Electronic Supplementary Material (ESI) for Food & Function.

Tea, coffee, and caffeine intake and risk of dementia and Alzheimer's Disease: a systematic review and meta-analysis of observational studies

Supplementary Material

目录

Supplemental Tables

Table S1. Systematic literature review search terms and strategy.

Search terms for PubMed (n=1221), until 11 June 2024
#1 ("Coffee"[Mesh]) OR ("Tea"[Mesh]) OR (coffee [Title/Abstract] OR caffeine [Title/Abstract] OR caffeinated [Title/Abstract] OR Chicory* [Title/Abstract] OR Coffea [Title/Abstract] OR 1,3,7-trimethylxanthine [Title/Abstract]) OR tea [Title/Abstract] 90078 results
#2 ("Dementia"[Mesh]) OR ("Alzheimer Disease"[Mesh]) OR (Dementias[Title/Abstract] OR Cognitive Dysfunction [Title/Abstract] OR Cognitive Defect [Title/Abstract] OR Cognitive Dysfunctions [Title/Abstract] OR Cognitive Decline[Title/Abstract] OR Cognitive Declines[Title/Abstract] OR Cognitive Impairments[Title/Abstract] OR Cognitive Impairment[Title/Abstract] OR Neurocognitive Disorder[Title/Abstract] OR Neurocognitive Disorders[Title/Abstract] OR Alzheimer's Diseases[Title/Abstract] OR Alzheimer's [Title/Abstract] OR Alzheimer[Title/Abstract]) 387693 results
#1 AND #2 1221 results
Search terms for Embase (n=2406), 11 June 2024
#1 'coffee'/exp OR 'coffee' OR 'tea'/exp OR 'tea' OR 'caffeine':ab,ti OR 'caffeinated':ab,ti OR 'chicory':ab,ti OR 'coffea':ab,ti OR '1,3,7-trimethylxanthine':ab,ti 133455 results
#2 'dementia'/exp OR 'dementia' OR 'alzheimer disease'/exp OR 'alzheimer disease' OR 'dementias':ab,ti OR 'cognitive defect':ab,ti OR 'cognitive dysfunction':ab,ti OR 'cognitive

dysfunctions':ab,ti OR 'cognitive decline':ab,ti OR 'cognitive declines':ab,ti OR 'cognitive impairments':ab,ti OR 'cognitive impairment':ab,ti OR 'neurocognitive disorder':ab,ti OR 'neurocognitive disorders':ab,ti OR 'alzheimer diseases':ab,ti OR 'alzheimer*':ab,ti 666856 results
#1 AND #2 2406 results
Search terms for Web of Science (n= 1985), 11 June 2024
TS= (("Coffee" OR "Tea" OR "caffeine" OR "Caffeinated" OR "Chicory" OR "Coffea" OR "1,3,7-trimethylxanthine") AND ("Dementia" OR "Dementias" OR "Cognitive Dysfunction" OR "Cognitive Defect" OR "Cognitive Dysfunctions" OR "Cognitive Decline" OR "Cognitive Declines" OR "Cognitive Impairments" OR "Cognitive Impairment" OR "Neurocognitive Disorder" OR "Neurocognitive Disorders" OR "Alzheimer Disease" OR "Alzheimer's Diseases" OR "Alzheimer's" OR "Alzheimer")) 1985 results

Table S2. The list of excluded studies during the full text screening stage

Exclusion reason	Reference number
Reviews, meta-analysis	1-85
Not the relevant exposure	86-113
Not the relevant outcome	114-213
Conference	214-261
Not cohort study	262-278
Same population study	279-281
Not available	282-284

References lists are attached at the end of this document.

Table S3. The category of exposures and the estimated effects of the included cohort studies on the association between tea intake and dementia and Alzheimer's Disease

Author, year	Date source (Sample size/cases)	Exposure	Dementia	AD
Abbel D, 2023	HUNT (dementia: 7381/985 AD:7381/572)	Tea:		
		0 cup/day	Reference	
		1 cup/day	0.92(0.74,1.16)	
		2 cups/day	0.92(0.74,1.14)	
		≥3 cups/day	1.01(0.76,1.33)	
		Coffee:		
		0-1 cup/day	Reference	Reference
		2-3 cups/day	1.11(0.81,1.51)	1.15(0.83,1.58)
		4-5 cups/day	0.94(0.69,1.28)	1.37(0.96,1.95)
		6-7 cups/day	1.04(0.74,1.46)	1.85(1.22,2.81)
		≥8 cups/day	1.09(0.77,1.54)	1.65(1.03,2.53)
Cornelis MC, 2022	MAP (dementia: 888/266 AD:888/252)	Caffeine		
		≤100 mg/day	Reference	Reference
		>100 mg/day	1.35(1.03,1.76)	1.41(1.07,1.85)
		Caffeine (male)		
		≤100 mg/day	Reference	Reference
		>100 mg/day	1.36(0.69,2.69)	1.56(0.76,3.18)
		Caffeine(female)		
		≤100 mg/day	Reference	Reference
		>100 mg/day	1.38(1.01,1.88)	1.41(1.02,1.94)
Zhang Y, 2021	UK Biobank (dementia: 365682/5069 AD:365682/2128)	Tea:		
		0 cup/day	Reference	Reference
		0.5-1 cup/day	0.92(0.82,1.03)	0.91(0.77,1.09)
		2-3 cups/day	0.92(0.84,1.01)	0.92(0.80,1.06)
		≥4 cups/day	0.89(0.82,0.98)	0.89(0.78,1.02)
		Coffee:		
		0 cup/day	Reference	Reference
		0.5-1 cup/day	0.94(0.87,1.02)	1.05(0.92,1.19)
		2-3 cups/day	0.93(0.85,0.98)	1.00(0.88,1.14)
		≥4 cups/day	0.96(0.88,1.06)	1.14(0.99,1.32)
Matsushita N, 2021	Murakami cohort (dementia: 13757/309)	Green tea:		
		Q1 (<60) ml/day	Reference	
		Q2 (≥60, <160) ml/day	0.68(0.46,1.03)	
		Q3 (≥160, <300) ml/day	0.99(0.59,1.66)	
		Q4 (≥300, <600) ml/day	0.76(0.53,1.08)	
		Q5 (≥600) ml/day	0.72(0.51,1.03)	
		Green tea（male）:		
		Q1 (<60) ml/day	Reference	
		Q2 (≥60, <160) ml/day	0.53(0.30,0.93)	
		Q3 (≥160, <300) ml/day	0.57(0.26,1.21)	
		Q4 (≥300, <600) ml/day	0.64(0.40,1.04)	

