

Cognitive Vitality Reports® are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-in-development, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

Green Tea

Evidence Summary

There are many health benefits of green tea, including decreased risk of dementia, cardiovascular disease, and all-cause mortality, but the majority of data are from observational studies.

Neuroprotective Benefit: Several prospective studies and short-term randomized controlled trials suggest promise for neuroprotection, but no clinical trials have tested whether it can prevent dementia.

Aging and related health concerns: Multiple meta-analyses report that green tea consumption is associated with decreased risks of mortality, cardiovascular disease, and some cancers, but many studies were carried out in Asia.

Safety: Multiple meta-analyses have concluded that green tea consumption at moderate amounts is safe with mild side effects, but it is worth paying attention to the source of the tea leaves, as those grown in areas of excessive pollution can have lead contamination.



What is it? Green tea is made from dried leaves of *Camellia sinensis*, a perennial evergreen shrub. Green tea contains caffeine, catechins (antioxidants), and L-theanine (an amino acid derivative) (See separate reports for caffeine, EGCG, and L-theanine). There are multiple types of green tea. Sencha, the most common type of green tea in Japan (and the US), is prepared by infusing the processed whole tea leaves in hot water. Gyokuro is a type of green tea that is produced from shading the tea leaves, increasing theanine and caffeine production while inhibiting catechin levels. Matcha is a type of green tea used in Japanese tea ceremony. The tea leaves are also shade-grown, to increase theanine and chlorophyll levels and to enhance flavor and color, then harvested and finely stone-ground. Matcha is consumed by adding hot water to the fine tea powder and mixing vigorously with a bamboo whisk. Matcha powder is also used as food coloring, for green tea ice cream, Japanese confectionary, and noodles.

Neuroprotective Benefit: Several prospective studies and short-term randomized controlled trials suggest promise for neuroprotection, but no clinical trials have tested whether it can prevent dementia.

Types of evidence:

- 2 double-blind randomized controlled trials (RCTs), 1 on cognitive function and the other on acute effects of green tea extract
- 2 prospective studies on the incidence of dementia and cognitive decline
- 2 observational studies (1 longitudinal, 1 cross-sectional) on cognitive function in old people
- 1 review on tea and cognitive health in late life

Human research to suggest prevention of dementia, prevention of decline, or improved cognitive function?

Two prospective studies have reported that greater green tea consumption is associated with lower risk of incident dementia [1; 2]. In the larger study (13,645 Japanese people over 65 years old), the hazard ratio for 5 or more cups/day was 0.73 (95% CI, 0.61-0.87) [2]. The smaller study (723 Japanese people over 60 years old) showed that compared with individuals who did not consume green tea at all, the incidence of overall cognitive decline (dementia or MCI) was 0.32 (95% CI: 0.16-0.64) among individuals who consumed green tea every day and 0.47 (95% CI: 0.25-0.86) among those who consumed green tea 1-6 days per week [1]. While positive effects of green tea drinking may be attributable to the benefits of social interactions and leisurely activities with peers [3], in the latter study they did not find an association between coffee or black tea consumption and incidence of dementia or MCI. (But other studies have shown protection with coffee intake—please see the report on coffee for details).

Two RCTs have evaluated the effects of green tea extracts on cognitive functions. In a double-blind RCT in 91 patients with MCI, the combination of green tea extract and L-theanine (1680 mg of LGNC-07, including 240 mg of L-theanine but no caffeine) for 16 weeks resulted in significant improvements in memory and attention, particularly in patients who had relatively severe baseline impairment (MMSE scores of 21-23)[4]. Brain theta waves were increased in the temporal, frontal, parietal, and occipital cortex after 3 hours, suggestive of cognitive alertness. A double-blind RCT examining the acute effects of a drink containing 27.5 g of green tea extract reported that the extract increased brain connectivity and that the magnitude of that effect correlated with improvement in working memory task performance [5].

In a population-based longitudinal cohort study in Chinese people aged 80-115 years old, tea drinking was associated with higher verbal fluency at baseline and throughout the follow-up period (up to 7 years) [6]. Thus, regular tea drinking is associated with better cognitive function at old age. In a cross-sectional study, low green tea consumption was associated with a higher prevalence of cognitive impairment in older Japanese people [7].

