations the same? *Motiv Emot*. 2019;43:400–411.
33. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Ann Intern Med*. 2009;151:W–94.
34. Williams KA, Sr, Patel H. Healthy plant-based diet: what does it really mean. *J Am Coll Cardiol*. 2017;70:423–425.
35. Wells G, Shea B, O'connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. [Internet]. 2014;
36. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol*. 2010;25:603–605.
37. Hedges L, Olkin I. *Statistical Methods for Meta-Analysis*. Cambridge, MA: Academic Press; 2014.
38. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Controlled Clin Trials*. 1986;7:177–188.
39. Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. *BMJ* 2003;327:557–560.
40. Zamani B, Daneshzad E, Siassi F, et al. Association of plant-based dietary patterns with psychological profile and obesity in Iranian women. *Clin Nutr*. 2020;39:1799–1808.
41. Daneshzad E, Keshavarz SA, Qorbani M, et al. Association of dietary acid load and plant-based diet index with sleep, stress, anxiety and depression in diabetic women. *Br J Nutr*. 2020;123:901–912.
42. Sánchez-Villegas A, Henríquez-Sánchez P, Ruiz-Canela M, et al. A longitudinal analysis of diet quality scores and the risk of incident depression in the SUN Project. *BMC Med*. 2015;13:197.
43. Northstone K, Joinson C, Emmett P. Dietary patterns and depressive symptoms in a UK cohort of men and women: a longitudinal study. *Public Health Nutr*. 2018;21:831–837.
44. Hosseinzadeh M, Vafa M, Esmailzadeh A, et al. Empirically derived dietary patterns in relation to psychological disorders. *Public Health Nutr*. 2016;19:204–217.
45. Liu ZM, Ho SC, Xie YJ, et al. Associations between dietary patterns and psychological factors: a cross-sectional study among Chinese postmenopausal women. *Menopause*. 2016;23:1294–1302.
46. Wang CJ, Yang TF, Wang GS, et al. Association between dietary patterns and depressive symptoms among middle-aged adults in China in 2016–2017. *Psychiatry Res*. 2018;260:123–129.
47. Baines S, Powers J, Brown WJ. How does the health and well-being of young Australian vegetarian and semi-vegetarian women compare with non-vegetarians? *Public Health Nutr*. 2007;10:436–442.
48. Beezhold B, Radnitz C, Rinne A, et al. Vegans report less stress and anxiety than omnivores. *Nutr Neurosci*. 2015;18:289–296.
49. Forestell CA, Nezzlek JB. Vegetarianism, depression, and the five factor model of personality. *Ecol Food Nutr*. 2018;57:246–259.
50. Lindeman M. The state of mind of vegetarians: psychological well-being or distress? *Ecol Food Nutr*. 2002;41:75–86.
51. Michalak J, Zhang XC, Jacobi F. Vegetarian diet and mental disorders: results from a representative community survey. *Int J Behav Nutr Phys Act*. 2012;9:67.
52. Rodríguez Jiménez J, Rodríguez JR, González MJ. [Indicators of anxiety and depression in subjects with different kinds of diet: vegetarians and omnivores]. *Bol Asoc Med P R*. 1998;90:58–68.
53. Timko CA, Hormes JM, Chubski J. Will the real vegetarian please stand up? An investigation of dietary restraint and eating disorder symptoms in vegetarians versus non-vegetarians. *Appetite*. 2012;58:982–990.
54. Hessler-Kaufmann JB, Meule A, Holzapfel C, et al. Orthorexic tendencies moderate the relationship between semi-vegetarianism and depressive symptoms. *Eat Weight Disord*. 2020;26:623–628.
55. Lavalley K, Zhang XC, Michalak J, et al. Vegetarian diet and mental health: cross-sectional and longitudinal analyses in culturally diverse samples. *J Affect Disord*. 2019;248:147–154.
56. Adler UC, Marques AH, Calil HM. Inflammatory aspects of depression. *Inflamm Allergy Drug Targets*. 2008;7:19–23.
57. Alzoubi A, Abunaser R, Khassawneh A, et al. The bidirectional relationship between diabetes and depression: a literature review. *Korean J Fam Med*. 2018;39:137–146.
58. Pan A, Keum N, Okereke OI, et al. Bidirectional association between depression and metabolic syndrome: a systematic review and meta-analysis of epidemiological studies. *Diabetes Care*. 2012;35:1171–1180.
59. Haghghatdoost F, Feizi A, Esmailzadeh A, et al. Association between the dietary inflammatory index and common mental health disorders profile scores. *Clin Nutr*. 2019;38:1643–1650.
60. Liu MW, Chen QT, Towne SD, Jr, et al. Fruit and vegetable intake in relation to depressive and anxiety symptoms among adolescents in 25 low- and middle-income countries. *J Affect Disord*. 2020;261:172–180.
61. Liu X, Yan Y, Li F, et al. Fruit and vegetable consumption and the risk of depression: a meta-analysis. *Nutrition*. 2016;32:296–302.
62. Mullee A, Vermeire L, Vanaelst B, et al. Vegetarianism and meat consumption: a comparison of attitudes and beliefs between vegetarian, semi-vegetarian, and omnivorous subjects in Belgium. *Appetite*. 2017;114:299–305.
63. Davey GK, Spencer EA, Appleby PN, et al. 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;6:259–269.
64. Tonstad S, Butler T, Yan R, et al. Type of vegetarian diet, body weight, and prevalence of type 2 diabetes. *Diabetes Care*. 2009;32:791–796.
65. Chiu TH, Huang H-Y, Chiu Y-F, et al. Taiwanese vegetarians and omnivores: dietary composition, prevalence of diabetes and IFG. *PLoS One*. 2014;9:e88547.
66. Lee H, Woo J, Chen Z, et al. Serum fatty acid, lipid profile and dietary intake of Hong Kong Chinese omnivores and vegetarians. *Eur J Clin Nutr*. 2000;54:768–773.
67. McEvoy CT, Temple N, Woodside JV. Vegetarian diets, low-meat diets and health: a review. *Public Health Nutr*. 2012;15:2287–2294.
68. Lowe MR, Thomas JG. Measures of restrained eating: Conceptual evolution and psychometric update. In: Allison DB, ed. *Handbook of Assessment Methods for Obesity and Eating Behaviors*. Los Angeles, CA: Sage; 2009:137–185.
69. Adjibade M, Julia C, Allès B, et al. Prospective association between ultra-processed food consumption and incident depressive symptoms in the French NutriNet-Santé cohort. *BMC Med*. 2019;17:78.
70. Pribis P, Pencak RC, Grajales T. Beliefs and attitudes toward vegetarian lifestyle across generations. *Nutrients*. 2010;2:523–531.