Title: Neuroinflammatory Markers sTREM2 and YKL-40 in Association with Alzheimer's Disease Pathology: A Systematic Review and Meta-Analysis

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Supplementary Methods. Search strategy

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sTREM2

Medline, EMBASE, PsycInfo

1	sTREM2 OR sTREM-2 OR “soluble TREM2” OR “soluble TREM-2” OR “soluble triggering receptor expressed on myeloid cells 2”
2	Alzheimer* OR AD.tw (title/abstract) OR neurodegenerat* OR dementia* OR aging* OR ageing* OR “mild cognitive impairment” OR “cogniti*
3	Biomarker* OR marker* OR protein* OR peptide* OR CSF OR “cerebrospinal fluid” OR blood* OR plasma OR serum OR “positron emission tomography” OR PET.tw (title/abstract)
4	2 AND 3
5	A<beta>* OR A-<beta>* OR <beta>-amyloid* OR amyloid*
6	Total-tau OR t-tau OR ttau OR ptau* OR p-tau* OR tau
7	NFL.tw (title/abstract) OR NEFL OR NF-L OR “neurofilament light chain”
8	4 OR 5 OR 6 OR7
9	1 AND 8

PubMed

((strem2 OR OR “strem-2” OR "soluble TREM2" OR “soluble TREM-2” OR "soluble triggering receptor expressed on myeloid cells 2") AND ((Alzheimer* OR AD OR neurodegenerat* OR dementia* OR aging* OR ageing* OR "mild cognitive impairment" OR cognitive) AND (biomarker* OR marker* OR protein* OR peptide* OR CSF OR "cerebrospinal fluid" OR blood* OR plasma OR serum OR "positron emission tomography" OR PET) OR (Abeta* OR A-beta* OR beta-amyloid* OR amyloid* OR total-tau OR t-tau OR ttau OR p-tau* OR tau OR NFL OR NEFL OR NF-L OR "neurofilament light chain")))

Scopus

((TITLE-ABS-KEY(strem2 OR strem-2 OR "soluble TREM2" OR “soluble TREM-2” OR "soluble triggering receptor expressed on myeloid cells 2")) AND ((TITLE-ABS-KEY(Alzheimer* OR AD OR neurodegenerat* OR dementia* OR aging* OR ageing* OR "mild cognitive impairment" OR "cognitive") AND TITLE-ABS-KEY(biomarker* OR marker* OR protein* OR peptide* OR CSF OR "cerebrospinal fluid" OR blood* OR plasma OR serum OR "positron emission tomography" OR PET) OR TITLE-ABS-KEY(Abeta* OR A-beta* OR beta-amyloid* OR amyloid* OR total-tau OR t-tau OR ttau OR p-tau* OR tau OR NFL OR NEFL OR NF-L OR "neurofilament light chain"))))

YKL-40

Medline, EMBASE, PsycInfo

1	YKL-40 OR YKL40 OR “Chitinase-3-like protein 1”OR CHI3L1 OR “Glycoprotein 39” OR GP-39 OR GP39 OR CGP-39
2	Alzheimer* OR AD.tw (title/abstract) OR neurodegenerat* OR dementia* OR aging* OR ageing* OR “mild cognitive impairment” OR “cogniti*
3	Biomarker* OR marker* OR protein* OR peptide* OR CSF OR “cerebrospinal fluid” OR blood* OR plasma OR serum OR “positron emission tomography” OR PET.tw (title/abstract)
4	2 AND 3

5	A<beta>* OR A-<beta>* OR <beta>-amyloid* OR amyloid*
6	Total-tau OR t-tau OR ttau OR ptau* OR p-tau* OR tau
7	NFL.tw (title/abstract) OR NEFL OR NF-L OR “neurofilament light chain”
8	4 OR 5 OR 6 OR7
9	1 AND 8

PubMed

((YKL-40 OR YKL40 OR "chitinase-3-like protein 1" OR CHI3L1 OR "Glycoprotein 39" OR GP-39 OR GP30 OR CGP-39) AND ((Alzheimer* OR AD OR neurodegenerat* OR dementia* OR aging* OR ageing* OR "mild cognitive impairment" OR cognitive) AND (biomarker* OR marker* OR protein* OR peptide* OR CSF OR "cerebrospinal fluid" OR blood* OR plasma OR serum OR "positron emission tomography" OR PET) OR (Abeta* OR A-beta* OR beta-amyloid* OR amyloid* OR total-tau OR t-tau OR ttau OR p-tau* OR tau OR NFL OR NEFL OR NF-L OR "neurofilament light chain")))

Scopus

((TITLE-ABS-KEY(YKL-40 OR YKL40 OR "chitinase-3-like protein 1" OR CHI3L1 OR "Glycoprotein 39" OR GP-39 OR GP30 OR CGP-39)) AND ((TITLE-ABS-KEY(Alzheimer* OR AD OR neurodegenerat* OR dementia* OR aging* OR ageing* OR "mild cognitive impairment" OR "cognitive") AND TITLE-ABS-KEY(biomarker* OR marker* OR protein* OR peptide* OR CSF OR "cerebrospinal fluid" OR blood* OR plasma OR serum OR "positron emission tomography" OR PET) OR TITLE-ABS-KEY(Abeta* OR A-beta* OR beta-amyloid* OR amyloid* OR total-tau OR t-tau OR ttau OR p-tau* OR tau OR NFL OR NEFL OR NF-L OR "neurofilament light chain"))))

Supplementary Table 2a. Studies investigating cross-sectional relationship between CSF sTREM2 and AD outcomes

Author, year	Cohort	Included in meta-analysis	N	Age (years), mean/ median	% Female	Education (years)	APOE (%e4)	MMSE (mean/ median)	Assay method for sTREM2	CSF sTREM2 levels pg/ml	AD markers assessed	Outcomes included in meta-analysis	Statistical method	Adjustments
Johnson et al. (2023)c	ABBY/BLAZE	Y	164	69.6 (7.8)	52	NA	72	21.7 (3.2)	NeuroToolKit	8903 (IQR=4150)	CSF Aβ40, Aβ42, Aβ42/40, tTau, pTau181	Aβ40, Aβ42, Aβ42/40, tTau, pTau181	Correlation	
Li et al. (2022)a	ADNI	Y	1035	73.16 (7.32)	43.8	16.01 (2.77)	47.4	27.25 (2.66)	MSD	NA	CSF Aβ42, pTau181	Aβ42, pTau181	Correlation (Pearson)	
Liu & Yu (2019)	ADNI	Y	1001	73.06 (7.35)	43.85	16.02 (2.78)	46.98	27.27 (2.63)	MSD	4097.31	CSF Aβ42, pTau181, tTau	tTau	Correlation (Spearman)	
Nabizadeh et al. (2024)	ADNI	Y	1001	73.02 (7.31)	43.6	16 (2.75)	44.7	27.25 (2.60)	MSD	4100.14 (2229.60)	PET Aβ (F18-AV45), PET tau ([18F]AV1451)	PET Aβ	Regression	Age, gender, and APOE ε4 status
Liu et al. (2024)	ADNI	N	545	72.6 (6.9)	42.57	14.5 (3.1)	42.9	28.15 (1.81)	MSD	3554.9 (2121.2)	CSF Aβ42, pTau181, tTau		Correlation (Pearson)	
Rauchmann et al. (2019)	ADNI	Y	497	73.75 (6.69)	49	15.83 (2.86)	43.9	NA	MSD and ELISA	3752.66 (2071.60)	CSF Aβ42, tTau, pTau181, NfL	Aβ42, tTau, pTau181, NfL	Regression	Age, sex, APOE ε4 status, education
Biel et al. (2025)	ADNI	N	454	73.38	46.3	16.22 (2.65)	NA	NA	MSD	3957.49 (2135.91)	CSF pTau181		Regression	Sex, age, education, clinical status, Aβ-PET
Wu et al. (2023)	ADNI	N	426	71.9 (7.0)	43.9	16.4 (2.6)	42	28.4 (1.6)	MSD	3874.1 (1960.6)	CSF Aβ42, pTau181		Regression	Age, sex, educational level, APOE ε4 gene, and general cognition
Ewers et al. (2020)	ADNI	N	300	72.56 (6.43)	45.33	16.38 (2.58)	54.67	28.21 (2.08)	MSD	4171.96 (2172.32)	PET Aβ (18F-		Regression	Baseline age, gender, education,

