Original Investigation

Coffee and Tea Intake, Dementia Risk, and Cognitive Function

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JAMA
Published Online: February 9, 2026
doi: 10.1001/jama.2025.27259

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Key Points

Question Is long-term intake of caffeinated and decaffeinated coffee associated with risk of dementia and cognitive outcomes?

Findings In this prospective cohort study of 131 821 individuals from 2 cohorts with up to 43 years of follow-up, 11 033 dementia cases were documented. Higher caffeinated coffee intake was significantly associated with lower risk of dementia. Decaffeinated coffee intake was not significantly associated with dementia risk.

Abstract

Importance Evidence linking coffee and tea to cognitive health remains inconclusive, and most studies fail to differentiate caffeinated from decaffeinated coffee.

Objective To investigate associations of coffee and tea intake with dementia risk and cognitive function.

Design, Setting, and Participants Prospective cohort study that included female participants from the Nurses' Health Study (NHS; n = 86 606 with data from 1980-2023) and male participants from the Health Professionals Follow-up Study (HPFS; n = 45 215 with data from 1986-2023) who did not have cancer, Parkinson disease, or dementia at study entry (baseline) in the US.

Exposures The primary exposures were intakes of caffeinated coffee, decaffeinated coffee, and tea. Dietary intake was collected every 2 to 4 years using validated food frequency questionnaires.

Main Outcomes and Measures The primary outcome was dementia, which was identified via death records and physician diagnoses. The secondary outcomes included subjective cognitive decline assessed by a questionnaire-based score (range, 0-7; higher scores indicate greater perceived decline; cases defined as those with a score ≥3) and objective cognitive function assessed only in the NHS cohort using telephone-based neuropsychological tests such as the Telephone Interview for Cognitive Status (TICS) score (range, 0-41) and a measure of global cognition (a standardized mean *z* score for all 6 administered cognitive tests).

Results Among 131 821 participants (mean age at baseline, 46.2 [SD, 7.2] years in the NHS cohort and 53.8 [SD, 9.7] years in the HPFS cohort; 65.7% were female) during up to 43 years of follow-up (median, 36.8 years; IQR, 28-42 years), there were 11 033 cases of incident dementia. After adjusting for potential confounders and pooling results across cohorts, higher caffeinated coffee intake was significantly associated with lower dementia risk (141 vs 330 cases per 100 000 person-years comparing the fourth [highest] quartile of consumption with the first [lowest] quartile; hazard ratio, 0.82 [95% CI, 0.76 to 0.89]) and lower prevalence of subjective cognitive decline (7.8% vs 9.5%, respectively; prevalence ratio, 0.85 [95% CI, 0.78 to 0.93]). In the NHS cohort, higher caffeinated coffee intake was also associated with better objective cognitive performance. Compared with participants in the lowest quartile, those in the highest quartile had a higher mean TICS score (mean difference, 0.11 [95% CI, 0.01 to 0.21]) and a higher mean global cognition score (mean difference, 0.02 [95% CI, −0.01 to 0.04]); however, the association with global cognition was not statistically significant ($P = .06$). Higher intake of tea showed similar associations with these cognitive outcomes, whereas decaffeinated coffee intake was not associated with lower dementia risk or better cognitive performance. A dose-response analysis showed nonlinear inverse associations of caffeinated coffee and tea intake levels with dementia risk and subjective cognitive decline. The most pronounced

Conclusions and Relevance Greater consumption of caffeinated coffee and tea was associated with lower risk of dementia and modestly better cognitive function, with the most pronounced association at moderate intake levels.

Introduction

Alzheimer disease (AD), the most common cause of dementia, currently affects more than 6 million people in the US, and is projected to nearly double to 13 million by 2050.[1] The clinical trajectory of dementia is often conceptualized as a continuum that may begin with subjective cognitive decline (a stage where individuals report perceived cognitive changes[2]), progressing to mild cognitive impairment with measurable deficits on objective cognitive testing,[3] and ultimately to clinical dementia.[4]

With limited treatment options and potential adverse effects of available therapies, early prevention is crucial. Among modifiable risk factors, dietary components have garnered increasing attention.[5] Coffee contains bioactive compounds, including caffeine and polyphenols, which may offer neuroprotection by reducing oxidative stress and neuroinflammation.[6] Experimental studies suggest that chronic caffeine exposure may influence AD-related processes, including amyloid and tau pathways, and AD pathogenesis is increasingly recognized as multifactorial, involving additional mechanisms such as lysosomal or autophagy dysfunction and neuroinflammatory or immune responses.[7-10] Moreover, caffeine has been linked to improved insulin sensitivity and vascular function, which may help protect against cognitive decline.[11]

Several prospective studies have examined coffee and caffeine intake with cognitive health, yet findings remain inconsistent.[12-16] Notably, the dose-response relationship between caffeine intake and cognitive decline or dementia risk varies across studies; some studies suggested increased risk at higher intake levels, whereas other studies indicated protective effects that stabilize at higher intake levels.[14,15] Most previous studies were limited by single dietary assessments and short follow-up periods, making it difficult to evaluate long-term effects on cognitive outcomes.[17] Furthermore, few studies have comprehensively assessed cognitive outcomes spanning the dementia continuum.

We used data from the Nurses' Health Study (NHS) and the Health Professionals Follow-up Study (HPFS) that had up to 43 years of follow-up with repeated dietary measurements and assessments of dementia, subjective cognitive decline, and objective cognitive function. We hypothesized that higher consumption of caffeinated coffee, tea, and caffeine was associated with lower dementia risk and better cognitive function.