		Q5 (≥600) ml/day	0.72(0.45,1.15)	
		Green tea（female）:		
		Q1 (<60) ml/day		
		Q2 (≥60, <160) ml/day	Reference	
		Q3 (≥160, <300) ml/day	0.90(0.50,1.62)	
		Q4 (≥300, <600) ml/day	1.94(0.94,4.00)	
		Q5 (≥600) ml/day	0.97(0.57,1.66)	
			0.75(0.44,1.27)	
		Coffee:		
		0	Reference	
		0.1-0.9 cup/day	1.05(0.8,1.38)	
		1-1.9 cups/day	0.69(0.48,0.98)	
		2-2.9 cups/day	0.76(0.5,1.14)	
		≥3 cups/day	0.53(0.31,0.89)	
		Coffee(male):		
		0	Reference	
		0.1-0.9 cup/day	0.61(0.37,1)	
		1-1.9 cups/day	0.44(0.22,0.89)	
		2-2.9 cups/day	0.44(0.22,0.89)	
		≥3 cups/day	0.23(0.1,0.54)	
		Coffee(female):		
		0	Reference	
		0.1-0.9 cup/day	0.74(0.44,1.24)	
		1-1.9 cups/day	1.1(0.65,1.87)	
		2-2.9 cups/day	1.1(0.65,1.87)	
		≥3 cups/day	1.16(0.58,2.3)	
		Caffeine:		
		Q1 (<92) mg/day	Reference	
		Q2 (≥92, <155) mg/day	0.89(0.66,1.19)	
		Q3 (≥155, <236) mg/day	0.65(0.46,0.91)	
		Q4 (≥236, <333) mg/day	0.55(0.37,0.8)	
		Q5 (≥333) mg/day	0.62(0.42,0.91)	
		Caffeine(male):		
		Q1 (<92) mg/day	Reference	
		Q2 (≥92, <155) mg/day	0.96(0.64,1.45)	
		Q3 (≥155, <236) mg/day	0.7(0.45,1.11)	
		Q4 (≥236, <333) mg/day	0.48(0.28,0.84)	
		Q5 (≥333) mg/day	0.45(0.25,0.81)	
		Caffeine(female):		
		Q1 (<92) mg/day	Reference	
		Q2 (≥92, <155) mg/day	0.8(0.52,1.24)	
		Q3 (≥155, <236) mg/day	0.57(0.35,0.95)	
		Q4 (≥236, <333) mg/day	0.6(0.35,1.03)	
		Q5 (≥333) mg/day	0.81(0.47,1.39)	
Fischer K, 2018	AgeCoDe (AD: 2622/418)	Green tea: Never vs. Every day		0.94(0.86,1.02)
		Coffee: Never vs. Every day		0.97(0.90,1.04)

Larsson SC, 2018	SIMPLER (AD: 28775/3755)	Coffee:		
		<1.0 cups/day		Reference
		1.0–2.9 cups/day		0.99(0.85,1.16)
		3.0–4.9 cups/day		1.03(0.88,1.21)
		≥5.0 cups/day		1.07(0.9,1.28)
		Coffee (male):		
		<1.0 cups/day		Reference
		1.0–2.9 cups/day		1.07(0.85,1.35)
		3.0–4.9 cups/day		1.03(0.82,1.31)
		≥5.0 cups/day		1.07(0.83,1.37)
		Coffee (female):		
		<1.0 cups/day		Reference
		1.0–2.9 cups/day		0.94(0.76,1.17)
		3.0–4.9 cups/day		1.03(0.83,1.28)
		≥5.0 cups/day		1.11(0.87,1.41)
Park SY, 2017	MEC (AD: 185855/1404)	Coffee:		
		none		Reference
		1–3 cups/month		1.01(0.72,1.41)
		1–6 cups/week		0.92(0.69,1.24)
		1 cup/day		0.90(0.71,1.14)
		2-3 cups/day		1.16(0.90,1.49)
		≥4 cups/day		1.33(0.86,2.04)
Tomata Y, 2016	Ohsaki Cohort (dementia: 13645/1186)	Green Tea:		
		<1 cup/day	Reference	
		1–2 cups/day	1.06(0.89,1.27)	
		3–4 cups/day	0.88(0.74,1.04)	
		≥5 cups/day	0.73(0.61,0.87)	
		Black tea:		
		<1 cup/day	Reference	
		1–2 cups/day	0.69(0.46,1.04)	
		3–4 cups/day	1.03(0.62,1.72)	
		≥5 cups/day	0.68(0.34,1.35)	
		Oolong tea:		
		<1 cup/day	Reference	
		1–2 cups/day	1.05(0.8,1.39)	
		3–4 cups/day	1.13(0.68,1.87)	
		≥5 cups/day	0.71(0.28,1.79)	
Sugiyama K, 2016	Ohsaki Cohort (dementia: 13137/1107)	Coffee:		
		Never	Reference	
		Occasionally	0.73(0.62,0.86)	
		1-2 cups/day	0.72(0.61,0.84)	
		≥3 cups/day	0.82(0.65,1.02)	
Paganini-Hill A, 2016	LWCS in 1980s (dementia: 587/268)	Caffeine:		
		<50 mg/day	Reference	
		50-199 mg/day	0.96(0.70,1.32)	
		200+ mg/day	1.04(0.76,1.43)	
	LWCS in 2003 or later (dementia: 338/154)	Caffeine:		
		<50 mg/day	Reference	
		50-199 mg/day	0.76(0.52,1.10)	
		200+ mg/day	0.66(0.43,0.99)	