											Florbetapir (AV45))			diagnosis, CSF p-tau181, APOE ε4, time between AV45 PET visits, and random intercept
Biel et al. (2023)	ADNI	N	271	73.10 (6.88)	41.33	16.29 (2.66)	72.8	/	MSD	3718.32 (2133.91)	pTau181		Regression	Age, sex, education, clinical status, APOE ε4
Wang et al. (2022)a	ADNI	N	255	75.3 (6.6)	39.12	15.69 (3.14)	49.32	26.79 (2.61)	MSD	4421.53 (2032.28)	CSF Aβ42, tTau, pTau181		Partial Correlation (Spearman)	Age, sex, education, and APOE4 status
Wang et al. (2023)	ADNI	N	233	75.19 (6.73)	39.91	15.68 (3.12)	48.95	NA	MSD	4582.85 (2390.09)	CSF Aβ42, tTau, pTau181		Regression	Age, sex, education, APOE ε4 status
Sheng et al. (2025)	ADNI	N	211	74.99 (7.16)	37.9	15.75 (2.90)	53.1	NA	MSD	4389.37 (2045.13)	CSF Aβ42, tTau, pTau181		Partial correlation (Spearman)	Age, gender, education, APOE ε4 status
Pillai et al. (2021)a	ADNI	N	182	74.78 (6.61)	44.2	15.61 (3.05)	55.2	26.89 (2.66)	MSD	4229.58 (2134.51)	CSF Aβ42, pTau181, tTau		Correlation (Pearson)	
Shi et al. (2022)	ADNI	N	151	74.35 (6.68)	46.36	16 (5.14)	54.97	26.75 (3.14)	MSD	4689.04 (2572.32)	CSF Aβ42, tTau, pTau181		Regression	Age, gender, and ApoE4
Zeng et al. (2022)	ADNI	N	117	72.42 (5.90)	54.86	16.60 (2.49)	32	29.05 (1.29)	MSD	2818.38 (1160)	CSF Aβ42, tTau, pTau181		Correlation (Spearman)	
Johnson et al. (2023)a	ALFA+	Y	398	61.08 (4.74)	61.3	13.5 (3.54)	53.8	29.17 (0.94)	NeuroToolKit	7570 (2110)	CSF Aβ40, Aβ42, Aβ42/40, tTau, pTau181	Aβ40, Aβ42, Aβ42/40, tTau, pTau181	Correlation	
Vila-Castelar et al. (2024)	ALFA+	Y	397	61.08 (4.71)	61.46	13.52 (3.55)	53.7	NA	NeuroToolKit	7940 (2250)	[18F] Flutemetamol PET, CSF Aβ42/40, pTau181	PET Aβ, Aβ42/40, pTau181	Regression	For PET/CSFAβ [Age, APOE4 status]; For ptau181 [age, Aβ 42/40)

Warmenhoven et al. (2024)	ALFA+	Y	353	60.9 (4.7)	60	13.5 (3.5)	54.8	NA	NeuroToolKit (NTK)	7940 (2231.12)	CSF Aβ40, Aβ42/40, pTau181, PET Aβ ([18F]flutemetamol)	PET Aβ	Correlation (Pearson)	
Falcon et al. (2020)	Alzheimer's Disease and other cognitive disorder unit, Hospital Clinic de Barcelona	Y	36	66.5 (5.5)	66.67	NA	NA	27.9 (1.7)	MSD	NA	CSF Aβ42, tTau	Aβ42, tTau	Correlation	
Hok-A-Hin et al. (2023)	Amsterdam Dementia Cohort	Y	247	67 (58-72)	27.3	NA	NA	27 (21-30)	ELISA	NA	CSF Aβ42, tTau, pTau181	Aβ42, tTau, pTau181	Correlation (Spearman)	
Park et al. (2021)	Asan Medical Center	Y	101	68.80 (9.86)	53.5	11.57 (4.73)	39.6	22.99 (4.90)	Solid phase proximity ligation assay	NA	CSF Aβ42, tTau, NfL	Aβ42, tTau, NfL	Correlation (Spearman)	
Pereira et al. (2022)	BioFINDER-2	Y	121	73.0 (59.0-88.0)	50.41	11 (7-22)	/	28 (23-30)	NeuroToolKit	11,600 (4700-29600) pg/ml	PET Aβ ([18F]flutemetamol), CSF Aβ42/40	PET Aβ, Aβ42/40	Correlation	
Li et al. (2022)b	CABLE	Y	1131	62.47 (10.34)	58.89	9 (9-12)	15.2	28 (27-30)	ELISA	18310.87 (12047.88–22914.61)	CSF Aβ42, tTau, pTau181,	Aβ42, tTau, pTau181	Regression	Age, gender, APOE ε4 status, education

Yin et al. (2024)	CABLE	N	1078	62.58 (10.06)	44.16	9.30 (4.36)	15.9	27.07 (3.18)	ELISA	17,886.95 (7002.11)	CSF Aβ42, tTau, pTau181		Regression	APOE ε4 status
Li et al. (2024)	CABLE	Y	994	61.99 (10.40)	44.1	9.67 (4.24)	16.8	27.34 (3.11)	ELISA	18005.12 (7104.00)	CSF Aβ42, pTau181, tTau	Aβ42, pTau181, tTau	Correlation	
Wang et al. (2024)a	CABLE	Y	924	61.8 (10.2)	58.22	9.7 (4.4)	15.15	27.8 (2.2)	ELISA	17478.8 (7116.8)	CSF Aβ40 Aβ42, Aβ42/40, tTau, pTau181	Aβ40, Aβ42/40	Regression	Age, sex, educational level, MMSE score, and APOE ε4 status
Wang et al. (2024)b	CABLE	N	877	61.33 (9.99)	40	10.03 (4.28)	15.5	28.29 (2.04)	ELISA	18258.01 (7382.76)	CSF Aβ42, tTau, pTau181		Regression	Age, sex, education, APOE ε4 status
Wang et al. (2022)b	CABLE	N	796	61.6 (10.2)	43.97	9.5 (4.3)	17.5	27.2 (3.1)	ELISA	17605 (7206.6)	CSF Aβ42, tTau, pTau181		Regression	Age, sex, education, and APOE ε4 status
Ma et al. (2020)	CABLE	N	659	62.22 (10.45)	39.9	9.74 (4.38)	15.9	27.78 (2.14)	ELISA	18,233.64 (6,743.21)	CSF Aβ42, Aβ40, tTau, pTau181		Regression	Age, gender, APOE ε4 status, education
Pillai et al. (2021)b	Cleveland Clinic	Y	48	68.10 (7.3)	41.7	15.37 (2.87)	77.1	24.8 (3.1)	MSD / Luminex	1226.22 (637.46)	CSF Aβ42, tTau, pTau181	Aβ42, tTau, pTau181	Correlation (Pearson)	
Halaas et al. (2020)	COGNORM-study	Y	115	71 (68-76)	53	14 (12-17)	NA	NA	ELISA	8000 (6000-11000)	CSF Aβ42, tTau, pTau181	Aβ42, tTau, pTau181	Correlation (Spearman)	
Heslegrave et al. (2016)	Community	Y	59	70.02 (7.72)	50	NA	43	22 (18.0-29.0)	Mass-spec	217.1 (157.5-282.0)	CSF Aβ42, tTau, pTau181	Aβ42, tTau, pTau181	Correlation (Spearman)	
Nordengen et al. (2019)	DDI + MCI-GO	Y	121	65.28 (7.96)	51.9	NA	50	26.55 (5.08)	ELISA	4000 (1710)	CSF Aβ42*, tTau, pTau181	tTau, pTau181	Correlation (Pearson)	