Methods

Study Design

The study protocol was approved by the institutional review boards of the Brigham and Women's Hospital

dance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

The NHS began in 1976 and enrolled 121 700 female registered nurses aged 30 to 55 years.[18] The HPFS started in 1986 and recruited 51 529 male health professionals aged 40 to 75 years at baseline.[19] Questionnaires were sent biennially to collect information on lifestyle factors and health conditions. In this analysis, the start of the study (baseline) was 1980 for the NHS cohort and was 1986 for the HPFS cohort, which is when diet was first assessed in both studies. In both cohorts, participants were excluded if they had a history of cancer, Parkinson disease, or dementia; reported implausible total energy intake (<500 or >3500 kcal/d for females in the NHS cohort; <800 or >4200 kcal/d for males in the HPFS cohort); or had missing intake for caffeinated beverages. After these exclusions, 86 606 female participants in the NHS cohort and 45 215 male participants in the HPFS cohort were included in the dementia analysis. The participant selection process and cohort-specific exclusions appear in eFigure 1 in **Supplement 1**.

Intake Assessment for Coffee, Tea, and Caffeine

Dietary intake was measured using validated semiquantitative food frequency questionnaires (FFQs) that were administered at baseline and every 2 to 4 years thereafter.[20] Participants reported how often, on average, they consumed each food and beverage, with a specified portion size. Caffeine intake was derived from intake levels of coffee, tea, soda, and chocolate by multiplying the frequency of consumption for each item by its caffeine content per serving (as estimated by the US Department of Agriculture food composition sources) and then summing across all items.[21] In our validation studies, the intake assessed by the FFQs showed strong correlations with those measured from 7-day dietary records ($r = 0.80$ for caffeine, $r = 0.84$ for coffee, and $r = 0.81$ for tea), demonstrating excellent validity.[20,22] In this study, the primary exposures were caffeinated coffee, decaffeinated coffee, and tea intake. In addition, total caffeine intake was analyzed as a secondary exposure.

Ascertainment of Dementia and Cognitive Function

Dementia was the primary outcome. Cases of dementia were identified through death records and biennial self-reported physician diagnoses of AD or other types of dementia. Death ascertainment was greater than 98% complete through state records, the National Death Index, next-of-kin confirmation, and postal authorities; a physician blinded to exposure data confirmed dementia as the underlying or contributory cause using death certificates, medical records, and autopsy reports.[23] *APOE4* genotype and plasma phosphorylated tau 217 (p-tau217) are established biomarkers reflecting AD-related genetic susceptibility and pathophysiology.[24,25] In the 2 included cohorts, *APOE4* carriers and participants with higher plasma p-tau217 levels had substantially higher risk of incident dementia, supporting the construct validity of the ascertainment for disease outcomes (eMethods in **Supplement 1**).[24]

As secondary outcomes, we assessed subjective cognitive decline and objective cognitive function. Subjective cognitive decline was assessed using cohort-specific 6- to 7-item questionnaires (with yes or no responses) covering general memory, executive function, attention, and visuospatial skills. The questionnaires were administered in the NHS cohort in 2012 and 2014 and in the HPFS cohort in 2008, 2012, 2016, 2018, and 2020. Each yes response was scored as 1 point and summed to create a subjective cognitive decline score (range, 0-7; higher scores indicate greater perceived decline). The wording for each item and the administration cycles appear in eTable 1 in **Supplement 1**. The validity of this score has been reported.[26]

For each participant, the mean score across all available questionnaires was ascertained. Individuals with subjective cognitive decline had a mean score of 3 or greater.[27] Among the 17139 participants in the NHS cohort who were older than 70 years, objective cognitive function was evaluated using telephone-based cognitive tests from 1995 to 2008 in 4 waves and comprising the following tests: (1) the Telephone Interview for Cognitive Status (TICS; score range, 0-41); (2) immediate recall of the East Boston Memory Test (EBMT); (3) delayed recall of the EBMT; (4) delayed recall of the 10-word list for the TICS; (5) a test of verbal fluency; and (6) the digit span backward test.[28] The high validity and reliability of these tests have been previously reported.[29]

We derived 3 cognitive scores: global cognition (combining all tests), verbal memory (including immediate and delayed recalls of the EBMT and the 10-word list for the TICS), and TICS score. Test-specific *z* scores were calculated and averaged to produce composite scores for global cognition and verbal memory at each time point.[26] Although a validated minimal clinically important difference has not been established for these telephone-based scores or standardized composite scores in large epidemiological studies, prior work suggests mild cognitive impairment in individuals with a 2- or 3-point lower score on the TICS-based measures vs adults without cognitive impairment.[30] Objective cognitive function was not assessed in the HPFS cohort.

Statistical Analysis

We modeled coffee, tea, and caffeine intake as time-dependent covariates. For each follow-up interval, intake was defined as the cumulative mean of all available FFQ assessments up to that time point (updated at each dietary assessment cycle) to represent long-term habitual intake and reduce within-person random error. Intake of caffeinated coffee, decaffeinated coffee, tea, and caffeine was then categorized into quantiles based on their respective distributions in each cohort.

We applied Cox proportional hazard models to estimate hazard ratios (HRs) and 95% CIs for dementia risk by comparing higher quantiles of intake with the lowest quantile. Follow-up for dementia began at baseline questionnaire return, with person-years accrued until the date of dementia diagnosis, death, or the

ates.[31] Participants contributed person-time in biennial intervals; exposures and covariates were updated at each dietary or questionnaire cycle. For dietary or covariate data that were intermittently missing, we carried forward the most recent value from the prior FFQ or other type of questionnaire. The models were jointly stratified by age (in months) and the calendar year of the current questionnaire cycle to flexibly adjust for age and period effects. The proportional hazards assumption was evaluated by fitting a model with a caffeine or beverage intake × follow-up interaction term and was assessed using a likelihood ratio test (all $P > .05$).