It is unclear whether benefits of life-long green tea consumption can be mimicked by late-in-life changes in tea drinking. Also, observational studies cannot tease apart the benefits of green tea with the benefits of avoiding alternatives to tea/coffee, such as sodas and other sugared beverages.

Human research to suggest benefits to patients with dementia: None available.

Mechanisms of action for neuroprotection identified from laboratory and clinical research: Green tea contains several compounds that may be neuroprotective, including caffeine, L-theanine, and green tea catechins (e.g., EGCG). Mechanisms of action for caffeine, EGCG, and L-theanine are discussed in the individual reports.

APOE4 interactions: No studies on green tea have examined whether it affects ApoE4 carriers differently from non-carriers. Some studies have examined the interactions between ApoE status and caffeine intake [8], which have produced inconclusive results. A pilot randomized crossover trial has shown that drinking 6 mugs of black tea daily was associated with some beneficial effects on factors associated with cardiovascular disease risk (triacylglycerol, blood coagulation factors) in E2 carriers but not in people with E3/E4 or E4/E4 genotype [9].

Aging and related health concerns: Multiple meta-analyses report that green tea consumption is associated with decreased risks of mortality, cardiovascular disease, and some cancers, but many studies were carried out in Asia.

Types of evidence:

- 2 Cochrane meta-analyses based on 14 and 11 RCTs examining the effects of green tea on weight loss and cardiovascular disease prevention, respectively
- 1 Cochrane meta-analysis based on 50 observational studies and 1 RCT on cancer risk
- 14 meta-analyses on age-related conditions (3 on cardiovascular disease and/or mortality, 3 on blood pressure, 6 on cancers, 1 on diabetes, and 1 on glucose and insulin sensitivity)
- 1 longitudinal study on mortality
- 1 European cohort study on diabetes incidence
- 1 review on coffee and tea for health and longevity

Mortality: DECREASED. Two meta-analyses of 18 and 22 prospective studies (each with over 800,000 total subjects) reported that tea consumption is associated with lower mortality [10; 11]. High green tea consumption specifically was associated with lower all-cause mortality (RR=0.80, 95% CI, 0.68-0.93) and cardiovascular disease mortality (RR=0.67, 95% CI, 0.46-0.96) compared to the lowest consumption [10]. The dose-response analysis indicated that for every additional cup of green tea/day, all-cause mortality and cardiovascular disease mortality was decreased by 4% and 5%, respectively.

Cardiovascular diseases: DECREASED. A meta-analysis of 8 observational studies and 1 RCT reported benefits of green tea consumption [12]. Those who drank 1-3 cups of green tea per day had a reduced risk of myocardial infarction (OR=0.81, 95% CI: 0.67-0.98) and stroke (OR=0.64, 95% CI: 0.47-0.86) compared to those who drank less than 1 cup/day. People who drank 4 cups or more per day had an even greater reduction of risk of myocardial infarction (OR=0.68, 95% CI: 0.56-0.84).

Cholesterol: BENEFIT. A meta-analysis of RCTs in healthy adults or those at high risk of cardiovascular disease reported that green tea produced statistically significant reductions in total cholesterol by 23.9 mg/dL (95% CI, -29.7 to -17.8)[13]. Another meta-analysis of mostly observational studies reported that people who drank over 10 cups of green tea per day had lower LDL compared to those who drank fewer than 3 cups/day [12].

Blood pressure: DECREASED. Three meta-analyses based on 10, 13, and 25 RCTs showed that consumption of green tea significantly reduced systolic blood pressure by 1.98-2.36 mmHg and diastolic



blood pressure by 1.70-1.92 mmHg [14; 15; 16]. These effects are typically seen after long-term intervention (12+ weeks).

Type 2 diabetes mellitus: DECREASED. While there is not enough data on green tea specifically, 1 meta-analysis and 1 large cohort study showed that tea consumption is associated with a reduced risk of type 2 diabetes [17; 18]. The meta-analysis including 16 cohorts (total of 545,517 subjects) showed that for every 2 additional cups/day of tea consumption, there was a 4.6% reduced risk of type 2 diabetes (95% CI, 0.9-8.1%)[18]. The large case cohort study was carried out in Europe and included 340,234 subjects across 8 European countries [17]. In this study too, tea consumption was associated with lower incidence of type 2 diabetes. The hazard ratio was 0.84 (95%CI, 0.71-1.00) when subjects who drank 4 or more cups/day were compared with non-drinkers.