Brosseron et al. (2022)	DELCODE	Y	308	70.74 (2.94)	52.2	NA	36.67	NA	ELISA	6080 (1540)	CSF Aβ42/40*, tTau, pTau181	tTau, pTau181	Partial Correlation (Spearman)	Age, sex, APOE status, BMI
Toppala et al. (2021)	Finnish population-based, nationwide Health2000 study	Y	11	68.1 (2.2)	54.5	NA	45.5	NA	ELISA	3647 (3370-4502)	PET Aβ [11C]PiB SUVR Composite score	PET Aβ	Correlation (Spearman)	
Brosseron et al. (2018)	German Center for Neurodegenerative Diseases (Bonn, Germany)	Y	331	71.02 (9.27)	42	13.91 (3.68)	NA	25.02 (4.42)	MSD	3879.94 (2428.32)	CSF Aβ40, Aβ42, Aβ42/40, tTau, pTau181	Aβ40, Aβ42, Aβ42/40, tTau, pTau181	Correlation (Spearman)	
Piccio et al. (2016)	Knight-ADRC	Y	180	72.74 (7.98)	51.4	NA	54.5	NA	ELISA	832 (163-2570)	CSF Aβ42, tTau, pTau181	Aβ42, tTau, pTau181	Correlation (Pearson)	
Pascoal et al. (2021)	McGill University Research Centre for Studies in Aging	Y	130	63.68 (19.41)	65.3	15.42 (3.39)	31.5	27.82 (4.04)	MSD	NA	CSF Aβ42/40, pTau181	Aβ42/40, pTau181	Correlation (Pearson)	
Henjum et al. (2016)	Memory Clinic of Skåne University Hospital	Y	100	66 (50-86)	50	NA	45	NA	ELISA	4400 (3000-7100)	CSF Aβ42, tTau, pTau181	Aβ42, tTau, pTau181	Correlation (Spearman)	

	(Norwegian cohort)													
Morenas-Rodríguez et al. (2019)	Memory Unit at Hospital de Sant Pau	Y	207	73 (6.5)	57.8	NA	45.1	25.7 (3.8)	ELISA	4600 (2300)	CSF Aβ42, tTau, pTau181	Aβ42, tTau, pTau181	Correlation (Pearson)	Age, sex
Ferri et al. (2021)	NA	Y	76	78.1 (4.6)	69.7	NA	46.10 %	22.1 (4.6)	ELISA	32600 (18100)	CSF Aβ42, tTau, pTau181	Aβ42, tTau, pTau181	Correlation (Spearman)	
Schmidt-Morgenroth (2023)	National Bioservice LLC	Y	77	66.6 (7.56)	55.8	NA	NA	26.7 (4.11)	Simple Plex	1577 (8080)	CSF Aβ42, tTau, pTau181	Aβ42, tTau, pTau181	Correlation (Spearman)	
Popovacki et al. (2023)	University Hospital Center "Zagreb"	Y	293	67.33 (10.03)	NA	NA	NA	23.41 (5.05)	ELISA	29167.03 (18,829.59)	CSF Aβ42, tTau, pTau181	Aβ42, tTau, pTau181	Correlation (Spearman)	
Doroszkiewicz et al. (2024)	University Hospital, Krakow, Poland	Y	80	75.5 (63.3-80.0)	70	NA	NA	22 (19-29)	Luminex	3805 (2124-4732)	CSF Aβ42, Aβ42/40, tTau, pTau181	Aβ42, Aβ42/40, tTau, pTau181	Correlation (Spearman)	
Winfree et al. (2023)	Vanderbilt Memory and Aging Project	Y	335	72 (6.33)	32.9	16 (2.80)	33	NA	MSD	3667 (1812.50)	CSF Aβ42, Aβ40, tTau, pTau181, NfL	Aβ42, Aβ42/40, tTau, pTau181, NfL	Correlation (Pearson)	
Moore et al. (2021)	Vanderbilt Memory and Aging Project	N	146	72 (6)	34	16 (3)	31	NA	ELISA	3668 (1812)	CSF Aβ42, pTau181, tTau, NfL		Correlation (Pearson)	

Van Hulle et al. (2021)	Wisconsin cohorts	Y	720	63.9 (9.0)	63.3	16 (2.6)	34.8	28.5 (2.5)	NeuroToolKit	8260 (2670)	CSF Aβ40, Aβ42, tTau, pTau181, NfL	Aβ40, Aβ42, tTau, pTau181, NfL	Correlation (Pearson)	
Johnson et al. (2023)b	Wisconsin cohorts	Y	546	61.39 (7.60)	66.8	16.25 (2.49)	35.7	29.34 (0.94)	NeuroToolKit	7670 (2380)	CSF Aβ40, Aβ42, Aβ42/40, tTau, pTau181	Aβ42/40	Correlation	

Note. Studies listed more than once contributed multiple datasets to the analysis.
*Value not reported; outcome unable to be included in meta-analysis

Supplementary Table 2b. Studies investigating cross-sectional relationship between CSF YKL-40 and AD outcomes

Author, year	Cohort	Included in meta-analysis	N	Age (years), mean/ median	% Female	Education (years)	APOE (%e4)	MMSE (mean/ median)	Assay method for YKL-40	CSF YKL-40 levels ng/ml	AD markers assessed	Outcomes included in meta-analysis	Statistical method	Adjustments
Lane et al. (2024)	12 centers (Canada, Finland, Germany, Netherlands, Sweden, UK)	Y	45	65.8 (5.8)	NA	NA	73	23.6 (2.3)	ELLA	NA	CSF Aβ42, pTau181	Aβ42, pTau181	Correlation (Pearson)	
Johnson et al. (2023)c	ABBY/BLAZE	Y	164	69.6 (7.8)	52	NA	72	21.7 (3.2)	NeuroToolKit	191.6 (IQR=103.9)	CSF Aβ40, Aβ42, Aβ42/40, tTau, pTau181	Aβ40, Aβ42, Aβ42/40, tTau, pTau181	Correlation	
Sheng et al. (2025)	ADNI	Y	211	74.99 (7.16)	37.9	15.75 (2.90)	53.1	NA	mass spectrometry with multiple reaction monitoring (MRM) and then normalized	NA	CSF Aβ42, tTau, pTau181	Aβ42, tTau, pTau181	Regression	Age, gender, education, APOE ε4 status
Sutphen et al. (2019)	ADNI	Y	148	75 (7.13)	38	16.01 (2.93)	68	27.475 (2.29)	ELISA	399.80 (36.16)	CSF Aβ42, tTau, pTau181	Aβ42, tTau, pTau181	Correlation (Spearman)	
Morar et al. (2022)	ADNI	N	140	74.93 (5.94)	39.28	15.85 (2.96)	43.57	27.31 (2.52)	ELISA	396.33 (134.15)	CSF Aβ42, pTau181, tTau		Correlation (Pearson)	