We constructed 2 multivariable models to examine the robustness of the associations. Model 1 adjusted for basic demographic characteristics, family history, and total energy intake; the latter was included to account for differences in body size and metabolic efficiency as well as to reduce measurement error associated with self-reported dietary assessment. Model 2 served as the primary fully adjusted model and additionally controlled for lifestyle factors, diet quality, social factors, and clinical comorbidities to isolate the independent association of caffeine and beverage intake from these potential confounders. The models for each type of beverage were additionally adjusted for the other caffeinated beverages (eg, decaffeinated coffee models adjusted for caffeinated coffee and tea intake). Most were treated as time-varying covariates; however, the covariates of family history of dementia and baseline history of depression, diabetes, hypertension, or hypercholesterolemia were not; additional details appear in the eMethods and in eFigure 2 in **Supplement 1**.

For the analyses of subjective and objective cognitive function, we used generalized estimating equation (GEE) models with an unstructured working correlation matrix and robust variance estimators to account for repeated measures within individuals. To assess the associations of caffeinated beverages and caffeine intake with subjective cognitive decline, we fitted GEE models with a log link to estimate the prevalence ratios and corresponding 95% CIs for subjective cognitive decline that were scaled to a 3-point increment in the subjective cognitive score. For the analyses of the objective cognitive measures (including TICS score, verbal memory *z* score, and global composite *z* score), we used GEE models with an identity link to quantify the multivariable-adjusted mean differences and compared higher quantiles of intake with the lowest. The GEE models were adjusted for the same covariates described above. Linear trends were assessed by modeling the median intake value as a continuous variable using Wald tests.

We then examined whether the associations between intake and the cognitive outcomes varied by smoking status, age, body mass index (calculated as weight in kilograms divided by height in meters squared), *APOE4* genotype, and AD polygenic risk score (PRS) tertiles. Subgroup analyses were conducted in subpopulations defined by each stratification variable. Effect modification was tested by including a main exposure × stratification variable interaction term. Significance was tested using likelihood ratio tests in the Cox proportional hazard models and Wald tests in the GEE models. We assessed potential nonlinear dose-

ables.[32] Nonlinearity was evaluated by comparing a model that includes only the linear term with one that additionally includes cubic spline terms, using the likelihood ratio test. We performed several sensitivity analyses to assess the robustness of our findings (additional details appear in the eMethods in **Supplement 1**).

Analyses of dementia risk and subjective cognitive function were performed separately within each cohort. Cohort-specific estimates were pooled using fixed-effects meta-analysis because the results were highly consistent and there was no evidence of between-cohort heterogeneity ($P > .05$ for heterogeneity). All statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc) with 2-sided tests; $P < .05$ was considered statistically significant.

Results

Participant Characteristics

A total of 131 821 participants (mean age, 46.2 years [SD, 7.2 years] in the NHS cohort and 53.8 years [SD, 9.7 years] in the HPFS cohort at baseline; 65.7% were female) were included in the primary analysis (eFigure 1 in **Supplement 1**). The age-standardized characteristics of participants by cohort and quartiles of caffeinated coffee intake appear in **Table 1**. In the highest quartile of caffeinated coffee intake, females consumed a median of 4.5 cups per day (1 cup was defined as an 8-oz [237-mL] serving of coffee or tea) vs 2.5 cups per day by males. Participants who reported a higher intake of caffeinated coffee tended to be younger, consumed more alcohol, were more likely to currently smoke, and had a higher total energy intake. The age-standardized characteristics of the 2 cohorts at the midpoint of follow-up appear in eTable 2 in **Supplement 1** by quartiles of caffeine intake, in eTable 3 by tertiles of decaffeinated coffee intake, and in eTable 4 by tertiles of tea intake.

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Table 1. Age-Standardized Characteristics by Quartiles of Caffeinated Coffee Intake at the Midpoint of Follow-Up in the Nurses' Health Study (NHS) and the Health Professionals Follow-up Study (HPFS)[a]

Age-Standardized Characteristics by Quartiles of Caffeinated Coffee Intake at the Midpoint of Follow-Up in the Nurses' Health Study (NHS) and the Health Professionals Follow-up Study (HPFS)a

Coffee and Tea Intake and Dementia Risk

The duration of follow-up was 43 years (4 327 851 person-years; median, 36.8 years [IQR, 28-42 years]).

100 000 person-years for the first quartile (lowest intake) of caffeinated coffee intake, 298 per 100 000 person-years for the second quartile, 229 per 100 000 person-years for the third quartile, and 141 per 100 000 person-years for the fourth quartile. In the multivariable-adjusted analyses, a higher level of caffeinated coffee intake was associated with a lower risk of dementia (Table 2). Compared with the first quartile (lowest intake) of caffeinated coffee intake, the pooled HR for dementia was 0.98 (95% CI, 0.93-1.04) for the second quartile, 0.81 (95% CI, 0.78-0.85) for the third quartile, and 0.82 (95% CI, 0.76-0.89) for the fourth quartile.

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Table 2. Associations of Coffee and Tea Intake With Dementia Risk in the Nurses' Health Study (NHS; n = 86 606 Participants) and the Health Professionals Follow-up Study (HPFS; n = 45 215 Participants)

Associations of Coffee and Tea Intake With Dementia Risk in the Nurses' Health Study (NHS; n = 86 606 Participants) and the Health Professionals Follow-up Study (HPFS; n = 45 215 Participants)

Similarly, higher tea intake was associated with lower dementia risk. The incidence rate of dementia was 321 per 100 000 person-years for the first tertile (lowest intake) of tea intake, 218 per 100 000 person-years for the second tertile, and 201 per 100 000 person-years for the third tertile. Compared with the first tertile (lowest intake) of tea, the HR was 0.91 (95% CI, 0.86-0.96) for the second tertile and 0.86 (95% CI, 0.83-0.90) for the third tertile. In contrast, decaffeinated coffee intake was not associated with dementia risk (Table 2).

