Review

Green Tea Consumption and Risk of Depression Symptoms: A Systematic Review and Meta-Analysis of Observational Studies

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Summary This systematic review and meta-analysis aimed to investigate the association between green tea consumption and depression symptom risk, using subgroup analyses concerning study design, geographical region of study, adjustment factors, age, cut-off for the highest consumption category, and depression assessment methods applied. We used PubMed to search for relevant literature. The inclusion criteria were studies that (a) investigated this association as a primary or secondary outcome; (b) published in English; (c) assessed and reported hazard ratios or odds ratios (ORs) and the corresponding 95% confidence intervals (CIs) for depression symptoms, or included sufficient information to allow their calculation; (d) included at least two groups differentiated based on green tea consumption (e.g., high and low); (e) reported the prevalence of depression symptoms in each group; and (f) reported the sample size for each group. Eight articles were found to meet all criteria. The results indicated that high green tea consumption is inversely associated with depression symptoms. The pooled OR was 0.66 (95% CI 0.58–0.74), and significant heterogeneity was not observed. Subgroup analysis showed that study design impacted results (cohort study [one study]: OR=0.29, 95% CI=0.04-2.14; cross-sectional study [seven studies]: OR=0.66, 95% CI=0.59-0.75). These findings suggest that green tea consumption reduces the risk of depression symptoms. This association was also observed in the cohort study included, but the results in which did not reach the significant level. Therefore, further cohort studies are needed to confirm the potential causal relationship in this regard. Key Words beverage, depression symptoms, green tea, meta-analysis, systematic review

Globally, depression is the most widespread mental health condition (1). Studies from several countries have reported that over 90% of individuals who attempt or commit suicide have at least one primary depressive symptom (2, 3). In addition, depression is ranked third in terms of the medical conditions with the most significant global disease burden (4).

A dietary activity that can combat depression is the consumption of green tea. The catechins in green tea have been shown to increase serum levels of noradrenaline and dopamine (5), which are believed to play a major role in combatting depression (6). In addition, theanine, a major amino acid in green tea, has also been shown to have anti-stress effects (7). As stress is known to be a causative factor in depression (8), theanine is consequently thought to have anti-depressive symptoms.

A previous meta-analysis of observational studies showed that green tea consumption is inversely associated with depression (9). This meta-analysis (9) examTherefore, the present systematic review and metaanalysis of observational studies aimed to analyze existing findings concerning the influence of green tea consumption on the risk of depression symptoms, stratifying the analyses in terms of study design, geographical region of study, adjustment factors, participant age, cut-off for the highest consumption category, and depression assessment methods applied.

Materials and Methods

Using the PubMed database, we conducted a systematic review and meta-analysis of observational studies

ined only four cross-sectional studies. In addition, although associations between green tea and depression symptoms may differ depending on age, gender, and country, and observations of the effect may differ depending on the depression assessment method applied, the study did not stratify these variables in its analysis. Since the publication of this meta-analysis (9), several additional studies on the topic of green tea and depression (10-12) have been published, suggesting it is now necessary to conduct another meta-analysis that incorporates these new findings.

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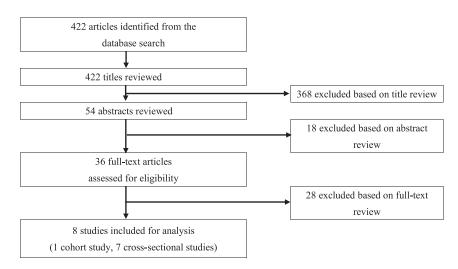


Fig. 1. Flowchart showing the study selection process.

to evaluate the association between green tea consumption and depression symptoms. This study was exclusively performed by the present investigators, and no librarians were part of the team. The study was conducted in accordance with the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (13).

