A Review and Meta-analysis of the Effect of Tea on the Prevention of Depression

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Introduction

Depression is a common public health problem affecting more than 264 million people of all ages around the world (James *et al*., 2018). It has a high prevalence of approximately 15% adults in high-income countries (Bromet *et al*., 2011), and 76% ~ 85% of people in low- or middle-income countries receive no treatment for their disorder, although there are known, effective treatments for mental disorders (Wang *et al*., 2007). Moreover, the incidence of depression is growing. Depression is estimated to result in nearly 800,000 people attempting suicide and dying each year (WHO, 2020), and it gives rise to an ascending risk of morbidity and mortality (Ng *et al*., 2007). Besides, several studies having shown that the prevalence of psychological problems among adolescents has increased significantly in recent years, and this trend is more pronounced at younger ages (Kim & Hagquist, 2018; Nair *et al.*, 2017; Twenge, 2011). Thus, it is very essential to establish prevention and treatment programmes from new perspectives. Some epidemiological evidence from the last 20 years suggests that lifestyles, such as alcohol drinking (Wang *et al*., 2012), smoking (Paperwalla *et al*., 2004), and diet (i.e., plant-based or Mediterranean) may play an important role in the development and healing of depression. Nevertheless, the impact of nutrition on depression, such as types of antioxidants or analogous compounds that may directly interact with the central nervous system, are still largely unexplored.

Tea is one of the most commonly consumed beverages in our daily life, to which drinking patterns, amounts, and types can vary a huge extent, according to different geographical and cultural backgrounds (Cheng, 2006). Because of tea consumption's widespread prevalence, even a small effect can have a significant impact on the population (Pan *et al*., 2003). In recent years, studies have found that tea intake is associated with depression. Animal studies have shown that tea extract has an antidepressant effect (Unno *et al*., 2011; Zhu *et al*., 2012). Moreover, Sun (2003) suggested that daily intake of morning/evening menopausal formula with tea extract could relieve depression and anxiety among menopausal women.

Therefore, a critical review and meta-analysis of observational studies were formed to compare the depression risk in high versus low tea drinkers, and to explore whether a dose-response association between tea intake and risk of depression existed. In the following chapters, the author describes how the research was selected. Following, the effects of tea drinking in different populations are

compared, and the studies included in the review are statistically analysed. Finally, the author critically discusses the antidepressant effects of tea consumption to draw conclusions.

Search Strategy

A systematic search was performed for articles in Embase (http://www.embase.com) and PubMed (https://www.pubmed.ncbi.nlm.nih.gov) databases through December 2020 written in the English language. The search terms were 'tea' or 'camellia sinensis' or 'theanine' combined with 'depression' or 'depressive symptom' or 'depressive disorder'. Furthermore, reference lists of the selected papers were also reviewed carefully to search for additional, previously unidentified studies. The previous studies' authors were not contacted for additional data.

Study Selection

Studies were eligible if they met the following inclusion criteria: (i) the study was conducted in humans and observationally designed, (ii) the exposure of interest was tea consumption, and the outcome of interest was depression, (iii) the frequency or dose of tea consumption were provided, (iv) the study assessed or reported a risk estimate (hazard ratios (HRs) or odds ratios (ORs) or relative risks (RR) and the corresponding 95% confidence interval (CI) for depression), and (v) the study used a credible depression measure. A credible depression measure was operationalised as, i) an international depression scale that has been measured and validated, or ii) a measuring tool that has been previously used in empirical studies and is considered reliable. Reporting ratios, such as HRs and ORs, were required to better harmonize the criteria for comparison and to perform meta-analyses. The most recent and comprehensive study was used if data were repeated in more than one study. Letters, replies, editorials, case reports, commentaries, and reviews without original data were excluded from this study.

Results

Eight of twenty-four studies were eligible for review, as summarized in Table 1 (Appendix). The remaining papers were excluded for one of two reasons: the study was a review, or it did not use risk ratios. Five of the articles included were cross-sectional studies, and three were prospective cohort designs. The total number of participants across the studies included in this current review was 21,358 people.