Zhang et al. (2018)	ADNI	N	121	74.76 (6.38)	37.19	15.99 (2.90)	44.62	27.05 (2.15)	ELISA	407.05 (142.69)	CSF Aβ42, pTau181		Correlation (Spearman)	
Wang et al. (2020)	ADNI	Y (subgroup anaysis only)	109	74.45 (5.97)	41.28	15.70 (2.17)	45.9	27.34 (1.39)	ELISA	370.99	CSF Aβ42, pTau181, tTau		Correlation (Spearman)	
Melah et al. (2016)	ADRC	Y	192	60.98 (7.55)	71.3	16.26 (2.51)	41	29.34 (0.886)	ELISA	142.761 (52.093)	CSF tTau, NfL	tTau, NfL	Regression	Age, sex, WMHr, APOE genotype status, and family history status
Johnson et al. (2023)a	ALFA+	Y	398	61.08 (4.74)	61.3	13.5 (3.54)	53.8	29.17 (0.94)	NeuroToolKit	140.1 (47.84)	CSF Aβ40, Aβ42, Aβ42/40, tTau, pTau181	Aβ40, Aβ42, Aβ42/40, tTau, pTau181	Correlation	
Vila-Castelar et al. (2024)	ALFA+	Y	397	61.08 (4.71)	61.46	13.52 (3.55)	53.7	NA	NeuroToolKit	147.31 (53.56)	[18F] Flutemetamol PET, CSF Aβ42/40, pTau181	PET Aβ, Aβ42/40, pTau181	Regression	For PET/CSFAβ [Age, APOE ε4 status]; For ptau181 [age, Aβ 42/40)
Pelkmans et al. (2023)	ALFA+	Y	384	61.1 [range 49.6 to 73.4]	61.2	13.5 (3.5)	54.2	29.2 [range 27.0 to30.0]	NeuroToolKit	145.3 (51.7)	PET Aβ ([18F]flutemetamol); CSF Aβ42/40, pTau181, NfL	NfL	Regression	Age, sex, APOE status
Warmenhoven et al. (2024)	ALFA+	Y	353	60.9 (4.7)	60	13.5 (3.5)	54.8	NA	NeuroToolKit	147.23 (52.86)	PET Aβ Centiloids ([18F]flutemetamol); CSF Aβ40, Aβ42/40, pTau181	PET Aβ	Correlation (Pearson)	
Muszyński et al. (2017)	Biomark APD – EU Joint	Y	86	NA	70.93	NA	NA	22	ELISA	NA	CSF Aβ42, Aβ42/40,	Aβ42, Aβ42/40,	Correlation (Spearman)	

	Programme for Neurodegenerative Disease Research (JPND)										tTau, pTau181	tTau, pTau181		
Daniilidou et al. (2024)	Co-STAR	Y	108	62.46 (7.76)	57.57	13.80 (3.31)	NA	NA	ELISA	140.84 (59.06)	CSF Aβ42, tTau, pTau181	Aβ42, tTau, pTau181	Correlation (Spearman)	
Nordengen et al. (2019)	DDI + MCI-GO	Y	121	65.28	52.07		50.41	26.55	MSD	180.59 (70.70)	CSF Aβ42*, tTau, pTau181	tTau, pTau181	Correlation (Pearson)	
Brosseron et al. (2022)	DELCODE	Y	308	70.74 (2.94)	52.2	NA	36.67	NA	ELISA	346.38 (145.98)	CSF Aβ42/40, tTau, pTau181	tTau, pTau181	Partial Correlation (Spearman)	Age, sex, APOE status, BMI
Hellwig et al. (2015)	Department of Psychiatry and Psychotherapy, Universitätsklinikum Erlangen	Y	95	70.57 (7.98)	53.68	NA	NA	23.37 (2.78)	ELISA	NA	CSF Aβ40, Aβ42, tTau, pTau181	Aβ40, Aβ42, tTau, pTau181	Correlation (Spearman)	
Idland et al. (2020)	Elective surgery patients	Y	99	72 (68–78)	49.49	14 (12-17)	NA	29 (28-30)	ELISA	225.210 (175.208–280.877)	CSF Aβ42, pTau181, tTau, NfL	Aβ42, tTau, pTau181, NfL	Correlation (Spearman)	Age
Bos et al. (2019)	EMIF-AD Multimodal Biomarker	Y	770	69.3 (8.3)	52	10.9 (3.9)	49	25.55 (3.93)	ELISA	172.91 (65.40)	CSF Aβ40, Aβ42*, Aβ42/40, tTau, pTau181, NFL	Aβ40, Aβ42/40, tTau, pTau181, NfL	Correlation (Spearman)	

	Discovery study													
Schaeverbeke et al. (2019)	EudraCT	Y	38	72 (4.7)	42.1	13.4 (3.1)	50	29 (1)	ELISA	369 (93)	CSF Aβ40, Aβ42, tTau, pTau181	Aβ40, Aβ42, tTau, pTau181	Correlation (Spearman)	
Toppala et al. (2021)	Finnish population-based, nationwide Health2000 study	Y	11	68.1 (2.2)	54.5	NA	45.5	NA	ELISA	133 (111-155)	PET Aβ [11C]PiB SUVR Composite score	PET Aβ	Correlation (Spearman)	
Antonell et al. (2014)	Hospital Clinic de Barcelona	Y	83	65.6 (9.1)	63.9	NA	32.6	27.4 (2.4)	ELISA	303 (97.2)	CSF Aβ42, tTau, pTau181	Aβ42, tTau, pTau181	Partial Correlation (Pearson)	Age
Rosén et al. (2014)	Hospital Clinic de Barcelona	Y	50	63.855 (4.35)	64	NA	30	25 (4.15)	ELISA	155.921 (47.11)	CSF Aβ42, tTau, pTau181	Aβ42, tTau, pTau181	Correlation (Spearman)	
Falcon et al. (2020)	Hospital Clinic de Barcelona	N	36	66.5 ± 5.5	66.67%	NA	NA	27.9 (1.7)	MSD	286.7 (84.2)	CSF Aβ42, pTau181		Correlation	
Teitsdottir et al. (2020)	Icelandic MCI study cohort	Y	52	68.62 (8.5)	36.54	13.19 (2.85)	NA	27.46 (1.58)	ELISA	185.46 (72.29)	CSF Aβ42, tTau, NfL	Aβ42, tTau, NfL	Correlation (Pearson)	
Teitsdottir et al. (2022)	Icelandic MCI study cohort	Y	46	70.72 (9.36)	54.35	13 (3.32)	NA	27.72 (1.57)	ELISA	189.2 (67.71)	CSF Aβ42, pTau181, tTau, NfL	pTau181	Correlation (Pearson)	
Baldacci et al. (2017)	IM2A (n=35) + DZNE (n=57) + Sahlgren	Y	108	70.83 (6.83)	52.8	NA	NA	25.55 (4.42)	ELISA	126.81 (50.45)	CSF Aβ42, tTau, pTau181	Aβ42, tTau, pTau181	Partial Correlation (Spearman)	Age, sex, site