Driscoll I, 2016	WHIMS (dementia: 6467/388)	Caffeine: <175 mg/day ≥175 mg/day	 Reference 0.74(0.56,0.99)	
Loftfield E, 2015	The PLCO Cancer Screening Trial (AD: 90317/8718)	Coffee: 0 0-1 cup/day 1 cup/day 2-3 cups/day ≥4 cups/day		 Reference 1.01(0.53,1.95) 0.66(0.32,1.36) 0.59(0.31,1.11) 0.72(0.33,1.58)
Noguchi-Shinohara M, 2014	Nakajima Project (dementia: 2845/490)	Green tea: None 1–6 days/week Every day Black tea: None 1–7 days/week	 Reference 0.90(0.34,2.35) 0.26(0.06,1.06) Reference 2.14(0.75,6.08)	
Mirza SS, 2014	Rotterdam Study (dementia: 5408/814)	Coffee: None 1–6 days/week Every day Coffee: 0–1 cup/day 1–3 cups/day 3 cups/day	 Reference 1.00(0.34,2.99) 0.70(0.22,2.17) Reference 0.88(0.67,1.16) 1.00(0.76,1.30)	
Gelber RP, 2011	HAAS (dementia: 3734/226; AD: 3734/118; Vad: 3734/80)	Coffee: 0 oz/day 4-8 oz/day 12-16 oz/day 20-24 oz/day ≥28 oz/day Caffeine： 0–115.5 mg/day >115.5–188.0 mg/day >188.0–277.5 mg/day >277.5–415.0 mg/day >415.0–2673.0 mg/day	 Reference 0.93(0.59,1.46) 1.24(0.78,1.97) 1.14(0.66,1.98) 1.09(0.59,2.00) Reference 1.21(0.74,1.96) 1.31(0.82,2.09) 1.47(0.92,2.35) 1.12(0.66,1.91)	 Reference 0.89(0.5,1.59) 1.09(0.60,2.00) 0.95(0.45,2.00) 0.59(0.23,1.54) Reference 1.20(0.65,2.23) 1.15(0.62,2.11) 1.07(0.57,2.00) 0.95(0.46,1.95)
Eskelinen MH, 2009	CAIDE (dementia:1409/61; AD:1409/48)	Tea: drinking 1 cup /day vs. not drinking Coffee: 0–2 cups/day 3–5 cups/day ＞5 cups/day	1.04(0.59,1.84) Reference 0.30(0.10,0.93) 0.83(0.32,2.15)	0.91(0.48,1.71) Reference 0.42(0.12,1.46) 1.01(0.33,3.08)
Laitala VS, 2009	Finnish Twin Cohort (dementia: 2606/445)	Coffee： 0–3 cups/day 3.5–8 cups/day ＞8 cups/day	 Reference 0.91(0.52,1.58) 1.94(0.86,4.38)	

Dai Q, 2006	Kame Project cohort (AD: 1589/270)	Tea: Less often than weekly 1–2 Times per week 3 Times or More per week	 Reference 1.49(0.43,5.16) 1.70(0.67,4.33)
Lindsay J, 2002	CSHA (AD: 4088/194)	Tea Coffee	1.12(0.78,1.61) 0.69(0.50,0.96)
Tyas SL, 2001	MSHA (AD: 694/36)	Tea Coffee	0.46(0.20,1.06) 1.03(0.47,2.30)

Abbreviation: AD, Alzheimer's disease; VaD, Vascular Dementia; NA, not available; HUNT, the Trøndelag Health Study of Norway; CSHA, Canadian Study of Health and Aging; MSHA, the Manitoba Study of Health and Aging; MEC, the Multiethnic Cohort study; HAAS, the Honolulu-Asia Aging Stud; HAAS, the Honolulu-Asia Aging Study; CAIDE, the Cardiovascular risk factors; Aging and Dementia study; MAP, the Rush Memory and Aging Project; AgeCoDe: the German Study on Ageing, Cognition and Dementia in Primary Care Patients study; SIMPLER, Swedish Infrastructure for Medical Population-based Life-course Environmental Research; WHIMS, the Women's Health Initiative Memory Study.

Table S4. Quality assessment of included cohort studies for the association of tea intake and dementia and Alzheimer's Disease

First author (year)	Study Selection				Comparability of cohorts		Outcome			Total
	a	b	c	d	e	f	g	h	i	
Dementia										
Abbel D, 2023	1	1	0	1	0	1	1	1	0	6
Zhang Y, 2021	1	1	0	1	1	1	1	1	1	8
Matsushita N, 2021	1	1	0	1	1	1	1	1	0	7
Tomata Y, 2016	1	1	0	1	1	1	1	1	1	8
Noguchi-Shinohara M, 2014	1	1	1	1	1	0	1	0	1	7
Eskelinen MH, 2009	1	1	0	1	1	1	1	1	0	7
AD										
Zhang Y, 2021	1	1	0	1	1	1	1	1	1	8
Fischer K, 2018	1	1	1	1	1	0	1	1	1	8
Eskelinen MH, 2009	1	1	0	1	1	1	1	1	0	7
Dai Q, 2006	1	1	1	1	1	0	1	1	1	8
Lindsay J, 2002	1	1	1	1	0	0	1	1	1	7
Tyas SL, 2001	1	1	1	1	0	0	1	1	0	6

a. Representativeness of the exposed cohort;
b. Selection of the non-exposed cohort;
c. Ascertainment of exposure;
d. Demonstration that outcome of interest was not present at start of study;
e. Comparability of cohorts on the basis of the design or analysis (adjusted for physical activity);
f. Comparability of cohorts on the basis of the design or analysis (adjusted for cardiovascular disease);
g. Assessment of outcome;
h. Was follow-up long enough for outcomes to occur;
i. Adequacy of follow-up of cohorts.