General Population's Tea Consumption and Depression

Three studies evaluated the relationship between tea consumption and depression symptoms among the general population. All of these studies found that, compared to non-drinkers, or people who rarely drank tea, daily tea drinkers were associated with a significantly decreased risk of having high depression scale scores or symptoms. However, percentage of change performed differently in the three studies. Kim *et al*. (2018) showed that those who drank three or more cups of tea a week had a 21% lower risk of depression compared to non-tea drinkers (odds ratio (OR) =0.79, 95%

confidence interval (CI) 0.63-0.99). Additionally, in Pham *et al.* (2013), the risk decreased 51% between individuals who drank 4 or more cups a day with individuals who drank less than one cup a day (OR=0.49, 95% CI 0.27-0.90). Finally, Hintikka *et al*. (2005) found that, in Finland, daily consumption may decrease the risk of tristimania (OR=0.47, 95% CI 0.27-0.83). Notably, no one in this study who drank over 5 cups a day showed measurable symptoms of a depressive disorder.

Older Population's Tea Consumption and Depression

Three articles assessed the relationship between tea and depression in older drinkers, especially in elder Asian populations. Two cross-sectional studies evaluated depression by using the same valid scales (Niu *et al*., 2009). Niu and colleagues (2009) found that any level of tea consumption can decrease the risk of getting a high scale depression score (equal to or more than 5 points). Their results showed, in Japanese community-dwelling participants, both 4+ cups of tea per day and 2-3 cups a day were associated with lower depression risks, compared to 1 or less per day (OR=0.56, 95% CI 0.39-0.81; OR=0.96, 95% CI 0.66-1.42, respectively), with relatively stable protective effects observed at higher doses. Feng and colleagues (2013) found slightly different effects. They found that old people living in groups in rural China, who consumed weekly or daily tea beverages, compared to non or irregular drinkers, also showed a statistically significant linearly decreasing risk in symptoms of depression (OR=0.86, 95% CI 0.56-1.32; OR=0.59, 95% CI 0.43-0.81, respectively) (Feng *et al*., 2013). Another prospective cohort study (Ng *et al*., 2020) explained the depressive tendency of drinking different types of tea. For people who were already depressed, drinking three or more cups of tea compared to non-tea drinkers reduced the risk of worsening depressive symptoms (OR=0.32, 95% CI 0.12-0.84), and the risk of new cases was lower among people who drank tea on a daily basis (OR=0.34, 95% CI 0.13-0.90). A similar result was obtained from Chinese tea (OR=0.46, 95% CI 0.31-0.99).

Association Between Tea and Depression by Gender

Two studies containing gender data were included in this review. Both were prospective cohort studies. Ruusune *et al*. (2010) reported no association between tea beverages and diagnosis of depression in middle-aged men in Eastern Finland (drinkers vs. non-drinkers RR=1.19, 95% CI 0.54-2.23). Notably, Ruusune and colleagues found that caffeine, one of the theoretically important components of tea, did not affect risk of depression. Moreover, Chen *et al*. (2010) found that using over 100g of dry tea leaves per month can decrease the risk of having a depressive disorder in women who survived breast cancer in Shanghai, China (OR=0.39, 95% CI 0.19-0.84).

Overall Estimate for Higher Tea consumption and Depression

As shown in Figure 1 (Appendix), based on all selected studies, the results of the highest-level categories were combined and a common RR for the association analysis of the higher level of tea consumption with depression risk was calculated using a fixed-effects model using Stata 15.0. The researcher found a significant 43% decrease in the risk of depression development for higher tea

consumption compared with low tea consumption (RR = 0.567, 95% CI: 0.444–0.691). Moderate heterogeneity was observed with Cochran's Q statistics (p = 0.120, I^2 = 38.9%). Subgroup analyses showed that reductions in depression risk were observed across different types of study designs, although they varied in magnitude (39% and 53% decreasing, respectively).