	ska University Hospital (n=16)													
Abu-Rumeileh et al. (2019)	Institute of Neurological Sciences of Bologna	Y	40	68.63 (8.16)	40	NA	NA	20.22 (4.87)	ELISA	240 (IQR=176–293)	CSF Aβ42/40, tTau, pTau181	Aβ42/40, tTau, pTau181	Correlation (Spearman)	
Deming et al. (2016)	Knight-ADRC	Y	379	70.86 (8.80)	60.95	NA	36.68	NA	ELISA	307.25 (108.45)	CSF Aβ42, tTau, pTau181	Aβ42, tTau, pTau181	Correlation (Pearson)	
Dage et al. (2023)	LEADS	Y	165	57.9 (5.0)	49	NA	51	NA	ELISA	240 (99)	CSF Aβ42/40, tTau, pTau181, NfL	Aβ42/40, tTau, pTau181, NfL	Correlation (Spearman)	
Olsson et al. (2013)a	Malmö cohort	Y	161	75.6 (7.5)	68.3	NA	NA	22.9 (5.7)	ELISA	222.6 (94.5)	CSF Aβ42, tTau, pTau181	Aβ42, tTau, pTau181	Correlation (Spearman)	
Janelidze et al. (2015)	Memory Clinic of Skåne University Hospital	Y	162	75.74 (7.16)	68.22	NA	57.12	23.92 (4.95)	ELISA	226.03 (69.16)	CSF Aβ40, Aβ42, Aβ42/40, tTau	Aβ40, Aβ42, Aβ42/40, tTau	Correlation	Age, gender
Wennström et al. (2015)	Memory Clinic of Skåne University Hospital	Y	44	63.7 (10.3)	52	NA	33	29 (1)	ELISA	NA	CSF Aβ42, tTau, pTau181	tTau, pTau181	Correlation (Spearman)	
Morenas-Rodríguez (2019)	Memory Unit at Hospital de Sant Pau	Y	207	73 (6.5)	57.8	NA	45.1	25.7 (3.8)	ELISA	277.8 (64.8)	CSF Aβ42, tTau, pTau181	Aβ42, tTau, pTau181	Correlation (Pearson)	Age

Alcolea et al. (2014)	Memory Unit at Hospital de Sant Pau	N	194	67.2 (9.25)	55.7	NA	36.7	26.3 (4.01)	ELISA	233.7 (61.0)	CSF Aβ42, tTau, pTau181		Correlation (Spearman)	Age
Alcolea et al. (2015)a	Memory Unit at Hospital de Sant Pau	Y	107	62.27 (9.10)	69.2	12.93 (5.06)	34.6	28.43	ELISA	210.39 (50.27)	CSF Aβ42, tTau, pTau181	Aβ42, tTau, pTau181	Correlation (Pearson)	
Khoonsari et al. (2019)	NA	Y	206	73.20 (9.54)	43.59	NA	NA	NA	Mass-spec	NA	CSF Aβ42, tTau, pTau181	Aβ42, tTau, pTau181	Correlation (Spearman)	
Schmidt-Morgenroth (2023)	National Bioservice LLC	Y	77	66.6 (7.56)	55.8	NA	NA	26.7 (4.11)	Simple Plex	197.9 (102.2)	CSF Aβ42, tTau, pTau181	Aβ42, tTau, pTau181	Correlation (Spearman)	
Alcolea et al. (2015)b	SIGNAL	Y	266	58.77 (7.77)	59	NA	25.28	29 (1.48)	ELISA	196.77 (48.68)	CSF Aβ42, tTau	Aβ42, tTau	Correlation (Spearman)	
Olsson et al. (2013)b	Stability study	Y	52	76.1 (7.9)	46.15	NA	NA	23.8 (0.5)	ELISA	NA	CSF Aβ42, tTau, pTau181	Aβ42, tTau, pTau181	Correlation (Spearman)	
Ferrari-Souza et al. (2022)	TRIAD	Y	121	70.14 (6.61)	56.19	14.93 (3.30)	39.64	27.62 (3.91)	ELISA	NA	PET Aβ ([18F]AZD 4694 SUVR); PET tau ([18F]MK-6240 temporal meta-ROI SUVR)	PET Aβ, PET tau	Regression	Age, sex, cognitive status, APOE ε4 status, CSF GFAP + PET-Aβ (for PET tau)/ PET-tau (for PET Aβ)
Kulczynska-Przybik et al. (2023)	University Hospital, Krakow, Poland	N	78	72 (median)	69.23	NA	NA	24.72	ELISA	375.95 (165.41)	CSF Aβ42/40, tTau, pTau181		Correlation (Spearman)	

Doroszkiewicz et al. (2023)	University Hospital, Krakow, Poland	N	71	73 (51–89)	70.4	NA	NA	24.92	ELISA	NA	CSF Aβ42/40, tTau, pTau181		Correlation (Spearman)	
Moore et al. (2021)	Vanderbilt Memory and Aging Project	Y	146	72 (6)	34	16 (3)	31	NA	ELISA	193.252 (65.031)	CSF Aβ42, tTau, pTau181, NfL	Aβ42, tTau, pTau181, NfL	Correlation (Pearson)	
Van Hulle et al. (2021)	Wisconsin cohorts	Y	720	63.9 (9.0)	63.3	16 (2.6)	34.8	28.5 (2.5)	NeuroToolKit	157.47 (66.98)	CSF Aβ40, Aβ42, tTau, pTau181, NfL	Aβ40, Aβ42, tTau, pTau181, NfL	Correlation	
Johnson et al. (2023)b	Wisconsin cohorts	Y	546	61.39 (7.60)	66.8	16.25 (2.49)	35.7	29.34 (0.94)	NeuroToolKit	134.0 (47.32)	CSF Aβ40, Aβ42, Aβ42/40, tTau, pTau181	Aβ42/40	Correlation	
Craig-Schapiro et al. (2010)	Wisconsin cohorts	Y	292	72.17 (7.32)	59.9	NA	40.9	27.67 (2.95)	ELISA	NA	PET Aβ ([11C]-PIB); CSF Aβ42, tTau, pTau181	PET Aβ	Correlation (Pearson)	

Note. Studies listed more than once contributed multiple datasets to the analysis.
*Value not reported; outcome unable to be included in meta-analysis

Supplementary Table 2c. Studies investigating cross-sectional relationship between blood-derived sTREM2 and AD outcomes