Table S5. Quality assessment of included cohort studies for the association of coffee intake and dementia and Alzheimer's Disease

First author (year)	Study Selection				Comparability of cohorts		Outcome			Total
	a	b	c	d	e	f	g	h	i	
Dementia										
Abbel D, 2023	1	1	0	1	0	1	1	1	0	6
Zhang Y, 2021	1	1	0	1	1	1	1	1	1	8
Matsushita N, 2021	1	1	0	1	1	1	1	1	0	7
Sugiyama K, 2016	1	1	1	1	1	1	1	1	1	9
Noguchi-Shinohara M, 2014	1	1	1	1	1	0	1	0	1	7
Mirza SS, 2014	1	1	1	1	0	0	1	1	1	7
Gelber RP, 2011	1	1	1	1	1	0	1	1	1	8
Eskelinen MH, 2009	1	1	0	1	1	1	1	1	0	7
Laitala VS, 2009	0	1	1	1	0	1	1	1	1	7
AD										
Abbel D, 2023	1	1	0	1	0	1	1	1	0	6
Zhang Y, 2021	1	1	0	1	1	1	1	1	1	8
Larsson SC, 2018	1	1	1	1	0	0	1	1	0	6
Fischer K, 2018	1	1	1	1	1	0	1	1	1	8
Park SY, 2017	1	1	0	1	1	1	1	1	1	8
Loftfield E, 2015	1	1	1	1	0	0	1	1	0	6
Gelber RP, 2011	1	1	1	1	1	0	1	1	1	8
Eskelinen MH, 2009	1	1	0	1	1	1	1	1	0	7
Lindsay J, 2002	1	1	1	1	0	0	1	1	1	7
Tyas SL, 2001	1	1	1	1	0	0	1	1	0	6

a. Representativeness of the exposed cohort;
b. Selection of the non-exposed cohort;
c. Ascertainment of exposure;
d. Demonstration that outcome of interest was not present at start of study;
e. Comparability of cohorts on the basis of the design or analysis (adjusted for physical activity);
f. Comparability of cohorts on the basis of the design or analysis (adjusted for cardiovascular disease);
g. Assessment of outcome;
h. Was follow-up long enough for outcomes to occur;
i. Adequacy of follow-up of cohorts.

Table S6. Quality assessment of included cohort studies for the association of caffeine intake and dementia and Alzheimer's Disease

First author (year)	Study Selection				Comparability of cohorts		Outcome			Total
	a	b	c	d	e	f	g	h	i	
Dementia										
Cornelis MC, 2022	1	1	0	1	1	1	1	1	1	8
Matsushita N, 2021	1	1	0	1	1	1	1	1	0	7
Paganini-Hill A, 2016	0	1	1	1	0	0	1	1	1	6
Driscoll I, 2016	1	1	1	1	1	1	1	1	1	9
Gelber RP, 2011	1	1	1	1	1	0	1	1	1	8
AD										
Cornelis MC, 2022	1	1	0	1	1	1	1	1	1	8
Gelber RP, 2011	1	1	1	1	1	0	1	1	1	8

a. Representativeness of the exposed cohort;
b. Selection of the non-exposed cohort;
c. Ascertainment of exposure;
d. Demonstration that outcome of interest was not present at start of study;
e. Comparability of cohorts on the basis of the design or analysis (adjusted for physical activity);
f. Comparability of cohorts on the basis of the design or analysis (adjusted for cardiovascular disease);
g. Assessment of outcome;
h. Was follow-up long enough for outcomes to occur;
i. Adequacy of follow-up of cohorts.

Table S7. Subgroup analysis of tea intake and risk of dementia and Alzheimer's Disease for the highest versus lowest meta-analysis.

Subgroups	No. of studies	Tea intake□			P_2
		RR (95% CI）	I^2 %	P_1	
Dementia					
Expsoure					
Tea	3	0.90(0.83,0.98)	0%	0.62	0.49
Green tea	3	0.72(0.61,0.84)	0%	0.38	0.19
Oolong tea	1	0.68(0.34,1.36)	--	--	0.29
Black tea	2	1.20(0.41,3.53)	58%	0.12	Ref
Mean age					
<70	3	0.89(0.82,0.97)	8%	0.34	Ref
≥70	3	0.74(0.63,0.88)	42%	0.18	0.06
No of participants					
<5000	2	0.61(0.16,2.29)	68%	0.08	Ref
≥5000	4	0.84(0.73,0.96)	51%	0.11	0.97
No of cases					
<500	3	0.76(0.56,1.03)	41%	0.18	Ref
≥500	3	0.86(0.73,1.00)	61%	0.08	0.53
Region					
Asia	3	0.72(0.61,0.84)	0%	0.38	Ref
Europe	3	0.90(0.83,0.98)	0%	0.62	0.01*
Follow-up years					
<10	3	0.72(0.61,0.84)	0%	0.38	Ref
≥10	3	0.90(0.83,0.98)	0%	0.62	0.01*
Exposure assessment					
Dietary record	1	0.72(0.51,1.02)	--	--	Ref
FFQ	2	0.56(0.23,1.35)	49%	0.16	0.99
others	3	0.90(0.83,0.98)	0%	0.62	0.22
Adjustment for PA					
No	2	0.84(0.61,1.16)	73%	0.05	Ref
Yes	4	0.87(0.79,0.97)	32%	0.22	0.98
Adjustment for CVD					
Yes	5	0.85(0.74,0.97)	39%	0.16	0.11
No	1	0.26(0.06,1.09)	--	--	Ref
Adjustment for ApoE E4 carrier status					
No	3	0.89(0.82,0.97)	8%	0.34	Ref
Yes	3	0.74(0.63,0.88)	42%	0.18	0.06