Discussion

The results of the current study show that regularly drinking tea may reduce the risk of depressive disorder, although this effect may be population specific and vary with type or dose of tea. Nevertheless, in all observed regions studied, results have shown varying degrees of a negative association between risk of depressive symptoms and tea intake, except one in Finland (Ruusunen *et al*., 2010). However, Ruusunen's findings should be treated with caution because the study was conducted on a narrow, specifically defined population. In contrast, a previous Finnish whole-population study confirmed the protective effect of tea drinks (Hintikka *et al*., 2005).

Concerning the population specificity of the effect of tea drinking on depressive disorder, there are several possible reasons for the different results that emerged in the two Finnish studies (Hintikka *et* al., 2005; Ruusunen *et al*., 2010). Firstly, the two studies used different study designs: the earlier study used a cohort design and the latter a cross-sectional design. Secondly, in Ruusunen *et al*. (2010), outcomes were measured with clinical depression scales, which would miss possible participants with only mild depressive symptoms or those who did not go to the hospital for examination and consultation. Thus, the actual effect may be underestimated. In addition, in the sample population selected for Ruusunen's study, the number of people with tea drinking habit prior to the study is very small, which is inconsistent with the frequency of tea drinking groups in Finland, and also leads to the fact that the study did not account for the quantity of tea drinking. Hintikka *et al*. (2005) used a scale with a sensitivity of 0.84 and a specificity of 0.81, which has been tested and used in several studies before. In addition to these two factors, Ruusunen *et al*. (2010) also looked at the effects of coffee and caffeine on the development of depression. These results suggest that caffeine may not be the main anti-depressant factor, and while they contradict some of the experimental findings (Unno *et al*., 2011; Zhu *et al*., 2012), they also suggest that further research on other common components of tea and coffee could be conducted.

Other possible effective components in tea can be discussed in conjunction with two studies in China and Japan (Chen *et al*., 2010; Pham *et al*., 2014). Both studies conducted in East Asian countries suggest that tea, especially green tea, may lower the risk of depression, and an important ingredient in green tea is folate. Meta-analysis results have shown both that an association with dietary folic acid intake and decreased depressive symptoms and that serum folic acid levels of depressed patients are lower than those of non-depressed patients (Sánchez *et al*., 2009). A cross-sectional study from Spain (Bender *et al*., 2017) focused on smoking and anxiety found a significant positive

association between low folic acid intake and the risk of depression among men (OR=2.18, 95% CI 1.08-4.38; OR=2.85, 95% CI 1.49-5.45).

Moreover, studies have shown (Zhu *et al*., 2012) that tea polyphenols have antioxidant activity in vivo and have antidepressant effects in mice models. Oral administration of epigallocatechin-3-gallate (one of the major catechins) has been shown in mouse models to prevent a decrease in brain dopamine concentrations (Levites *et al*., 2001), a key neurotransmitter in the neurochemistry of depression. In addition, theanine, which accounts for half of the amino acid content of tea leaves, can increase brain dopamine and serotonin in animal models (Yokogoshi *et al*., 1998), and its dysfunction has been considered a credible etiological candidate for depression (Delgado, 2000). A similar effect of theanine has also been found in human participants (Kimura *et al*., 2007).

In addition, Pham *et al*. (2014) observed a significant interaction in men (OR=0.23, 95%CI 0.07-0.73), suggesting that we can investigate whether green tea does not have an antipsychotic effect in postmenopausal women. Chen *et al*. (2010) also found a risk reduction effect of physical activity for both mild and clinical depression. These two studies suggest that drinking a lot of tea is often associated with other lifestyle habits that help to relieve and prevent depressive symptoms, forming a healthy lifestyle pattern. This provides a reference for experts to formulate relevant treatment plans as well as living and dietary guidelines, based on existing evidence.