Eligibility criteria. The inclusion criteria were observational studies that (a) investigated the association between green tea consumption and depression symptoms as a primary or secondary outcome; (b) were published in the English language; (c) assessed and reported hazard ratios (HRs) or odds ratios (ORs) and the corresponding 95% confidence intervals (CIs) for depression symptoms, or included sufficient information to allow their calculation; (d) included at least two groups divided in terms of green tea consumption (e.g., high and low); (e) reported the prevalence of depression symptoms in each group; and (f) reported the total sample size in each group. We excluded randomized clinical trials, quasi-experimental studies, and crossover studies.

Search strategy and selection criteria. Studies published before 14 January 2021 were retrieved from the PubMed electronic database by one investigator (AY). A search strategy was designed that featured the use of keywords such as "tea" or "catechin" or "camelia sinensis" and "depression" or "depressive." We did not contact any authors of the studies that were extracted.

Data extraction and quality assessment. The retrieved articles were screened for eligibility by two researchers (AY and TK). Those deemed to be eligible were advanced to full-text review. The quality of reporting in each study was assessed by two researchers (AY and TK) using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) instrument. For each study, the coded variables included authors, year of publication, study design, country, sample size (*n*), proportion of females in the sample (%), age range (in terms of mean age \pm standard deviation; SD), ORs (95% CIs), green tea consumption categories (highest vs. lowest), depression assessment method, adjustment factors, and STROBE score.

Statistical analysis. The meta-analysis was conducted using RevMan V.5.3. Effect sizes (ESs) were measured using ORs and 95% CIs; the ORs indicated the risk of depression symptoms depending on level of green tea consumption (high in relation to low). An inverse variance random-effects model was used to calculate the pooled ESs. Funnel plots were used to evaluate publication bias. Heterogeneity across studies was tested using Q-statistics, and the I^2 index was used to assess inconsistency (14).

Results

The search strategy yielded 422 articles. The titles of all 422 articles were examined, after which 368 articles were excluded. The abstracts of the remaining 54 articles were then examined, after which 36 articles were selected for full-text readings. Of these 36, eight met all inclusion criteria. Figure 1 shows a flowchart depicting the study-selection process.

Characteristics of the studies

The significant characteristics of the selected studies are listed in Table 1. The oldest study to meet the inclusion criteria was published in 2006 (15). Four different countries were represented in the article sample: five were conducted in Japan (10, 15–18) and one each was conducted in Korea (11), China (19), and Singapore (12), respectively. One of the eight studies was a cohort study (12), while seven used a cross-sectional study design (10, 11, 15–19). In the cohort study (12), the follow-up was 4.0 y. The sample sizes ranged from 89 to 9,576, and the ages of the participants ranged from 20 to 94 y.

All studies used the food frequency questionnaire to assess green tea consumption, and did not examine how green tea is drunk (e.g., slowly or quickly), type of tea leaves, origin, brewing method, and temperature of green tea. In addition, it was unclear whether or not they were targeting green tea in plastic bottles.

Depression symptoms were assessed using the following instruments: the 30-item Geriatric Depression Scale