Glucose/insulin sensitivity: BENEFIT/MIXED. A meta-analysis of 17 RCTs (total of 1133 subjects) reported that green tea extracts (tea catechins, EGCG, polyphenols, or tea extract) was associated with decreased fasting glucose and glycated hemoglobin (HbA1c, used for diagnosing prediabetes and diabetes) [19]. Glucose was decreased by -0.09 mmol/L (95% CI: -0.15, -0.03 mmol/L) and HbA1c concentration was decreased by 0.30% (95% CI, -0.37 to -0.22%). No significant effects on fasting insulin concentrations were observed. In a smaller meta-analysis of 7 RCTs in people at risk of type 2 diabetes, green tea consumption did not significantly decrease levels of fasting glucose, fasting insulin, HbA1c, and HOMA(IR)(index for insulin resistance) [20].

Weight: INCONCLUSIVE. A Cochrane meta-analysis based on 14 RCTs in overweight or obese adults reported that green tea consumption for at least 12 weeks was associated with weight loss, but the magnitude of change was small and not likely to be clinically important [21]. Green tea had no effect on the maintenance of weight loss.

Liver cancer: DECREASED. Based on a meta-analysis of 8 observational studies, green tea consumption was associated with a moderate reduction in risk for primary liver cancer (RR=0.79, 95% CI, 0.68-0.93) [22].

Breast cancer: DECREASED. Several meta-analyses have linked green tea consumption with decreased incidence of breast cancer and its recurrence. In a meta-analysis of four studies, high green tea consumption was associated with a reduced risk of breast cancer compared to non/lowest green tea consumption (OR = 0.78, 95% CI, 0.61-0.98)[23]. Another meta-analysis showed that breast cancer incidence was reduced with increased green tea consumption (more than 3 cups/day) in case-control

studies (RR=0.81, 95% CI, 0.75-0.88) but failed to find an association in cohort studies [24]. The same meta-analysis reported that high green tea consumption was associated with lower breast cancer recurrence (RR = 0.73, 95% CI: 0.56-0.96). A third meta-analysis also reported that the highest level of green tea consumption was associated with a significantly lower risk of breast cancer recurrence in early stage (stages I and II) cancers (RR=0.56, 95% CI, 0.38-0.83) [25]. But this meta-analysis did not find a significant effect of green tea consumption on breast cancer incidence (RR=0.89, p=0.28).

Black tea appears to not be as protective, despite coming from the same plant as green tea. Conflicting results were observed in case-control (OR = 0.91, 95% CI, 0.84-0.98) versus cohort studies (OR = 1.15, 95% CI = 1.02-1.31), with the latter showing a modest increase in breast cancer risk with black tea consumption [23]. A different meta-analysis showed that black tea consumption is not associated with the risk of breast cancer [26].

Lung cancer: DECREASED. In a meta-analysis of 22 observational studies (12 studies on green tea, 14 on black tea), there was a borderline significant association between highest green tea consumption and reduced risk of lung cancer (RR=0.78, 95% CI, 0.61-1.00) [27]. An increase in green tea consumption by 2 cups/day was associated with an 18% reduced risk of developing lung cancer (RR=0.82, 95% CI, 0.71-0.96). For black tea, no statistically significant association was observed (highest versus non/lowest, RR=0.86, 95% CI=0.70-1.05).

Endometrial Cancer: DECREASED. A meta-analysis of 7 observational studies showed that tea consumption may reduce the risk of endometrial cancer (RR for ever-drinkers vs non/lowest drinkers was 0.85, 95% CI, 0.77-0.94) [28]. An increase in tea intake by 2 cups/day was associated with a 25% decreased risk of endometrial cancer. The protective effect was more evident for green tea compared to black tea.

Prostate cancer: DECREASED. In a large meta-analysis of various cancers, observational studies with higher methodological quality and 1 RCT suggested that men consuming higher quantities of green tea or green tea extracts have a decreased risk of prostate cancer (RR ranged from 0.24-0.99)[29].