In dose-analysis, Both Niu *et al*. (2009) and Feng *et al*. (2013) found that the risk of depression decreased with increased frequency and quantity of tea consumed. Niu *et al*. (2009) found more significant decreases in those who consumed 4 or more cups of tea per day, while Feng *et al*. (2013) found a protective effect of weekly and daily tea consumption. Markedly, Feng and colleague's found a negative linear relationship between tea consumption depressive symptoms, with the significant effect more pronounced in the daily tea drinkers. These findings are consistent with a meta-analysis of dose-response analyses that found a linear relationship between tea consumption and risk of depression, with a 37% reduction in risk of depression for every 3 cups of tea consumed per day (Dong *et al*., 2015).

Ng *et al*. (2020) explored the antidepressant effects of different types of tea. Here, the emphasis was placed on Chinese and Western tea, finding a favourable response of Chinese tea in terms of antidepressant effects. The study summarized the effect of tea as "preventing the aggravation of symptoms in existing cases and reducing the occurrence of new cases." These authors provide a framework for the treatment and prevention of depression in the future. It is worth noting that Asia-based studies may use different classifications. A study conducted by Li *et al*. (2016) in eastern China divided tea into black tea, green tea, and other types of tea. Such classification is more in line with the Chinese diet and traditional cultural habits. This study showed that black tea was associated with a lower risk of depression, but there was no such association between green tea and other types

of tea. Also, higher volume or concentration of black tea consumption was significantly related to a lower prevalence of depressive symptoms.

There are several possible explanations for Pham *et al*. (2014)'s conclusions. The content of relative bioactive components (especially catechins) in green tea depends on the pre-drying treatment of leaves (certain levels of fermentation and heating of tea leaves during the manufacturing process lead to the polymerization of Mono-polyphenolic compounds such as catechins, resulting in conformational changes that alter their properties). Other factors that influence catechin content include geographical location and growing conditions (e.g., soil, climate, agricultural practices, chemical fertilizers), type of green tea (e.g., blend, decaffeinated, instant), and preparation for brewing (e.g., amount of product used, brewing time, temperature) (Cabrera *et al.*, 2006; Lin *et al*., 2003). Therefore, the discussion of different populations and the analysis of key components will be an important focus for follow-up studies.

Previous research has shown that not only the type of tea but also the ingredients added to it can affect the mental health of participants. Guo *et al*. (2014) surveyed an elderly American population (n= 263,923 people) that showed that drinking four or more cups or cans of cold or hot tea per day was not associated with self-reported depressive symptoms. However, at the same time, a higher risk of depression was observed in those who drank iced tea with added artificial sugar, as opposed to those who did not add sugar, which was associated with a lower risk of self-reported depression. On this basis, we can make a more detailed classification of the types of tea.

Limitations

Several further limitations for the studies included in this review have been shown in Table 1 (Appendix). What is more, the representativeness and generalisability of Niu *et al*. (2009), Chen *et al*. (2010), and Feng *et al*. (2013) may be low, because the selected populations are relatively specialised, such as women with breast cancer and elderly populations. Moreover, the lack of causal inference is common weakness of the five cross-sectional studies included. They cannot observe the changing process of depression by using camelia sinensis. Although almost all of the included studies had relatively large sample sizes, the percentage of tea drinkers in individual studies was low enough to affect the results of subsequent analyses.

Reporting bias may also limit this study. Firstly, only studies written in English and published after 2000 have the chance to be evaluated and selected. The search was limited to Embase/PubMed databases; articles published in other databases were excluded. For this reason, very limited articles were searched. This could be an issue because, perhaps, a large number of research from non-English using countries, especially Asian countries, which contain abundant tea drinkers, were possibly excluded. As not every paper reported different types of tea drinks, the literature reviewed

in this paper was not analysed by classification, only the higher categorisations (doses) used in each paper were summarized and analysed, which also limits the current study's results.