AD					
Mean age					
<70	1	0.89(0.78,1.02)	--	--	Ref
⩾70	5	0.95(0.87,1.03)	24%	0.26	0.45
No of participants					
<5000	5	0.95(0.87,1.03)	24%	0.26	Ref
⩾5000	1	0.89(0.78,1.02)	--	--	0.45
No of cases					
<500	5	0.95(0.87,1.03)	24%	0.26	Ref
⩾500	1	0.89(0.78,1.02)	--	--	0.45
Region					
Europe	3	0.93(0.86,0.99)	0%	0.80	Ref
North America	3	0.97(0.51,1.85)	59%	0.09	0.49
Follow-up years					
⩾10	4	0.93(0.86,1.00)	0%	0.56	0.79
<10	2	0.78(0.33,1.84)	73%	0.06	Ref
Exposure assessment					
others	5	0.91(0.81,1.03)	29%	0.23	0.68
FFQ	1	0.94(0.86,1.02)	--	--	Ref
Adjustment for PA					
Yes	4	0.93(0.86,1.00)	0%	0.56	0.79
No	2	0.78(0.33,1.84)	73%	0.06	Ref
Adjustment for CVD					
Yes	2	0.89(0.78,1.02)	0%	0.95	0.44
No	4	0.95(0.87,1.03)	43%	0.15	Ref
Adjustment for ApoE E4 carrier status					
No	3	0.90(0.79,1.02)	49%	0.14	Ref
Yes	3	0.94(0.87,1.03)	0%	0.46	0.54

FFQ, food frequency questionnaire; PA, physical activity; RR, relative risk; CI, confidence interval.

P_1: P value for heterogeneity within each subgroup.

P_2: P value for heterogeneity between subgroups with meta-regression analysis.

Table S8. Sensitivity analysis of tea intake and dementia and Alzheimer's Disease for the highest versus lowest meta-analysis

Study omitted	RR (95% CI)
Dementia	
Abbel D, 2023	0.81(0.70,0.94)
Zhang Y, 2021	0.81(0.67,0.98)
Matsushita N, 2021	0.86(0.74,0.99)
Tomata Y, 2016	0.89(0.82,0.96)
Noguchi-Shinohara M, 2014	0.85(0.74,0.97)
Eskelinen MH, 2009	0.83(0.72,0.95)
AD	
Zhang Y, 2021	0.95(0.87,1.03)
Fischer K, 2018	0.91(0.81,1.03)
Eskelinen MH, 2009	0.93(0.87,1.00)
Dai Q, 2006	0.93(0.86,0.99)
Lindsay J, 2002	0.92(0.86,0.99)
Tyas SL, 2001	0.93(0.87,1.00)

Table S9. Subgroup analysis of coffee intake and risk of dementia and Alzheimer's Disease for the highest versus lowest meta-analysis.

Subgroups	No. of studies	Coffee intake			P_2
		RR (95% CI）	I^2 %	P_1	
Dementia					
Outcome					
Dementia	9	0.95(0.87,1.02)	25%	0.22	Ref
VaD	2	1.10(0.46,2.62)	72%	0.06	0.13
Mean age					
<70	4	0.95(0.87,1.04)	46%	0.14	Ref
⩾70	5	0.93(0.76,1.13)	18%	0.3	0.86
No of participants					
<5000	4	1.13(0.75,1.70)	0%	0.43	Ref
≥5000	5	0.93(0.86,1.02)	43%	0.13	0.37
No of cases					
<500	5	0.90(0.56,1.45)	49%	0.10	Ref
≥500	4	0.95(0.88,1.03)	0%	0.49	0.52
Region					
Europe	5	0.98(0.90,1.06)	0%	0.49	Ref
Asia	3	0.72(0.51,1.00)	11%	0.32	0.03*
North America	1	1.09(0.59,2.01)	--	--	0.28
Follow-up years					
≥10	6	0.98(0.90,1.06)	0%	0.62	0.03*
<10	3	0.72(0.51,1.00)	11%	0.32	Ref
Exposure assessment					
Dietary record	3	0.87(0.55,1.38)	63%	0.07	Ref
others	4	0.97(0.89,1.06)	0%	0.39	0.66
FFQ	2	0.82(0.65,1.02)	0%	0.79	0.52
Adjustment for PA					
No	4	0.98(0.80,1.19)	44%	0.15	Ref
Yes	5	0.85(0.64,1.13)	24%	0.26	0.43
Adjustment for CVD					
Yes	6	0.92(0.79,1.07)	50%	0.08	0.61
No	3	1.00(0.78,1.27)	0%	0.80	Ref
Adjustment for ApoE E4 carrier status					
No	6	0.95(0.87,1.02)	50%	0.07	Ref
Yes	3	0.95(0.59,1.51)	0%	0.76	0.99
AD					

Mean age						
<70	5		1.12(0.98,1.27)	0%	0.44	Ref
⩾70	5		0.95(0.82,1.11)	26%	0.25	0.05
No of participants						
<5000		6	0.9(0.75,1.08)	2%	0.4	Ref
≥5000		4	1.11(1.00,1.24)	0%	0.54	0.03*
No of cases						
<500		5	0.87(0.69,1.09)	20%	0.29	Ref
≥500		5	1.11(1.00,1.23)	0%	0.69	0.05
Region						
Europe		5	1.04(0.94,1.15)	8%	0.36	Ref
North America		5	0.87(0.61,1.22)	40%	0.15	0.16
Follow-up years						
≥10		8	1.04(0.94,1.14)	11%	0.35	0.04*
<10		2	0.73(0.54,0.99)	0%	0.36	Ref
Exposure assessment						
Dietary record		2	0.91(0.58,1.43)	5%	0.31	Ref
others		4	0.94(0.67,1.31)	61%	0.05	0.82
FFQ		4	1.00(0.91,1.09)	14%	0.32	0.61
Adjustment for PA						
No		5	0.91(0.72,1.16)	34%	0.20	Ref
Yes		5	1.05(0.91,1.21)	40%	0.15	0.34
Adjustment for CVD						
Yes		3	1.13(0.98,1.29)	0%	0.91	0.05
No		7	0.96(0.82,1.11)	34%	0.17	Ref
Adjustment for ApoE E4 carrier status						
Yes		3	1.13(0.98,1.29)	0%	0.91	0.05
No		7	0.96(0.82,1.11)	34%	0.17	Ref

VaD, Vascular Dementia; FFQ, food frequency questionnaire; PA, physical activity; RR, relative risk; CI, confidence interval.