Author, year	Cohort	N	Age (years), mean/ median	% Female	Education (years)	APOE (%e4)	MMSE (mean/ median)	sTREM2 measured in:	Assay method for sTREM2	sTREM2 levels pg/ml	AD markers assessed	Statistical method	Adjustments
Ferri et al. (2021)	NA	76	78.1 (4.6)	69.7	NA	46.10%	22.1 (4.6)	Plasma	ELISA	39100 (15000)	CSF Aβ1-42, T-tau, p-tau181	Correlation (Spearman)	/
Park et al. (2021)	Asan Medical Center	101	68.80 (9.86)	53.5	11.57 (4.73)	39.6	22.99 (4.90)	Plasma	Solid phase proximity ligation assay	NA	CSF Aβ42, T-tau, NfL	Correlation (Spearman)	/
Zhao et al. (2022)	CABLE	150	62.73 (8.13)	50.67	11.57 (3.27)	29.33	25.97 (2.63)	Plasma	ELISA	NA	CSF Aβ1-42	Correlation (Pearson)	/
Brosseron et al. (2023)	DELCODE	309	70.74 (6.28)	51.78	/	36.7	/	Serum	ELISA	8540 (1557)	CSF Aβ42/40, p-tau181, t-tau; Plasma NfL	Correlation (Spearman)	Age, sex, BMI, APOE

Supplementary Table 2d. Studies investigating cross-sectional relationship between blood-derived YKL-40 and AD outcomes

Author, year	Cohort	N	Age (years), mean/ median	% Female	Education (years)	APOE (%e4)	MMSE (mean/ median)	YKL-40 measured in:	Assay method for YKL-40	YKl-40 levels pg/ml	AD markers assessed	Statistical method	Adjustments
Brosseron et al. (2023)	DELCODE	309	70.74 (6.28)	51.78	/	36.7	/	Serum	ELISA	92.95 (214.06)	CSF Aβ42/40, p-tau181, t-tau; Plasma NfL	Correlation (Spearman)	Age, sex, BMI, APOE
Craig-Schapiro et al. (2010)	WU-ADRC	237	NA	NA	NA	NA	NA	Plasma	ELISA	NA	PET Aβ ([11C]-PIB) CSF Aβ42, T-tau, P-tau181	Correlation (Pearson)	/
Prins et al. (2022)	Centre for Human Drug Research	121	NA	NA	NA	NA	NA	Plasma	ELISA	NA	CSF Aβ42	Correlation	/
Vergallo et al. (2020)	INSIGHT-preAD	302	76.07 (3.51)	63.69	NA	80.25	NA	Plasma	ELISA	NA	PET Aβ (18F-Florbetapir)	Regression	Age, sex, APOE ε4 allele

Supplementary Table 2e. Studies investigating longitudinal relationships between sTREM2 or YKL-40 and AD outcomes

Author, year	Cohort	Follow up period	N	Age (years), mean/ median	% Female	Education (years)	APOE (%e4)	MMSE (mean/ median)	sTREM2 or YKL-40 measured in:	Assay method for sTREM2 or YKL-40	AD markers assessed	Statistical method	Adjustments
sTREM2													
Biel et al. (2023)	ADNI	2.00 years (0.08)	95	NA	NA	NA	NA	NA	CSF	MSD	p-tau181	Regression	Age, sex, education, clinical status, APOE ε4
Ewers et al. (2020)	ADNI	2.17 years (0.6)	300	72.56 (6.43)	45.33	16.38 (2.58)	54.67	28.21 (2.08)	CSF	MSD	PET Aβ (18F-Florbetapir (AV45))	Regression	Baseline age, gender, education, diagnosis, CSF p-tau181, APOE ε4, time between AV45 PET visits, and random intercept
Li et al. (2022)a	ADNI	12, 24, 36, 48months	360	NA	NA	NA	NA	NA	CSF	MSD	CSF Aβ42, p-tau181	Correlation (Pearson)	
Nabizadeh et al. (2024)	ADNI	12months to up to 48 months	1001	73.02 (7.31)	43.6	16 (2.75)	44.7	27.25 (2.60)	CSF	MSD	PET Aβ (F18-AV45), PET tau ([18F]AV1451)	Regression	Age, gender, and APOE ε4 status
Zeng et al. (2022)	ADNI	Aβ-PET (4.79years ± 2.05)	117	72.42 (5.90)	54.86	16.60 (2.49)	32	29.05 (1.29)	CSF	MSD	[18F] florbetapir PET annual change	Correlation (Spearman)	
Pereira et al. (2022)	BioFINDER-2 (A^+ individuals only)	Second scan 1.8 years (0.15-2.56); Third scan 3.73 (1.34-4.0) years	115	73.0 (59.0 - 88.0)	50.41	11 (7.0-22.0)	NA	28.0 (23.0-30.0)	CSF	NeuroToolKit	PET Aβ ([18F]flutemetamol)	Regression	Time, age, sex, presence of cognitive impairment
YKL-40													
Vergallo et al. (2020)	INSIGHT-preAD	24M	255	NA	NA	NA	NA	NA	Plasma	ELISA	PET Aβ (18F-Florbetapir)	Regression	Age, sex, APOE ε4 allele

Supplementary Table 2. Summary of heterogeneity statistics for meta-analyses of associations between sTREM2/YKL-40 and AD biomarkers

	k	Q (df, p-value)	I^2	τ^2	τ
sTREM2					
PET Aβ	3	Q(2) = 0.9946, p = .6082	0%	0 (SE = 0.0079)	0
CSF Aβ42/40	9	Q(8) = 24.7769, p = .0017	73.34%	0.0088 (SE = 0.0064)	0.0935
CSF Aβ42	19	Q(18) = 87.19, p < .001	81.8%	0.0171 (SE = 0.0079)	0.131
CSF Aβ40	4	Q(3) = 16.4768, p = .0009	81.13%	0.0117 (SE = 0.0121)	0.1083
CSF pTau181	19	Q(18) = 40.8847, p = .0016	55.12%	0.0046 (SE = 0.0031)	0.0675
CSF tTau	20	Q(19) = 44.4650, p = .0008	58.25%	0.0055 (SE = 0.0035)	0.0741
CSF NfL	3	Q(2) = 10.1313, p = .0063	88.43%	0.0257 (SE = 0.0302)	0.1604
YKL-40					
PET Aβ	3	Q(2) = 2.6930, p = .2602	0.04%	0.0000 (SE = 0.0065)	0.0018
CSF Aβ42/40	7	Q(6) = 59.0300, p < .0001	88.75%	0.0289 (SE = 0.0204)	0.1701
CSF Aβ42	19	Q(18) = 64.9410, p < .0001	72.65%	0.0164 (SE = 0.0083)	0.1282
CSF Aβ40	6	Q(5) = 78.0822, p < .0001	95.06%	0.0613 (SE = 0.0433)	0.2476
CSF pTau181	23	Q(22) = 129.1445, p < .0001	81.72%	0.0266 (SE = 0.0109)	0.1631
CSF tTau	23	Q(22) = 127.9719, p < .0001	81.26%	0.0243 (SE = 0.0100)	0.1558
CSF NfL	5	Q(4) = 8.5869, p = .0723	54.78%	0.0040 (SE = 0.0057)	0.0632

Supplementary Table 3a. Adjusted associations between CSF sTREM2 and AD biomarkers