Conclusion

To sum up, findings in this review suggest that tea consumption may be an independent protective factor to the risk of depression. In addition, this study also reflects that the effect of tea intake level may be different among different populations, which may provide a reference for the development of dietary guidelines for recommended intake. At the same time, professionals may also want to add tea drinking to depression treatment and prevention plans, to be used in combination with clinical treatments such as medicine and psychological counselling. Given that tea is an economical drink most people consume without untoward reactions, its potency in controlling and preventing the exacerbation of depression should be realized, although further explorations such as effective groups and components are still necessary.

Recommendations for Future Research

More sophisticated methodology to specify the effect of tea and its related materials should be prioritised in future research. For the general population, more extensive methods for depression diagnosis should be used, such as different self-report scales combined with professional clinical diagnosis, to reduce the incidence of underreporting. Moreover, more sensitive depression scales can help categorize the type and level of depression when exploring this association. For a special community, such as menopausal women and older populations, the anti-depressive or preventive effect of high doses of tea should be verified. At the same time, more interventional studies, prospective studies, or randomized trials are needed to enrich current types and strengthen the inference of causality. Finally, possible mechanisms and confounding factors must be explored to identify the particular antidepressant components or the idiographic type of tea that are associated soothing effects.

Appendix

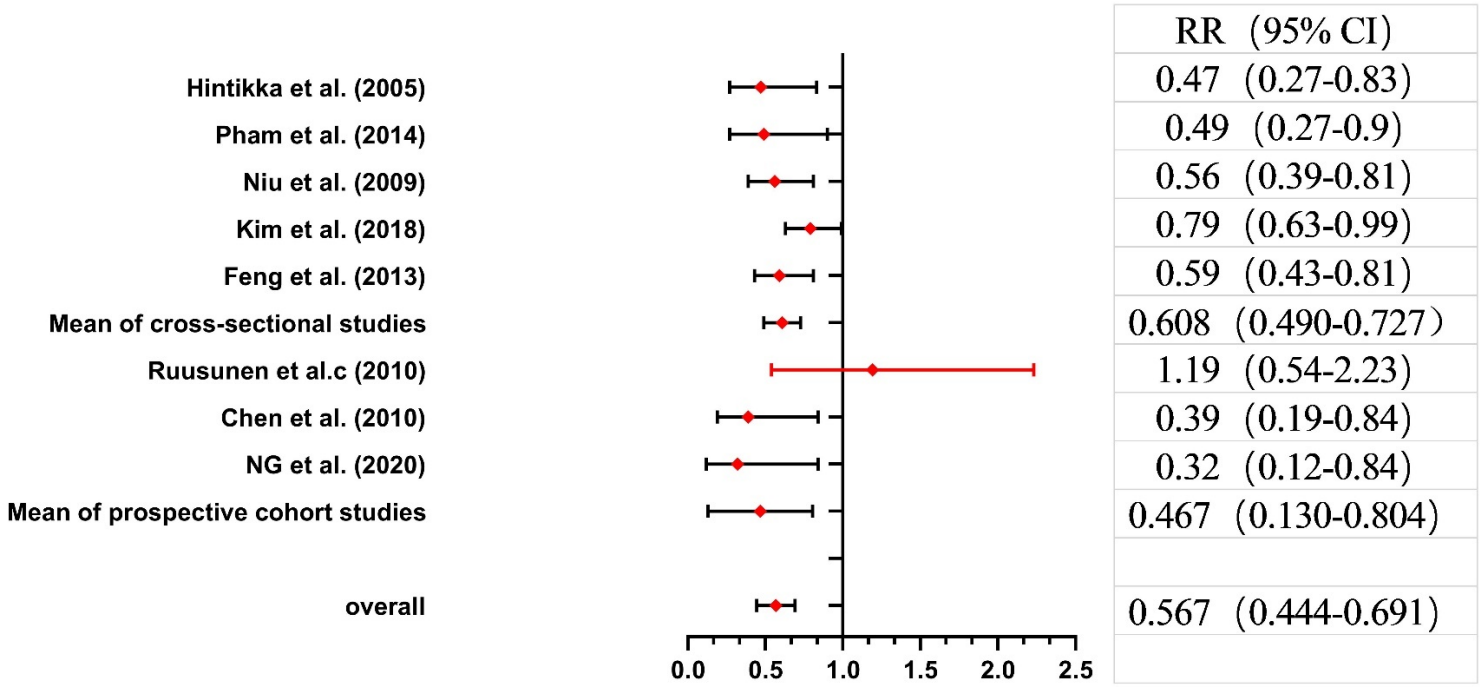

Figure 1 Relative Risks of depression comparing the highest with the lowest categories of tea consumption.

**RR = Relative Risk, CI = Confidence Intervals*

Table 1 Summary of selected research articles with key features, connections, and limitations.

Author(s) (Year) and Area	Study Aim	Design and Assessment Tool	Sample Characteristics	Exposure of Interest	Outcome of Interest	Main Results	Limitations
Anu Ruusunen et al. (2013). Eastern Finland.	Determine the association between the intake of coffee, tea and caffeine and depression.	Population-based cohort study using HPL* score.	2232 middle-aged men without psychiatric disorder at baseline.	Caffeine intake in tea and coffee consumption.	severe depression diagnosed by a physician	No associations were observed between depression and intake of tea (drinkers vs. non-drinkers; RR*=1.19, 95% CI* 0.54, 2.23).	Compared to the large sample size, the cases were relatively few. Only severe patients requiring hospitalisation were obtained in the study because of no national register.