P_1: P value for heterogeneity within each subgroup.

P_2: P value for heterogeneity between subgroups with meta-regression analysis.

Table S10. Sensitivity analysis of coffee intake and dementia and Alzheimer's Disease for the highest versus lowest meta-analysis

Study omitted	RR (95% CI）
Dementia	
Abbel D, 2023	0.93(0.85,1.02)
Zhang Y, 2021	0.92(0.77,1.10)
Matsushita N, 2021	0.96(0.89,1.04)
Sugiyama K, 2016	0.96(0.89,1.05)
Noguchi-Shinohara M, 2014	0.95(0.88,1.02)
Mirza SS, 2014	0.93(0.82,1.04)
Gelber RP, 2011	0.94(0.87,1.02)
Eskelinen MH, 2009	0.95(0.88,1.02)
Laitala VS, 2009	0.94(0.87,1.01)
AD	
Abbel D, 2023	1.00(0.88,1.13)
Zhang Y, 2021	0.97(0.91,1.04)
Larsson SC, 2018	0.98(0.84,1.14)
Fischer K, 2018	1.00(0.85,1.19)
Park SY, 2017	0.99(0.87,1.11)
Loftfield E, 2015	1.01(0.90,1.13)
Gelber RP, 2011	1.01(0.91,1.13)
Eskelinen MH, 2009	1.00(0.90,1.13)
Lindsay J, 2002	1.04(0.94,1.14)
Tyas SL, 2001	1.00(0.89,1.13)

Table S11. Subgroup analysis of caffeine intake and risk of dementia for the highest versus lowest meta-analysis.

Subgroups	No. of studies	Caffeine intake			P_2
		RR (95% CI)	I^2 %	P_1	
Dementia					
Gender					
Female	3	0.95(0.63, 1.44)	77%	0.01	0.64
Male	2	0.77(0.26, 2.28)	83%	0.02	Ref
Mean age					
<70	2	0.81(0.45,1.44)	68%	0.08	Ref
⩾70	3	1.01(0.72,1.44)	78 %	0.01	0.47
No of participants					
<5000	3	1.20(0.98,1.46)	0%	0.45	Ref
≥5000	2	0.70(0.55,0.87)	0%	0.47	< 0.01*
Region					
North America	4	1.03(0.78,1.37)	67%	0.03*	0.13
Asia	1	0.62(0.42,0.91)	--	--	Ref
Follow-up years					
≥10	3	0.91(0.70,1.20)	39%	0.2	0.98
<10	2	0.93(0.43,1.99)	91%	<0.01	Ref
Exposure assessment					
FFQ	2	1.00(0.56,1.81)	89%	<0.01	0.62
Dietary record	2	0.81(0.45,1.44)	68%	0.08	Ref
others	1	1.04(0.76,1.43)	--	--	0.63
Adjustment for PA					
No	2	0.87(0.62,1.22)	59%	0.12	Ref
Yes	3	0.99(0.61,1.60)	81%	<0.01	0.71
Adjustment for CVD					
Yes	3	0.86(0.54,1.37)	86%	<0.01	0.52
No	2	1.06(0.81,1.39)	0%	0.81	Ref
Adjustment for ApoE E4 carrier status					
Yes	2	1.30(1.02,1.65)	0	0.54	0.02
No	3	0.79(0.59,1.05)	56.60%	0.10	Ref

FFQ, food frequency questionnaire; PA, physical activity; RR, relative risk; CI, confidence interval.

P_1: P value for heterogeneity within each subgroup.

P_2: P value for heterogeneity between subgroups with meta-regression analysis.

Table S12. Sensitivity analysis of caffeine intake and dementia for the highest versus lowest meta-analysis

Study omitted	RR (95% CI）
Dementia	
Cornelis MC, 2022	0.84(0.65,1.08)
Matsushita N, 2021	1.03(0.78,1.37)
Paganini-Hill A, 2016	0.91(0.63,1.32)
Driscoll I, 2016	1.00(0.72,1.40)
Gelber RP, 2011	0.91(0.65,1.27)

Table S13. GRADE evidence profile for observational studies of tea, coffee, and caffeine between dementia and Alzheimer's Disease.

Exposure	Outcome	№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Relative risk (95% CI)	Certainty
Tea	Dementia	6	Observational studies	Not serious	Not serious	Not serious	Serious[a]	Dose-response gradient[g]	0.84(0.74,0.96)	⊕⊕◯◯ LOW
Tea	AD	6	Observational studies	Not serious	Not serious	Not serious	Serious[b]	Dose-response gradient[h]	0.93(0.87,1.00)	⊕⊕◯◯ LOW
Coffee	Dementia	9	Observational studies	Not serious	Not serious	Not serious	Serious[c]	Dose-response gradient[i]	0.95(0.87,1.02)	⊕⊕◯◯ LOW
Coffee	AD	10	Observational studies	Not serious	Not serious	Not serious	Serious[d]	Dose-response gradient[j]	1.01(0.90,1.12)	⊕⊕◯◯ LOW
Caffeine	Dementia	5	Observational studies	Not serious	Not serious	Not serious	Serious[e]	Dose-response gradient[k]	0.94(0.70,1.25)	⊕⊕◯◯ LOW
Caffeine	AD	2	Observational studies	Not serious	Not serious	Not serious	Serious[f]	None	1.34(1.04,1.74)	⊕◯◯◯ Very low

[a] Serious imprecision for tea intake and dementia, as the 95%CI (0.74-0.96) overlapped with the minimally important difference for clinical benefit (RR 0.95).