STROBE score	wid- ccu- mor-	and and me), no), level evel size city city PA+ take use	ohol e of 17	16
Adjustments factors	Age, gender, education, housing type, single/divorced/wid- owed, living alone, physical activity, social activity and occu- pational activity score, smoking, alcohol, number of comor- bidities, MMSE	Age (years, continuous) and residential block (Hokkaido and Tohoku, Kanto, Hokuriku and Tokai, Kinki, Chugoku and Shikoku, and Kyushu), living status (alone or not alone), current smoking (yes or no), alcohol drinking (yes or no), marital status (married or unmarried), physical activity level (total metabolic equivalents hours/d: METs, continuous), size of residential area (city with a population ≥ 1 million, city with a population <1 million, and town and village), BMI (kg/m ² , continuous), education level (junior high school, high school junior college, and university and higher), EPA+ DHA intake (mg/1,000 kcal, continuous), folate intake ($\mu g/1,000$ kcal, continuous), and dietary supplement use (yes or no).	Age, gender, BMI, income level, education level, alcohol intake, smoking status, and physical activity, intake of energy, vegetable, fruit, red meat, fish, and coffee	None
Depression assessment	15-item GDS (cutoff 5)	CES-D (cutoff 16)	Participants who reported at least one 'yes' were regarded as having depression. 'Have you ever been diagnosed with depression by a physician?': 'Do you have depression at pres- ent?': 'Are you getting treat- ment for depression at pres- ent?': 'In the past year, have you felt sadness or despair con- tinuously for 2 or more weeks that was severe enough to interfere with daily life?'	Japanese version of the HADS (cutoff 10)
OR (95% CI), green tea category (highest vs. lowest)	0.29 (0.04, 2.14), ≥1 cup/d vs. none	0.85 (0.62, 1.17), median (range) 390 (320–788) g/1,000 kcal vs. 22 (0–99) g/1,000 kcal	0.79 (0.63, 0.99), ≥3 cups/w vs. never	0.84 (0.28, 2.57), ≥3 cups/d vs.
Mean age±SD (Age range)	67	65–94	46.2±0.5 (depression) 43.9±0.3 (non- depression)	62.8±7.8
Sample size (n) , female $(\%)$	3,004, 65.0	1,922, 100	9,576, 59.8	89, 38.2
Study design, country	Cohort (4 y), Singapore	Cross- sectional, Japan	Cross- sectional, Korea	Cross- sectional, Iapan
Author (y) (reference number)	Ng et al. (2021) (12)	Kimura et al. (10)	Kim and Kim (2018) (11)	Omagari et al. (2014)

Table 1. General description of the included studies.

Table 1. (
Author (y) (reference number)	Study design, country	Sample size (n) , female $(\%)$	Mean age±SD (Age range)	OR (95% CI), green tea category (highest vs. lowest)	Depression assessment	Adjustments factors	STROBE score
Pham et al. (2014) (18)	Cross- sectional, Japan	537, 40.6	20-68	0.54 (0.29, 1.00), ≥4 cups/d vs. ≤1 cup/d	CES-D (cutoff 16)	Age, gender, workplace history of cancer, CVD, diabetes mel- litus or chronic hepatitis, marital status, living status, over- time work, job position, occupational physical activity, non-occupational physical activity, current smoking, alcohol drinking, BMI, <i>n</i> -3 PUFA intake, red meat intake, vegetable and fruit consumption, coffee consumption, serum CRP con- centrations, serum folate concentration	19
Feng et al. (2013) (19)	Cross- sectional, China	1,368, 59.3	≥68.6	0.68 (0.47, 0.97), one to five times per week or at least once a day vs. never or <1 time per month	15-item GDS (cutoff 5)	Age, gender, education level, leisure activity score, number of comorbidities, and MMSE score	18
Niu et al.	Cross-	1,058,	1 - - - - - - - - - - - - - - - - - - -	0.56 (0.39, 0.81), ≥4 cups/d vs. ≤1 cup/d	30-item GDS (cutoff≥11: mild and severe depression symptom)	Age, gender, BMI, hypertension, diabetes, history of cardio- vascular diseases, cancer or arthritis, high CRP, history of smoking and drinking habits, physical activity, cognitive sta- tus, impaired instrumental activities of daily living, self-re-	
(16)	sectional, Japan	57.4	- /.++0.0/	0.48 (0.31, 0.75), ≥4 cups/d vs. ≤1 cup/d	30-item GDS (cutoff≥14: severe depression symptoms)	- ported body pain, educational level, living alone, marital status, serum albumin concentration, total energy intake, intake per 2,000 kcal of energy intake as protein and folate, black or oolong tea consumption, coffee consumption, lack of perceived social support and visiting friends	Т
Kuriyama et al. (2006) (15)	Cross- sectional, Japan	1,003, 57.6	≥ 70	0.62 (0.44, 0.87), ≥2 cups/d vs. ≤3 cups/w	30-item GDS (cutoff 11)	None	20