Coffee and Tea Intake and Subjective Cognitive Decline

The associations of caffeinated coffee and tea intake with subjective cognitive decline were broadly similar to those observed for dementia risk. After the 2 cohorts were pooled, the prevalence of subjective cognitive decline was 9.5% for the first quartile of caffeinated coffee intake, 9.8% for the second quartile, 8.7% for the third quartile, and 7.8% for the fourth quartile. In the pooled multivariable-adjusted analyses comparing the highest with the lowest quartile of caffeinated coffee intake, the prevalence ratio was 0.85 (95% CI, 0.78-0.93; $P < .001$) for subjective cognitive decline (Table 3).

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Table 3. Associations of Coffee and Tea Intake With Subjective Cognitive Decline in the Nurses' Health Study (NHS) and the Health Professionals Follow-up Study (HPFS)

After the 2 cohorts were pooled, the prevalence of subjective cognitive decline was 9.5% in the first tertile of tea intake, 9.2% in the second tertile, and 8.1% in the third tertile. In the pooled multivariable-adjusted analyses comparing the highest with the lowest tertile of tea intake, the prevalence ratio was 0.86 (95% CI, 0.80-0.93; $P<.001$) for subjective cognitive decline. In contrast, after the 2 cohorts were pooled, the prevalence of subjective cognitive decline was 8.5% for the first tertile of decaffeinated coffee, 8.8% in the second tertile, and 9.7% in the third tertile. In the pooled multivariable-adjusted analyses comparing the highest with the lowest tertile of decaffeinated coffee intake, the prevalence ratio was 1.16 (95% CI, 1.08-1.24; $P<.001$).

Coffee and Tea Intake and Objective Cognitive Function

In the analysis of objective cognitive function in the NHS cohort only, higher intake of caffeinated coffee was associated with modestly better cognitive performance. Specifically, participants in the highest quartile had a TICS score that was 0.11 units higher compared with the lowest quartile (mean difference, 0.11 [95% CI, 0.01 to 0.21]; $P=.03$) (**Table 4**). Given that the mean annual decline in the NHS cohort is approximately 0.18 points per year for the TICS score, this difference is equivalent to the cognitive decline observed over approximately 0.6 years. Furthermore, this difference represents roughly 5% of the 2- to 3-point score gap typically observed between cognitively healthy adults and those with mild cognitive impairment.[30] The association of higher caffeinated coffee intake with global cognition was directionally similar but did not reach statistical significance for participants in the highest intake quartile compared with the lowest quartile (mean difference, 0.02 [95% CI, −0.01 to 0.04]; $P=.06$).

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Table 4. Associations of Coffee and Tea Intake With Objective Cognitive Function in the Nurses' Health Study (NHS)

Associations of Coffee and Tea Intake With Objective Cognitive Function in the Nurses' Health Study (NHS)

Similarly, the highest tea intake tertile was associated with a TICS score that was 0.16 units higher compared with the lowest tertile (mean difference, 0.16 [95% CI, 0.08 to 0.25]; $P=.001$), was 0.05 units higher for the verbal memory score (mean difference, 0.05 [95% CI, 0.03 to 0.07]; $P<.001$), and 0.04 units

est decaffeinated coffee intake tertile was associated with a verbal memory score that 0.03 units lower compared with the lowest tertile (mean difference, −0.03 [95% CI, −0.05 to −0.01]; *P* = .01).

Caffeine Intake and Cognitive Outcomes

In the secondary analyses, higher caffeine intake showed patterns consistent with those observed for caffeinated coffee (eTable 5 in **Supplement 1**). After the cohorts were pooled, participants in the highest quartile of caffeine intake had a lower risk of dementia compared with the lowest quartile (92 vs 401 per 100 000 person-years, respectively; HR, 0.78 [95% CI, 0.72-0.84]; *P* < .001) and a lower prevalence of subjective cognitive decline (7.7% vs 10.0%; prevalence ratio, 0.77 [95% CI, 0.71-0.85]; *P* < .001). In addition, the highest quartile of caffeine intake was associated with modestly better objective cognitive performance compared with the lowest quartile (participants had a TICS score that was 0.14 units higher; mean difference, 0.14 [95% CI, 0.04-0.24]; *P* = .02).

Dose-Response Analyses

The dose-response analyses revealed nonlinear inverse associations between intake of caffeinated coffee, tea, or caffeine with dementia risk (**Figure** and eFigures 3-4 in **Supplement 1**). Specifically, consumption of approximately 2 to 3 cups per day of caffeinated coffee, 1 to 2 cups per day of tea, or 300 mg/d of caffeine was associated with the lowest risk of dementia compared with no consumption; greater differences were not observed at higher intake levels (**Figure** and eFigures 3-4 in **Supplement 1**). Notably, similar nonlinear patterns were also observed for subjective cognitive decline and objective cognitive performance, reinforcing the notion that a daily intake of 2 to 3 cups of caffeinated coffee (around 300 mg of caffeine) was associated with optimal cognition. Decaffeinated coffee intake was not significantly associated with lower dementia risk or better cognitive performance in the dose-response analysis (eFigure 5 in **Supplement 1**).