[b] Serious imprecision for tea intake and AD, as the 95%CI (0.87-1.00) overlapped with the minimally important difference for clinical benefit (RR 0.95).

[c] Serious imprecision for coffee intake and dementia, as the 95%CI (0.87-1.02) overlapped with the minimally important difference for clinical benefit (RR 0.95).

[d] Serious imprecision for coffee intake and AD, as the 95%CI (0.90-1.12) overlapped with the minimally important difference for clinical harm (RR 1.05).

[e] Serious imprecision for caffeine intake and dementia, as the 95%CI (0.70-1.25) overlapped with the minimally important difference for clinical benefit (RR 0.95).

[f] Serious imprecision for caffeine intake and AD, as the 95%CI (1.04-1.74) overlapped with the minimally important difference for clinical harm (RR 1.05).

[g] Upgrade for a dose-response gradient, as the MKSPLINE dose-response analyses showed a significant nonlinear inverse relationship between tea consumption and dementia ($P = 0.006 < 0.01$).

[h] Upgrade for a dose-response gradient, as the MKSPLINE dose-response analyses showed a linear inverse relationship between tea consumption and AD ($P = 0.31 > 0.05$).

[i] Upgrade for a dose-response gradient, as the MKSPLINE dose-response analyses showed a nonlinear inverse relationship between coffee consumption and dementia ($P = 0.042 < 0.05$).

[j] Upgrade for a dose-response gradient, as the MKSPLINE dose-response analyses showed a linear inverse relationship between coffee consumption and AD (P = 0.17> 0.05).

[k] Upgrade for a dose-response gradient, as the MKSPLINE dose-response analyses showed a linear inverse relationship between caffeine consumption and dementia (P = 0.86> 0.05).

Supplemental Figures

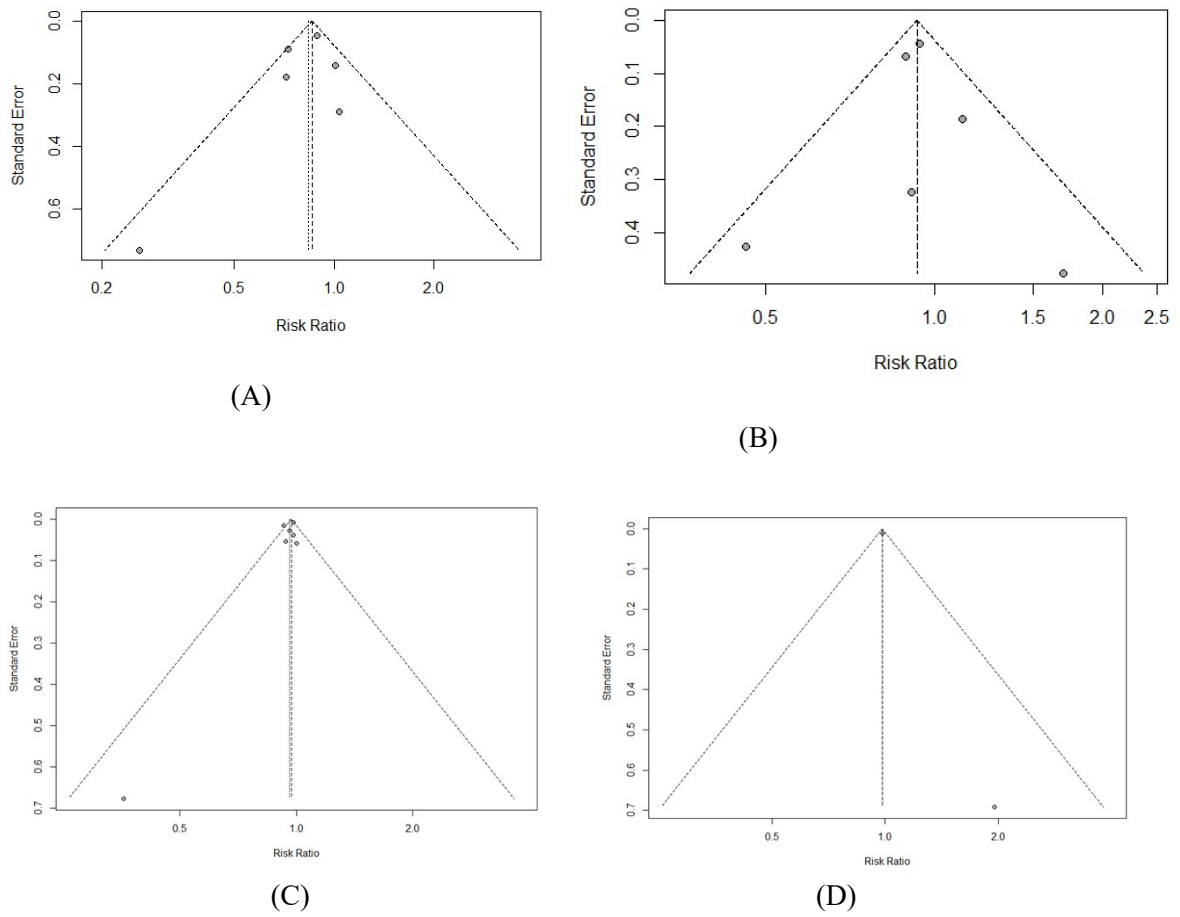
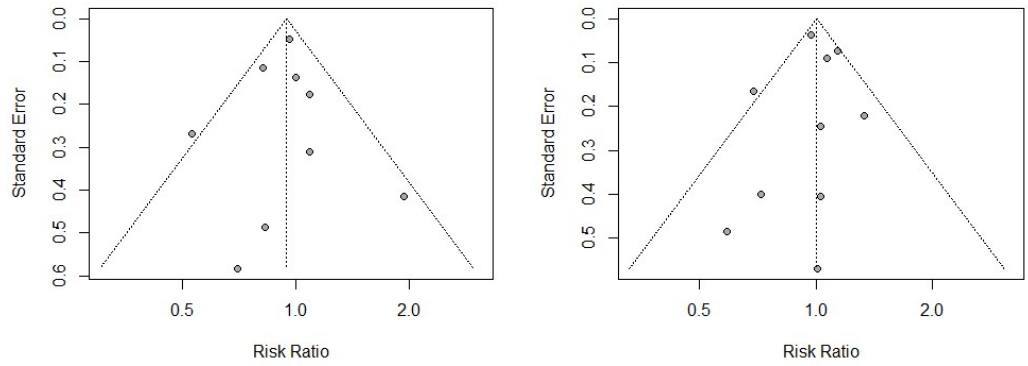
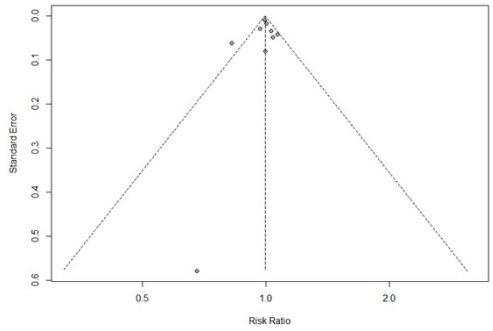