Study	Adjustment	N	Reported effect size	r_p conversion
Aβ40				
Wang et al. (2024)	Age, sex, APOE status, education, MMSE	924	β = 0.367, p < .001	Unable to be estimated*
Aβ42				
Morenas-Rodríguez et al. (2019)	Age, sex	207	r = 0.152	
Rauchmann et al. (2019)	Age, sex, APOE status, education	497	β = 0.03, p = 0.61	0.023
Li et al. (2022)b	Age, sex, APOE status, education	1031	β = 0.352, 95% CI [0.2867, 0.4164], p < .001	0.32
	Pooled r_p	**1735**	**r_p = 0.17, 95% CI [-0.01, 0.34], p = .0651**	
Aβ42/40				
Wang et al. (2024)a	Age, sex, APOE status, education, MMSE	924	β = -0.064, p = .051	-0.064
Vila-Castelar et al. (2024)	Age, APOE status	397	b = 0.001, 95% CI [0, 0.002], p = .136	0.099
	Pooled r_p	**1321**	**r_p = 0.01, 95% CI [-0.15, 0.17], p = .8717**	
T-tau				
Morenas-Rodríguez et al. (2019)	Age, sex	207	r = 0.179	
Brosseron et al. (2022)	Age, sex, APOE status, BMI	308	r = 0.405	
Rauchmann et al. (2019)	Age, sex, APOE status, education	497	β = 0.06, p < 0.001	Unable to be estimated*
Li et al. (2022)b	Age, sex, APOE status, education	1031	β = 0.354, 95% CI [0.2941, 0.4142], p < .001	0.339
	Pooled r_p	**2043**	**r_p = 0.32, 95% CI [0.19, 0.43], p < .0001**	
p-tau181				
Morenas-Rodríguez et al. (2019)	Age, sex	207	r = 0.204	
Brosseron et al. (2022)	Age, sex, APOE status, BMI	308	r = 0.429	

Rauchmann et al. (2019)	Age, sex, APOE status, education	497	β = 0.24, p < 0.001	Unable to be estimated*
Li et al. (2022)b	Age, sex, APOE status, education	1031	β = 0.315, 95% CI [0.2533, 0.3771], p < .001	0.30
Vila-Castelar et al. (2024)	Age, APOE status	397	b = 0.49, 95% CI [0.20, 0.78], p < .001	0.165
	Pooled r_p	**2440**	**r_p = 0.28, 95% CI [0.16, 0.39], p < .0001**	
NfL				
Rauchmann et al. (2019)	Age, sex, APOE status, education	497	β = 0.21, p = 0.03	0.097
Aβ PET				
Nabizadeh et al. (2024)	Age, sex, APOE status	1001	β = 0.026, p = .448	0.024
Vila-Castelar et al. (2024)	Age, APOE status	397	b = 0.19, 95% CI [-0.71, - 1.10], p = .678	0.021
	Pooled r_p	**1398**	**r_p = 0.02, 95% CI [-0.03, 0.08], p = .3876**	

Supplementary Table 3b. Adjusted associations between CSF YKL-40 and AD biomarkers

Study	Adjustment	N	Reported effect size	r_p conversion
Aβ40				
Janelidze et al. (2015)	Age, sex	162	r = 0.417	
Aβ42				
Idland et al. (2020)	Age	99	r = 0.01	
Antonell et al. (2014)	Age	83	r = -0.07	
Baldacci et al. (2017)	Age, sex, site	108	r = 0.002	
Janelidze et al. (2015)	Age, sex	162	r = 0.136	
Morenas-Rodríguez et al. (2019)	Age	207	r = -0.163	
Sheng et al. (2025)[†]	Age, sex, APOE status, education	211	β = 0.028, p = .672	0.03
	Pooled r_p	**870**	**r_p = -0.01, 95% CI [-0.10, 0.08], p = .8417**	

Aβ42/40				
Janelidze et al. (2015)	Age, sex	162	r = -0.313	
Vila-Castelar et al. (2024)	Age, APOE status	397	b = 0, p = .203	0.064
	Pooled r_p	**557**	**r_p = -0.12, 95% CI [-0.47, 0.25], p = .5190**	
T-tau				
Janelidze et al. (2015)	Age, sex	162	r = 0.5	
Idland et al. (2020)	Age	99	r = 0.67	
Antonell et al. (2014)	Age	83	r = 0.469	
Baldacci et al. (2017)	Age, sex, site	108	r = 0.554	
Morenas-Rodríguez (2019)	Age	207	r = 0.572	
Brosseron et al. (2022)	Age, sex, APOE status, BMI	308	r = 0.476	
Sheng et al. (2025)[†]	Age, sex, APOE status, education	211	β = 0.488, p <.001	Unable to be estimated*
Melah et al. (2016)	Age, sex, APOE genotype status, family history status, white matter hyperintensity ratio	192	β = 0.553, p <.001	Unable to be estimated*
	Pooled r_p	**1370**	**r_p = 0.54, 95% CI [0.48, 0.59], p < .0001**	
p-tau181				
Idland et al. (2020)	Age	99	r = 0.62	
Antonell et al. (2014)	Age	83	r = 0.431	
Baldacci et al. (2017)	Age, sex, site	108	r = 0.574	
Morenas-Rodríguez (2019)	Age	207	r = 0.589	
Brosseron et al. (2022)	Age, sex, APOE status, BMI	308	r = 0.487	
Vila-Castelar et al. (2024)	Age, APOE status	397	b = 0.079, 95% CI [0.066, 0.092], p < .001)	0.516

Sheng et al. (2025)[†]	Age, sex, APOE status, education	211	β = 0.444, p < .001	Unable to be estimated*
	Pooled r_p	**1413**	**r_p = 0.53, 95% CI [0.49, 0.57], p < .0001**	
NfL				
Idland et al. (2020)	Age	99	r = 0.35	
Melah et al. (2016)	Age, sex, APOE status, family history status, white matter hyperintensity ratio	192	β = 0.254, p < .001	Unable to be estimated*
Pelkmans et al. (2023)	Age, sex, APOE status	384	b = 0.22 (SE = 0.02)	0.492
	Pooled r_p	**675**	**r_p = 0.44, 95% CI [0.30, 0.56], p < .0001**	
Aβ PET				
Ferrari-Souza et al. (2022)	Age, sex, cognitive status, APOE status, CSF GFAP, PET-tau	121	β = −0.14, 95% CI [-0.30, 0.03], t = -1.66, p = .100	-0.154
Vila-Castelar et al. (2024)	Age, APOE status	397	b = 0.060, 95% CI [0.02, 0.1], p = .004	0.147
	Pooled r_p	518	**r_p = 0.01, 95% CI [-0.28, 0.29], p = .9673** Not used due to vast differences in covariate inclusion	

Note. Regression coefficients (b, β) were converted to partial correlations (r_p) as follows: $r_p = t / \sqrt{t^2 + df}$. Degrees of freedom (df) were defined as $df = N - K - 1$ (N = total sample size; K = number of covariates); the t-statistic, if not reported, was calculated as t = β/SE(β). If not reported, the standard error (SE) was calculated from the 95% CI: SE(β) = (Upper – Lower)/(2*1.96). If only the p-value was reported, the t-statistic was calculated from the two-sided p-value: $|t|=t_{1-p/2}(df)$, with sign taken from β).

*For studies that reported only threshold p-values (e.g., "p < .001"), the associated test statistic was unable to be reliably estimated and hence r_p was not calculated.

[†]Effects of three YKL-40 surrogate peptides quantified by targeted mass spectrometry (ILGQQVPYATK, SFTLASSETGVGAPISGPGIPGR, VTIDSSYDIAK) were reported; we treated peptides as technical replicates and used the median effect size for analysis.