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Figure. Line Graphs Assessing Caffeinated Coffee Intake

One cup was defined as an 8-oz serving of coffee or tea. Restricted cubic spline models were used to estimate dose-response relationships. All the models were adjusted (see table footnotes). For dementia and subjective cognitive decline, data were pooled. Objective cognitive function (global *z* score) was assessed only in the Nurses' Health Study (NHS). Cox proportional hazards were used in A. Generalized estimating equations were used in B (with log link function and dietary data from 2006-2010 for the NHS cohort and 2002-2006 for the Health Professionals Follow-up Study cohort) and in C (with identity link function and dietary data from 1990-1998). In C, a mean difference of 0.10 corresponds to one-tenth of an SD; positive differences indicate better cognitive performance.

Sensitivity and Subgroup Analyses

The inverse associations for caffeinated coffee, tea, and caffeine intake were consistent with our main findings (eTable 6 in **Supplement 1**). The associations between intake levels of caffeine and caffeinated beverages and dementia risk remained robust in the 4-year lag analysis (eTable 7 in **Supplement 1**) and were slightly more pronounced in analyses with a lag period of less than 12 years (eTable 8 in **Supplement 1**). The results were also stable across multiple additional sensitivity analyses including additional adjustment for metformin, aspirin, and lipid-lowering and antihypertensive medication use with multiple imputation of missing baseline caffeinated beverage intake (eTable 9 in **Supplement 1**). Similarly, the positive relationships with objective cognitive function persisted after excluding participants who reported significant changes in coffee intake in 1980 in the NHS cohort (eTable 10 in **Supplement 1**); change of coffee intake at the baseline was not assessed in the HPFS cohort.

The associations between intake of caffeine and caffeinated beverages and all the cognitive outcomes did not vary significantly across subgroups defined by different levels of body mass index, smoking status, *APOE4* genotype, or AD PRS (eTables 11-13 in **Supplement 1**). The inverse associations with dementia risk were stronger among participants aged 75 years or younger. In the pooled multivariable-adjusted analyses comparing the highest with the lowest quartile of caffeine intake, the HR was 0.65 (95% CI, 0.56-0.76; $P < .001$) among participants 75 years of age or younger and the HR was 0.81 (95% CI, 0.75-0.88; $P < .001$) among participants older than 75 years (eTable 11 in **Supplement 1**). Interactions by age were not significant for subjective cognitive decline or objective cognitive function; however, the analyses of objective function included only participants aged 70 years or older (eTables 12-13 in **Supplement 1**).

Discussion

In 2 large prospective cohorts including US female and male participants with repeated dietary assessments and extended follow-up, higher intake levels for caffeinated coffee, tea, and caffeine were associated with a reduced risk of dementia. These findings were further corroborated by the associations observed between caffeine and caffeinated beverage intake levels and lower prevalence of subjective cognitive decline and modestly better cognitive function. Notably, the strongest associations were observed at moderate consumption levels; there were no additional advantages observed at higher intake levels. These associations were independent of genetic predisposition (including *APOE4* genotype and AD PRS) and major risk factors of dementia and cognitive decline, and the findings were consistent across 2 independent cohorts.

Our findings are consistent with prior studies reporting protective associations of caffeine and coffee intake with cognitive decline.[33-36] For instance, an umbrella review of a meta-analysis[33] reported a 10% lower dementia risk associated with consumers of caffeine compared with nonconsumers. Another meta-analy-

tion (separately or in combination) was associated with lower dementia risk. In addition, another umbrella review of meta-analyses[36] identified an inverse association between coffee consumption and AD risk. However, prior studies have generally dichotomized coffee intake, limiting the ability to fully examine dose-response relationships.[36] Our study, which included 2 studies that collected detailed and repeated dietary assessments, observed a nonlinear inverse relationship across intake levels without incremental differences at higher intake levels. This pattern is biologically plausible because the absorption, transportation, metabolism, and storage of caffeine and other bioactive compounds in coffee and tea have physiological limits.[37,38] Specifically, enzymatic activities in caffeine metabolism (particularly those activities mediated by *CYP1A2*) may saturate at higher doses, contributing to this threshold effect.[39] Moreover, excessive caffeine intake may negatively affect sleep quality or increase anxiety, potentially offsetting its possible neuroprotective benefits.[6] This pattern is also consistent with prior studies on coffee consumption and cardiovascular disease risk in which moderate intake was associated with the greatest benefits.[40]

The observed differences in objective cognitive test scores were modest in magnitude. For example, the mean difference in the TICS score comparing the highest vs lowest caffeinated coffee intake category was 0.11 points, and the corresponding estimate for global cognition *z* score was small and did not reach statistical significance. These differences correspond to a mean age difference of 0.6 and 0.4 years in the 2 cohorts included in this study. The minimal clinically important differences for TICS score and the composite outcomes assessed with the *z* score are not well established for this specific study context; accordingly, these results should be interpreted as small mean differences at the population level rather than as change that could translate into clinically detectable improvement for an individual. We also note that objective cognitive outcomes were not uniformly significant across metrics, which may reflect limited sensitivity of some measures, differences in cognitive domains captured, or chance variation.