158

	High Green Tea Consi	Imption	Low Green Tea Consu	mption		Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% Cl
Kuriyama et al., 2006	223	725	71	170	11.8%	0.62 [0.44, 0.87]	2006	-#-
Niu et al., 2009	136	488	114	286	14.6%	0.58 [0.43, 0.79]	2009	
Feng et al., 2013	58	323	165	714	12.5%	0.73 [0.52, 1.02]	2013	
Omagari et al., 2014	8	50	7	38	1.1%	0.84 [0.28, 2.57]	2014	
Pham et al., 2014	24	97	89	269	5.0%	0.66 [0.39, 1.13]	2014	_ → _{
Kim et al., 2018	153	1326	682	3828	39.5%	0.60 [0.50, 0.73]	2018	=
Kimura et al., 2020	101	498	110	498	15.0%	0.90 [0.66, 1.22]	2020	
Ng et al., 2021	1	158	50	2352	0.4%	0.29 [0.04, 2.14]	2021	
Total (95% CI)		3665		8155	100.0%	0.66 [0.58, 0.74]		•
Total events	704		1288					
Heterogeneity: Tau ² = 0).00; Chi ² = 6.76, df = 7 (i	^o = 0.45); P	² = 0%					0.01 0.1 1 10 100
Test for overall effect: Z	= 6.96 (P < 0.00001)							Lower risk Higher risk

Fig. 2. Forest plot indicating the association between green tea consumption and depression symptoms. CI: confidence interval.

Table 2. Summary of ORs for the association between green tea consumption and depression symptoms by study characteristics.

	No. of studies	OR	95% CI
All studies	8	0.66	0.58, 0.74
Study design			
Cross-sectional study	7	0.66	0.59, 0.75
Cohort study	1	0.29	0.04, 2.14
Geographical region of study			
Singapore	1	0.29	0.04, 2.14
Japan	5	0.69	0.57, 0.84
Korea	1	0.60	0.50, 0.73
China	1	0.73	0.52, 1.02
Adjustment for smoking, alcohol drinking, physical a	ctivity, and BMI		
Yes	6	0.67	0.57, 0.78
No	2	0.64	0.46, 0.88
Age			
>60	6	0.70	0.59, 0.83
Cut-off for the highest consumption category ¹			
\geq 3 cups/d	3	0.61	0.47, 0.80
<3 cups/d	4	0.63	0.54, 0.72
Depression assessment			
Validity	7	0.70	0.60, 0.81
No validity	1	0.60	0.50, 0.73

CI, confidence interval; OR, odds ratio.

¹The study by Kimura et al. (10) was not included because the frequency of green tea intake was unknown.

(GDS), the 15-item GDS, the Center for Epidemiological Studies Depression Scale (CES-D), the Patient Health Questionnaire-9 (PHQ-9), the Japanese version of the Hospital Anxiety and Depression Scale (HADS); one study did not use a validated questionnaire to measure depression. Among the eight studies, six adjusted for possible confounding factors, including gender, age, total energy intake, smoking, alcohol use, and physical activity. Two studies did not adjust for possible confounding factors.

Quality assessment

The study quality assessment results, conducted using the STROBE instrument, are shown in Table S1 (Supplemental Online Material), while the individual quality assessment analysis of each included study is shown in Table S2 (Supplemental Online Material). The quality score for the cohort study was 20, and the scores for the seven cross-sectional studies were between 16 and 20, with an average score of 19. The main issues associated with the studies were inadequate descriptions of efforts made to address potential sources of bias (item 9 on the STROBE checklist) and inadequate descriptions of sample-size calculations (item 10).

Association between green tea and depression symptoms

For the eight articles examined in this research, the pooled OR was 0.66 (95% CI=0.58–0.74) and there was not significant heterogeneity (p=0.45, I^2 =0%; see Fig. 2). In the subgroup analyses, study design was found to impact results (cohort study [one study]: OR= 0.29, 95% CI=0.04–2.14; cross-sectional study [seven studies]: OR=0.66, 95% CI=0.59–0.75; as shown in Table 2).