Jukka Hintikka et al. (2005). Finland.	Investigated the relationship between the frequency and amount of tea drinking and the prevalence of depression in general population.	Cross-sectional study using BDI*.	2011 individuals between 25-64 years old.	Frequency and daily amount of tea drinking.	BDI score (equal or greater than 15).	Those who drink tea daily may have a significantly reduced risk of being depressed (adjusted OR* 0.47, 95% CI 0.27–0.83). No participants who daily tea intake was five cups or more had depression.	Lost one third of aimed baseline sample. No structured assessments were made when diagnosing depression. No questions were asked about the type of tea consumed, nor about other types of caffeinated beverages.

Author(s) (Year) and Area	Study Aim	Design and Assessment Tool	Sample Characteristics	Exposure of Interest	Outcome of Interest	Main Results	Limitations
Xiaoli Chen et al. (2010). Netherlands.	Examine the association of lifestyle factors and supplement use with depression among breast cancer survivors.	Population-based cohort study using CES-D*.	1399 breast cancer survivors.	Time, type and amount of tea consumption.	CES-D score (10 to 15: mild depression, and equal to or more than 16: clinical depression).	Regular tea consumption (more than 100 g dried tea leaves/mo) was inversely associated with mild depression (OR, 0.54;95%CI, 0.30 to 0.98), clinical depression (OR 0.76; 95% CI, 0.43 to 1.35), and overall depression (OR, 0.64; 95% CI, 0.41 to 0.99).	Included only one way to assess depression, and depression status at baseline was unknown. Prevalence of some specific lifestyle factors in study population is low. Have no enough power to evaluate differences between mild and clinical depression
Ngoc Minh Pham et al. (2014). North-eastern Kyushu, Japan.	Examine the association between the consumption of green tea, coffee and caffeine and depressive symptoms.	Cross-sectional study using CES-D.	537 men and women aged 20-68 years.	Consumption of green tea and coffee and the amount of caffeine intake	Depressive symptoms (measured by score more than 16).	Compared with participants consuming less than 1 cup green tea/d, those consuming 2-3 cups/d and more than 4 cups/d had a 41% and 51% significantly lower prevalence odds of depressive symptoms, respectively (P for trend=0.01).	Not conclude whether or not consumption of green tea or coffee decreases depressive symptoms. Food contain caffeine were not specifically asked. No detailed history of depressive episodes and use of antidepressants.