Notably, few studies are able to differentiate between caffeinated and decaffeinated coffee intake.[36] Our analysis revealed that the significant association was exclusive to caffeinated coffee and tea, and no similar association was observed with decaffeinated coffee consumption. This finding suggests that caffeine may be the primary putative neuroprotective agent underlying the observed association. An alternative explanation may be the confounding by indication when individuals switch to decaffeinated coffee due to caffeine intolerance or other underlying health concerns that could predispose them to cognitive decline. Consequently, the increased prevalence of subjective cognitive decline or decreasing verbal memory score among decaffeinated coffee drinkers at high intake levels might reflect this preexisting vulnerability rather than a direct beverage effect. Further research is warranted to elucidate the mechanistic pathways by which caffeinated and decaffeinated coffee influences cognitive health. In addition, we observed stronger associations in individuals younger than 75 years of age. One may speculate that the induction period for dementia may be more prominent in younger individuals, allowing earlier exposures to exert stronger pre-

The neuroprotective effects of caffeine are supported by multiple potential mechanisms. Caffeine, primarily through its antagonism of adenosine A1 and A2A receptors, modulates synaptic transmission and attenuates Aβ accumulation.[42] Experimental studies have shown that caffeine lowers Aβ levels, suppresses β- and γ-secretase activity, enhances neuronal plasticity, and stimulates mitochondrial function and prosurvival signaling pathways.[43] In addition, caffeine may lower brain proinflammatory cytokines and mitigate neuroinflammation, which are key contributors to cognitive decline and the development of AD.[44] The ability of caffeine to improve insulin sensitivity and reduce the risk of type 2 diabetes, which is a major risk factor for dementia, further contributes to its protective effect on cognitive health.[11] Beyond caffeine, coffee and tea contain bioactive compounds like polyphenols, chlorogenic acid, and catechins, which offer antioxidant and vascular benefits by reducing oxidative stress and improving cerebrovascular function.[45] Furthermore, tea components such as epigallocatechin-3-gallate and L-theanine may provide additional benefits by enhancing relaxation and neuroprotection.[46]

Limitations

Several limitations warrant consideration. First, the FFQs have been validated for coffee and tea intake, but they did not capture granular details regarding the specific type of tea consumed (eg, green vs black tea; caffeinated vs decaffeinated tea) or specific coffee preparation methods (eg, bean origin, roast level, or brewing technique). Variations in these factors can influence the concentration of caffeine and other bioactive compounds; consequently, we were unable to perform more specific subtype analyses of tea or coffee preparations.

Second, reverse causation cannot be fully excluded because early or prodromal cognitive changes may influence beverage consumption patterns or reduce the accuracy of self-reported dietary intake. However, to mitigate this concern, we excluded participants with major chronic diseases at baseline and conducted a variety of sensitivity analyses, including time-lagged analyses and the exclusion of participants who reported significant changes in coffee intake at baseline, all of which yielded consistent findings.

Third, despite adjustment for a broad range of confounders and medication use, residual confounding from unmeasured factors, including some neuroactive drugs not captured across follow-up, remains possible. Fourth, because this is an observational study, the observed associations cannot establish causality. Fifth, objective cognitive testing was available only in the NHS cohort, limiting independent replication of those results.

Sixth, dementia ascertainment relied on death records and self-reported physician diagnoses with medical record confirmation when available. Even though the inclusion of participants who are health professionals supports a higher validity of reporting compared with the general population, misclassification of dementia status remains possible, and we could not evaluate AD dementia separately. Seventh, each cohort was

Conclusions

Greater consumption of caffeinated coffee and tea was associated with lower risk of dementia and modestly better cognitive function, with the most pronounced association at moderate intake levels.

Article Information

Accepted for Publication: December 29, 2025.

Published Online: February 9, 2026. doi:10.1001/jama.2025.27259

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Obtained funding: Eliassen, Willett, D. Wang.

Administrative, technical, or material support: Gu, Eliassen, Willett, Hu, Stampfer.

Supervision: M. Wang, Stampfer, D. Wang.

Conflict of Interest Disclosures: Dr Hu reported receiving research support from the Analysis Group. No other disclosures were reported.

Funding/Support: This study was supported by research grants UM1 CA186107, U01 HL145386, U01 CA167552, R01 HL60712, P30 DK46200, R00 DK119412, R01 AG077489, RF1 AG083764, and R01

Role of the Funder/Sponsor: The National Institutes of Health had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Data Sharing Statement: See Supplement 2.

Additional Contributions: We are indebted to the participants in the Nurses' Health Study and the Health Professionals Follow-up Study for their continuing outstanding level of cooperation and we thank the staff for these 2 study cohorts for their valuable contributions. We also acknowledge the contributions from central cancer registries supported through the US Centers for Disease Control and Prevention's National Program of Cancer Registries and the National Cancer Institute's Surveillance, Epidemiology, and End Results Program. The participating central cancer registries were in Alabama, Alaska, Arizona, Arkansas, California, Colorado, Connecticut, Delaware, Florida, Georgia, Hawai'i, Idaho, Indiana, Iowa, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Mississippi, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Puerto Rico, Rhode Island, South Carolina, Tennessee, Texas, Utah, Virginia, West Virginia, Washington, and Wyoming. These cancer registries were supported by state agencies, universities, or cancer centers.

References

1. Alzheimer's Association. 2024 Alzheimer's disease facts and figures. *Alzheimers Dement*. 2024;20(5):3708-3821. doi:10.1002/alz.13809
PubMed | Google Scholar | Crossref

2. Jessen F, Amariglio RE, van Boxtel M, et al; Subjective Cognitive Decline Initiative (SCD-I) Working Group. A conceptual framework for research on subjective cognitive decline in preclinical Alzheimer's disease. *Alzheimers Dement*. 2014;10(6):844-852. doi:10.1016/j.jalz.2014.01.001
PubMed | Google Scholar | Crossref

3. Sperling RA, Aisen PS, Beckett LA, et al. Toward defining the preclinical stages of Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement*. 2011;7(3):280-292. doi:10.1016/j.jalz.2011.03.003
PubMed | Google Scholar | Crossref

5. Morris MC. Nutrition and risk of dementia: overview and methodological issues. *Ann N Y Acad Sci*. 2016;1367(1):31-37. doi:10.1111/nyas.13047
PubMed | Google Scholar | Crossref

6. van Dam RM, Hu FB, Willett WC. Coffee, caffeine, and health. *N Engl J Med*. 2020;383(4):369-378. doi:10.1056/NEJMra1816604
PubMed | Google Scholar | Crossref