We also conducted subgroup analyses for adjustment factors, participant age, cut-off for the highest consumption category, and depression assessment methods

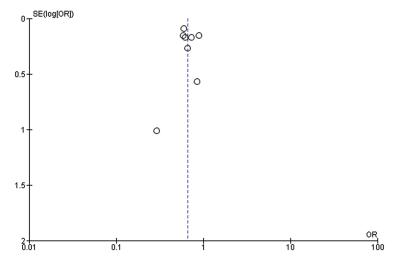


Fig. 3. Funnel plot illustrating the association between green tea consumption and depression symptoms. SE: standard error; OR: odds ratio.

applied, but observed no difference in results (as shown in Table 2).

Figure 3 features a funnel plot for the association between green tea consumption and depression symptoms. The figures are symmetrical.

Discussion

To evaluate the association between green tea consumption and the risk of depression symptoms, we conducted a comprehensive analysis of eight studies that focused on this topic. The results of this meta-analysis indicated that high green tea consumption is inversely associated with depression symptoms. This could be because green tea contains catechins and theanine, which have antidepressant effects (5-7).

Study-quality assessments demonstrated that the reports were of excellent quality, scoring between 16 and 20. The main issues associated with the studies were inadequate descriptions of efforts made to address potential sources of bias (item 9 on the STROBE checklist) and inadequate descriptions of sample-size calculations (item 10).

A previous meta-analysis (9) examined four cross-sectional studies that reported the relationship between green tea consumption and depression symptoms, in which, no stratification by participant age, gender, or country, nor by the study design or depression assessment methods was conducted. Thus, to the best of our knowledge, this is the first systematic review and metaanalysis to investigate, among observational studies, the relationship between green tea consumption and depression symptoms by conducting subgroup analyses. We added three cross-sectional studies (10, 11, 15) and one cohort study (12) to the four studies included in the previous meta-analysis (9), and the results were found to vary by study design. Therefore, the association between green tea consumption and depressive symptoms may be a reverse causality. We also conducted subgroup analyses in terms of age, category of green tea consumption, depression assessment method,

and adjustment factors other than study design, but no differences were found among the results.

Several previous meta-analyses have reported that green tea, as well as other teas, may reduce the risk of depression (9, 20). In addition, the eight studies used for meta-analysis in this study did not examine how green tea is drunk (e.g., slowly or quickly). Therefore, we could not rule out the possibility that it was the act of drinking tea rather than the effect of green tea consumption that suppressed depressive symptoms.

All studies used in this meta-analysis did not examine the type of tea leaves, origin, or brewing method. In addition, it was unclear whether or not they were targeting green tea in plastic bottles. Future studies examining the relationship between green tea consumption and depression should also investigate these factors. The main variables investigated in the present study were defined differently across the articles examined. For example, the green tea category was assessed using a variety of methods. Different outcome assessment methods were also used, including the 30-item GDS, the 15-item GDS, the CES-D, the PHQ-9, the Japanese version of the HADS; two studies did not use a validated questionnaire to measure depression. Therefore, the cut-off value for a reduction in depression-symptoms risk was unclear.

This review has two limitations. First, publication bias may have existed, given the possibility that studies that obtained negative results were not published. Second, this study only reviewed English-language manuscripts, excluding studies in other languages.

In conclusion, the results of this study suggest that the consumption of green tea reduces the risk of depression symptoms. This association was also observed in the cohort study included, but the results in which did not reach the significant level. Therefore, further cohort studies are needed to confirm the potential causal relationship in this regard.

Authorship

Research conception and design: AY; statistical analysis and interpretation of the data: AY; writing of the manuscript: AY, TK, TH, and AT.

All authors contributed to the final version of this manuscript. All authors read and approved the final manuscript.

Disclosure of state of COI

No conflict of interests to be declared.

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Data availability statement Not applicable.

Supporting information

Supplemental online material is available on J-STAGE.

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