Author(s) (Year) and Area	Study Aim	Design and Assessment Tool	Sample Characteristics	Exposure of Interest	Outcome of Interest	Main Results	Limitations
Kaijun Niu et al. (2009). Sendai City, Japan.	investigate the relations between green tea consumption and depressive symptoms in elderly Japanese.	Cross-sectional study using GDS*.	1058 community dwelling elderly Japanese individuals aged over 70 y.	Green tea consumption categories in tertile.	Depressive symptoms (GDS score: mild more than 11; severe more than 14).	Compared with green tea consumption of less than 1 cup/d: 2–3 cups green tea/d (OR 0.96; 95% CI: 0.66, 1.42) and more than 4 cups green tea/d (OR 0.56; 95% CI: 0.39, 0.81). Similar relations were also observed in the case of severe depressive symptoms.	People chosen from public facility may not represent elderly general population well. The GDS is not for making a clinical diagnosis of depressive episodes. Whether depressive symptoms lead to a decline in green tea consumption could not be known.
Jiwon Kim and Jihye Kim (2018). Korea.	Investigated the associations of green tea, coffee, and caffeine consumption with self-report lifetime depression in the Korean population.	Cross-sectional study using several questions.	9576 participants aged 19 years or older.	Frequent green tea consumption (more than 3 cups/week).	Self-report lifetime depression (at least one ‘yes’).	Frequent green tea consumers had 21% lower prevalence of depression (OR = 0.79, 95% CI = 0.63–0.99, p for trend = 0.0101) than green tea non-consumers.	Cannot identify causal relationships because of the study design. Potential misjudgement for depression because of the assessment tool.

Author(s) (Year) and Area	Study Aim	Design and Assessment Tool	Sample Characteristics	Exposure of Interest	Outcome of Interest	Main Results	Limitations
Ng et al. (2020). Singapore.	Investigated whether tea consumption was associated with changes in depressive symptoms over time among Asian older adults.	Population-based prospective cohort study using GDS.	3177 Singapore residents aged 50 and above.	Type and frequency of tea consumption.	Improvement or deterioration of depression (change 5 or more in GDS score).	Compared to non-tea drinkers, ≥3 cups of tea of all kinds were significantly less likely to have worsened GDS symptoms: OR=0.32, 95% CI=0.12, 0.84. The risk of incident GDS (≥5) depression was significantly lower (OR=0.34, 95%CI=0.13, 0.90) for daily consumption of all types of tea (OR=0.46, 95%CI=0.21,0.99).	Small counts by daily consumption of individual black/oolong or green tea. Large attrition from loss to follow-up, due to deaths and loss of contact and refusals. The incidence of depression was under-estimated.

Author(s) (Year) and Area	Study Aim	Design and Assessment Tool	Sample Characteristics	Exposure of Interest	Outcome of Interest	Main Results	Limitations
Lei Feng et al. (2013). Shandong, China.	Examined the association between tea consumption and depressive symptoms in Chinese older people and the mediating role of cerebrovascular disease in the association.	Population-based cross-sectional study using GDS.	1368 community-dwelling individuals aged 60 or older.	Regular tea consumption.	High depressive symptoms (GDS score of 5 or older).	Compared with no or irregular tea consumption, controlling, OR of having high depressive symptoms were 0.86 (95% confidence interval (CI) = 0.56–1.32) for weekly and 0.59 (95% CI = 0.43–0.81) for daily tea consumption (P for linear trend = .001);	Residual confounding might still have affected the results. Caution is still needed when generalizing these results to other rural populations. No information on biomarkers of tea intake was collected.

**HPL = Human Population Laboratory Depression Scale (18 items)*

**BDI = Beck Depression Inventory (21 items)*

**CES-D = The Center for Epidemiological Studies-Depression Scale (20 items)*

**GDS = the Geriatric Depression Scale (15 or 30 items)*

**95% CI = 95% Confidence Intervals, RR = Relative Risk, OR = Odds Ratio.*

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