Safety: Multiple meta-analyses have concluded that green tea consumption at moderate amounts is safe with mild side effects, but it is worth paying attention to the source of the tea leaves, as those grown in areas of excessive pollution can have lead contamination.

Types of evidence:

- 2 Cochrane meta-analyses based on 14 and 11 RCTs examining the effects of green tea on weight loss and cardiovascular disease prevention, respectively
- 1 Cochrane meta-analysis based on 50 observational studies and 1 RCT
- 3 case studies on excessive tea drinking and skeletal fluorosis
- Several articles on tea leaf contamination from soil and pollution

Meta-analyses: There are 3 Cochrane meta-analyses that have included analysis of the safety profile of green tea. A Cochrane meta-analysis based on 14 RCTs in overweight or obese adults (total of 703 subjects) reported that side effects from green tea consumption were mild and none of the serious adverse events observed were related to the intervention [21]. In another Cochrane meta-analysis based on 11 RCTs in healthy adults and those at high risk of cardiovascular disease (total of 821 subjects), side effects were mild and no significant differences in adverse events were observed between green tea and placebo groups [13]. In another Cochrane meta-analysis based mostly on observational studies (27 case-control studies, 23 cohort studies, and 1 RCT) that included a total of over 1.6 million subjects, green tea was judged to be safe at moderate and regular amounts (3 to 5 cups per day, up to 1200 ml/d) [29].

Drug interactions: Three drugs are known to interact with green tea, but the interactions are judged to be minor and minimally clinically significant (drugs.com). The three drugs are warfarin (also known as Coumadin™ and Jantoven™), anisindione (or Miradon™), and dicumarol. Caffeine in green tea can also interact with some drugs (drugs.com).

Lead: Tea leaves can absorb lead from the soil, and according to the ConsumerLab.com analysis, tea from some manufacturers contained up to 2.5 µg of lead per serving, compared to no measurable amounts from products that sourced tea leaves from Japan [30]. Green tea from areas with excessive pollution may contain higher amounts of lead [31]. While lead is not thought to readily seep into the fluid from steeping, lead contamination is a concern if you are drinking matcha, as the whole tea leaves are consumed.



Fluoride: Fluoride is known to prevent dental cavities and tap water is fluoridated in many areas of the US. While tea is safe when consumed in moderate amounts, long-term and excessive amounts of tea consumption can cause bone problems from fluoride in tea leaves. A case study reported that a 47 year-old woman who consumed a pitcher of tea made from 100 to 150 tea bags (estimated fluoride levels, > 20 mg/d) every day for 17 years developed skeletal fluorosis [32]. Several other case studies have also reported skeletal fluorosis in people who consumed gallons of tea daily for several decades [33; 34].

Sources and dosing: There are multiple types of green tea. Sencha, the most common type of green tea in Japan, contains 40~60 mg of caffeine, 8~25 mg of L-theanine, and 25~60 mg of EGCG in a cup (200 mL). Gyokuro, a type of green tea that is produced from shading the tea leaves, contains 240 mg of caffeine, 85 mg of L-theanine, and 86 mg of EGCG per cup. Matcha is powdered Japanese green tea often used in Japanese tea ceremony and contains 25 mg of caffeine, 36 mg of L-theanine, and 17-109 mg of EGCG per serving (80 ml) [35], along with vitamins A, B-complex, C, E, K, and trace minerals. No clinical studies have compared these different types of green tea for long-term health associations. In observational studies, high green tea consumption has often been defined as those who consumed over 7 cups of tea in Asia and over 2 cups of tea in the US [28].

Research underway: A clinical trial is testing whether a brain health supplement (BBG-1001) that contains green tea extract, turmeric, fish oil, and vitamin D can slow cognitive decline in people with mild cognitive impairment ([NCT02741804](https://clinicaltrials.gov/ct2/show/study/NCT02741804)). This study is scheduled to be completed in May 2019. This study has not started recruiting participants yet.

Search terms:

Pubmed, Google: Green tea

- + cognitive, + memory, + dementia, + meta-analysis, + systematic review, + ApoE4, + cancer, + cardiovascular, + diabetes, + safety

Clinicaltrials.gov: Green tea, EGCG, L-theanine, matcha

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