7. Barranco Quintana JL, Allam MF, Serrano Del Castillo A, Fernández-Crehuet Navajas R. Alzheimer's disease and coffee: a quantitative review. *Neurol Res*. 2007;29(1):91-95. doi:10.1179/174313206X152546
PubMed | Google Scholar | Crossref

8. Socała K, Szopa A, Serefko A, Poleszak E, Wlaź P. Neuroprotective effects of coffee bioactive compounds: a review. *Int J Mol Sci*. 2020;22(1):107. doi:10.3390/ijms22010107
PubMed | Google Scholar | Crossref

9. Van Eldik LJ, Carrillo MC, Cole PE, et al. The roles of inflammation and immune mechanisms in Alzheimer's disease. *Alzheimers Dement (N Y)*. 2016;2(2):99-109. doi:10.1016/j.trci.2016.05.001
PubMed | Google Scholar | Crossref

10. Kim Y, Ha TY, Lee MS, Chang KA. Regulatory mechanisms and therapeutic implications of lysosomal dysfunction in Alzheimer's disease. *Int J Biol Sci*. 2025;21(3):1014-1031. doi:10.7150/ijbs.103028
PubMed | Google Scholar | Crossref

11. Duarte JM, Agostinho PM, Carvalho RA, Cunha RA. Caffeine consumption prevents diabetes-induced memory impairment and synaptotoxicity in the hippocampus of NONcZNO10/LTJ mice. *PLoS One*. 2012;7(4):e21899. doi:10.1371/journal.pone.0021899
PubMed | Google Scholar | Crossref

12. Liu QP, Wu YF, Cheng HY, et al. Habitual coffee consumption and risk of cognitive decline/dementia: a systematic review and meta-analysis of prospective cohort studies. *Nutrition*. 2016;32(6):628-636. doi:10.1016/j.nut.2015.11.015
PubMed | Google Scholar | Crossref

13. Panza F, Solfrizzi V, Barulli MR, et al. Coffee, tea, and caffeine consumption and prevention of late-life cognitive decline and dementia: a systematic review. *J Nutr Health Aging*. 2015;19(3):313-328. doi:10.1007/s12603-014-0563-8
PubMed | Google Scholar | Crossref

15. Nila IS, Villagra Moran VM, Khan ZA, Hong Y. Effect of daily coffee consumption on the risk of Alzheimer's disease: a systematic review and meta-analysis. *J Lifestyle Med*. 2023;13(2):83-89. doi:10.15280/jlm.2023.13.2.83
PubMed | Google Scholar | Crossref

16. Zhu Y, Hu CX, Liu X, Zhu RX, Wang BQ. Moderate coffee or tea consumption decreased the risk of cognitive disorders: an updated dose-response meta-analysis. *Nutr Rev*. 2024;82(6):738-748. doi:10.1093/nutrit/nuad089
PubMed | Google Scholar | Crossref

17. Chen JQA, Scheltens P, Groot C, Ossenkoppele R. Associations between caffeine consumption, cognitive decline, and dementia: a systematic review. *J Alzheimers Dis*. 2020;78(4):1519-1546. doi:10.3233/JAD-201069
PubMed | Google Scholar | Crossref

18. Colditz GA, Manson JE, Hankinson SE. The Nurses' Health Study: 20-year contribution to the understanding of health among women. *J Womens Health*. 1997;6(1):49-62. doi:10.1089/jwh.1997.6.49
PubMed | Google Scholar | Crossref

19. Rimm EB, Giovannucci EL, Willett WC, et al. Prospective study of alcohol consumption and risk of coronary disease in men. *Lancet*. 1991;338(8765):464-468. doi:10.1016/0140-6736(91)90542-W
PubMed | Google Scholar | Crossref

20. Yuan C, Spiegelman D, Rimm EB, et al. Validity of a dietary questionnaire assessed by comparison with multiple weighed dietary records or 24-hour recalls. *Am J Epidemiol*. 2017;185(7):570-584. doi:10.1093/aje/kww104
PubMed | Google Scholar | Crossref

21. Sisti JS, Hankinson SE, Caporaso NE, et al. Caffeine, coffee, and tea intake and urinary estrogens and estrogen metabolites in premenopausal women. *Cancer Epidemiol Biomarkers Prev*. 2015;24(8):1174-1183. doi:10.1158/1055-9965.EPI-15-0246
PubMed | Google Scholar | Crossref

22. Gu X, Wang DD, Sampson L, et al. Validity and reproducibility of a semiquantitative food frequency questionnaire for measuring intakes of foods and food groups. *Am J Epidemiol*. 2024;193(1):170-179. doi:10.1093/aje/kwad170
PubMed | Google Scholar | Crossref

23. Rich-Edwards JW, Corsano KA, Stampfer MJ. Test of the National Death Index and Equifax nationwide death search. *Am J Epidemiol*. 1994;140(11):1016-1019. doi:10.1093/oxfordjournals.aje.a117191

24. Liu Y, Gu X, Li Y, et al. Interplay of genetic predisposition, plasma metabolome and Mediterranean diet in dementia risk and cognitive function. *Nat Med*. 2025;31(11):3790-3800. doi:10.1038/s41591-025-03891-5
PubMed | Google Scholar | Crossref

25. Ashton NJ, Brum WS, Di Molfetta G, et al. Diagnostic accuracy of a plasma phosphorylated tau 217 immunoassay for Alzheimer disease pathology. *JAMA Neurol*. 2024;81(3):255-263. doi:10.1001/jamaneurol.2023.5319
Article | PubMed | Google Scholar | Crossref