Fig. S1 Funnel plots for detection of publication bias of included studies for highest vs. lowest intake meta-analysis of tea intake and risk of dementia(A)and Alzheimer's Disease (B)； and for per 1 cup increase intake and risk of dementia(C)and Alzheimer's Disease (D).

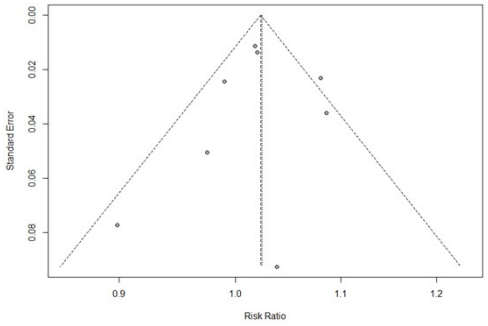


(A)

(B)



(C)



(D)

Fig. S2 Funnel plots for detection of publication bias of included studies for highest vs. lowest intake meta-analysis of coffee intake and risk of dementia(A) and Alzheimer's Disease (B); and for per 1 cup increase intake and risk of dementia(C)and Alzheimer's Disease (D).

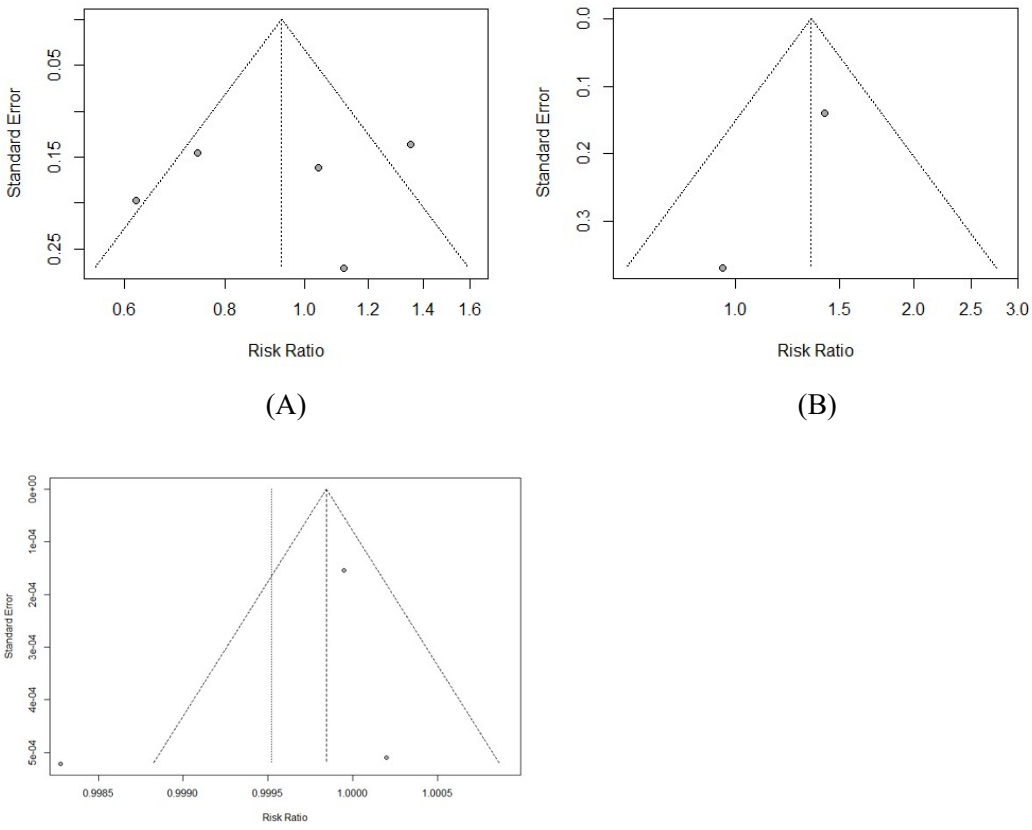


Fig. S3 Funnel plots for detection of publication bias of included studies for highest vs. lowest intake meta-analysis of caffeine intake and risk of dementia (A)and Alzheimer's Disease (B); and for per 50 mg increase intake and risk of dementia(C).

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