26. Li Y, Li Y, Gu X, et al. Long-term intake of red meat in relation to dementia risk and cognitive function in US adults. *Neurology*. 2025;104(3):e210286. doi:10.1212/WNL.0000000000210286
PubMed | Google Scholar | Crossref

27. Yuan C, Fondell E, Bhushan A, et al. Long-term intake of vegetables and fruits and subjective cognitive function in US men. *Neurology*. 2019;92(1):e63-e75. doi:10.1212/WNL.0000000000006684
PubMed | Google Scholar | Crossref

28. Logroscino G, Kang JH, Grodstein F. Prospective study of type 2 diabetes and cognitive decline in women aged 70-81 years. *BMJ*. 2004;328(7439):548. doi:10.1136/bmj.37977.495729.EE
PubMed | Google Scholar | Crossref

29. Kang JH, Grodstein F. Regular use of nonsteroidal anti-inflammatory drugs and cognitive function in aging women. *Neurology*. 2003;60(10):1591-1597. doi:10.1212/01.WNL.0000065980.33594.B7
PubMed | Google Scholar | Crossref

30. Knopman DS, Roberts RO, Geda YE, et al. Validation of the Telephone Interview for Cognitive Status-Modified in subjects with normal cognition, mild cognitive impairment, or dementia. *Neuro-epidemiology*. 2010;34(1):34-42. doi:10.1159/000255464
PubMed | Google Scholar | Crossref

31. Fisher LD, Lin DY. Time-dependent covariates in the Cox proportional-hazards regression model. *Annu Rev Public Health*. 1999;20:145-157. doi:10.1146/annurev.publhealth.20.1.145
PubMed | Google Scholar | Crossref

32. Desquilbet L, Mariotti F. Dose-response analyses using restricted cubic spline functions in public health research. *Stat Med*. 2010;29(9):1037-1057. doi:10.1002/sim.3841
PubMed | Google Scholar | Crossref

33. Gill H, Patel N, Naik N, et al. An umbrella review of meta-analysis to understand the effect of cof-

PubMed | Google Scholar | Crossref

34. Xu W, Tan L, Wang HF, et al. Meta-analysis of modifiable risk factors for Alzheimer's disease. *J Neurol Neurosurg Psychiatry*. 2015;86(12):1299-1306. doi:10.1136/jnnp-2015-310548
PubMed | Google Scholar | Crossref

35. Matsushita N, Nakanishi Y, Watanabe Y, et al. Association of coffee, green tea, and caffeine with the risk of dementia in older Japanese people. *J Am Geriatr Soc*. 2021;69(12):3529-3544. doi:10.1111/jgs.17407
PubMed | Google Scholar | Crossref

36. Poole R, Kennedy OJ, Roderick P, Fallowfield JA, Hayes PC, Parkes J. Coffee consumption and health: umbrella review of meta-analyses of multiple health outcomes. *BMJ*. 2017;359:j5024. doi:10.1136/bmj.j5024
PubMed | Google Scholar | Crossref

37. Manach C, Scalbert A, Morand C, Rémésy C, Jiménez L. Polyphenols: food sources and bioavailability. *Am J Clin Nutr*. 2004;79(5):727-747. doi:10.1093/ajcn/79.5.727
PubMed | Google Scholar | Crossref

38. Nehlig A. Interindividual differences in caffeine metabolism and factors driving caffeine consumption. *Pharmacol Rev*. 2018;70(2):384-411. doi:10.1124/pr.117.014407
PubMed | Google Scholar | Crossref

39. Guo J, Zhu X, Badawy S, et al. Metabolism and mechanism of human cytochrome P450 enzyme 1A2. *Curr Drug Metab*. 2021;22(1):40-49. doi:10.2174/18755453MTEyCOTgcx
PubMed | Google Scholar | Crossref

40. Ding M, Bhupathiraju SN, Satija A, van Dam RM, Hu FB. Long-term coffee consumption and risk of cardiovascular disease: a systematic review and a dose-response meta-analysis of prospective cohort studies. *Circulation*. 2014;129(6):643-659. doi:10.1161/CIRCULATIONAHA.113.005925
PubMed | Google Scholar | Crossref

41. Singh-Manoux A, Kivimaki M, Glymour MM, et al. Timing of onset of cognitive decline: results from Whitehall II prospective cohort study. *BMJ*. 2012;344:d7622. doi:10.1136/bmj.d7622
PubMed | Google Scholar | Crossref

42. Dall'Igna OP, Fett P, Gomes MW, Souza DO, Cunha RA, Lara DR. Caffeine and adenosine A(2a) receptor antagonists prevent beta-amyloid (25-35)-induced cognitive deficits in mice. *Exp Neurol*. 2007;203(1):241-245. doi:10.1016/j.expneurol.2006.08.008
PubMed | Google Scholar | Crossref

doi:10.3233/JAD-2009-1087
PubMed | Google Scholar | Crossref

44. Arendash GW, Schleif W, Rezai-Zadeh K, et al. Caffeine protects Alzheimer's mice against cognitive impairment and reduces brain beta-amyloid production. *Neuroscience*. 2006;142(4):941-952. doi:10.1016/j.neuroscience.2006.07.021
PubMed | Google Scholar | Crossref

45. Svilaas A, Sakhi AK, Andersen LF, et al. Intakes of antioxidants in coffee, wine, and vegetables are correlated with plasma carotenoids in humans. *J Nutr*. 2004;134(3):562-567. doi:10.1093/jn/134.3.562
PubMed | Google Scholar | Crossref

46. Song J, Xu H, Liu F, Feng L. Tea and cognitive health in late life: current evidence and future directions. *J Nutr Health Aging*. 2012;16(1):31-34. doi:10.1007/s12603-011-0139-9
PubMed | Google Scholar | Crossref