Supplementary Table 4. Meta-regressions (*b*, 95% CI, *p*) for eligible cross-sectional associations between sTREM2/YKL-40 and AD biomarkers by age, proportion of female participants, years of education, APOE ε4 positive, and MMSE.

	Age	**% Female**	**Years of education**	**% APOE ε4 positive**	**MMSE**
sTREM2					
PET Aβ	NA	NA	NA	NA	NA
CSF Aβ42/40	NA	NA	NA	NA	NA
CSF Aβ42	b = -0.010, 95% CI [-0.025, 0.005], p = .191	b = 0.005, 95% CI [-.0007, 0.0112], p = .0856	b = -0.0158, 95% CI [-0.0534, 0.0217], p = .4089	b = 0.0001, 95% CI [-0.0063, 0.0066], p = .9694	b = 0.014, 95% CI [–0.019, 0.047], p = .391
CSF Aβ40	NA	NA	NA	NA	NA
CSF pTau181	b = 0.0001, 95% CI [-0.0102, 0.0105], p = .9778	**b = 0.004, 95% CI [0.001, 0.007], p = .024**	b = 0.004, 95% CI [-0.0224, 0.0304], p = .7674	b = -0.0022, 95% CI [-0.0056, 0.0012], p = .2010	b = 0.0077, 95% CI [-0.0146, 0.0299], p = .4996
CSF tTau	b = -0.001, 95% CI [-0.0121, 0.0101], p = .8582	**b = 0.0042, 95% CI [0.0006, 0.0078], p = .0226**	b = 0.0125, 95% CI [-0.0068, 0.0318], p = .2058	b = -0.0022, 95% CI [-0.0062, 0.0018], p = .2774	b = 0.0191, 95% CI [-0.0002, 0.0384] , p = .0526
CSF NfL	NA	NA	NA	NA	NA
YKL-40					
PET Aβ	NA	NA	NA	NA	NA
CSF Aβ42/40	NA	NA	NA	NA	NA
CSF Aβ42	b = -0.0117, 95% CI [-0.0246, 0.0012], p = .0755	b = 0.0028, 95% CI [-0.0037, 0.0094], p = .3948	b = -0.0268, 95% CI [-0.1072, 0.0536], p = .5138	b = 0.0035, 95% CI [-0.0014, 0.0084], p = .1656	b = 0.0022, 95% CI [-0.0242, 0.0286], p = .8707
CSF Aβ40	NA	NA	NA	NA	NA
CSF pTau181	**b = -0.0229, 95% CI [-0.0354, -0.0105], p = 0.0003,**	b = 0.0048, 95% CI [-0.0031, 0.0127], p = 0.2374	b = -0.0156, 95% CI [-0.0741, 0.0430], p = 0.6022	b = -0.0019, 95% CI [-0.0080, 0.0042], p = 0.5479	b = 0.0273, 95% CI [-0.0029, 0.0574], p = 0.0765

CSF tTau	b = -0.0131, 95% CI[-0.0265, 0.0002], p = 0.0532	b = 0.0058, 95% CI [-0.0011, 0.0126], p = 0.0991	b = -0.0085, 95% CI [-0.0753, 0.0584], p = 0.8039	b = 0.0012, 95% CI [-0.0049, 0.0073], p = 0.7047	b = 0.0251, 95% CI [-0.0033, 0.0536], p = 0.0833
CSF NfL	NA	NA	NA	NA	NA

Supplementary Table 5. Studies and diagnostic classifications used for sTREM2 and YKL-40 subgroup analyses

Author, date	Diagnostic classification	N	Criteria	sTREM2 (pg/mL) or YKL-40 (ng/mL) concentration	Outcomes analysed
sTREM2 studies					
Liu & Yu (2019)	Healthy control	224	NA	4206.102	Aβ42, T-tau, p-tau181
Heslegrave et al. (2016)	Healthy control	22	Patients seeking treatment for non-neurodegenerative disorders	195.6 (131.0-240.7)	Aβ42, T-tau, p-tau181
Henjum et al. (2016)	Healthy control	50	NIA-AA	4400 (3000-5700)	Aβ42, T-tau, p-tau181
Schmidt-Morgenroth et al. (2023)	Healthy control	45	MMSE ≥ 29, no neurodegenerative disorder (but with osteoarthritis), aged <55	1416 (5948)	Aβ42, T-tau, p-tau181
Van Hulle et al. (2021)	Healthy control	616	NA	8010 (2470)	Aβ42, T-tau, p-tau181
Liu & Yu (2019)	SCD	72	NA	3801.212	Aβ42, T-tau, p-tau181
Hok-A-Hin et al. (2023)	SCD	67	NIA-AA	NA	Aβ42, T-tau, p-tau181
Nordengen et al. (2019)	SCD	18	SCD-I framework, CSF Aβ-positive	4600	T-tau, p-tau181
Liu & Yu (2019)	MCI	511	NIA-AA	4045.94	Aβ42, T-tau, p-tau181
Hok-A-Hin et al. (2023)	MCI	92	NIA-AA	NA	Aβ42, T-tau, p-tau181
Pillai et al. (2021)	MCI	48	NIA-AA	1226.22 (637.46)	Aβ42, T-tau, p-tau181
Brosseron et al. (2018)	MCI	130	Clinical or neuropsychological evidence of cognitive decline below age-dependent norms but with preserved daily function	4071 (2544)	Aβ42, T-tau, p-tau181
Doroszkiewicz et al. (2024)	MCI	18	NA	3376 (3081–4279)	Aβ42, T-tau, p-tau181
Henjum et al. (2016)	MCI	21	NIA-AA	4100 (2400-5900)	Aβ42, T-tau, p-tau181
Schmidt-Morgenroth (2023)	MCI	32	NIA-AA	1805 (1003)	Aβ42, T-tau, p-tau181
Van Hulle et al. (2021)	MCI	54	NIA-AA	9560 (3270)	Aβ42, T-tau, p-tau181
Nordengen et al. (2019)	MCI	40	NIA-AA, CSF Aβ-positive	4000	p-tau181
Johnson et al. (2023)	AD	164	NINCDS-ADRDA	8930 (IQR = 4150)	Aβ42, T-tau, p-tau181
Liu & Yu (2019)	AD	194	NIA-AA	4216.861	Aβ42, T-tau, p-tau181
Hok-A-Hin et al. (2023)	AD	38	NIA-AA	NA	Aβ42, T-tau, p-tau181
Heslegrave et al. (2016)	AD	37	IWG-2 criteria	231.2 (172.5-305.4)	Aβ42, T-tau, p-tau181
Brosseron et al. (2018)	AD	116	NIA-AA	4315 (2235)	Aβ42, T-tau, p-tau181
Doroszkiewicz et al. (2024)	AD	42	NIA-AA	3805 (2968–4732)	Aβ42, T-tau, p-tau181
Henjum et al. (2016)	AD	29	NIA-AA	4800 (3500-7100)	Aβ42, T-tau, p-tau181
Ferri et al. (2021)	AD	76	IWG-2 criteria	32600 (18100)	Aβ42, T-tau, p-tau181
Van Hulle et al. (2021)	AD	50	NIA-AA	9920 (3520)	Aβ42, T-tau, p-tau181
YKL-40 studies					
Wang et al. (2020)	Healthy control	35	MMSE ≥ 24 + CDR = 0	335	Aβ42, T-tau, p-tau181

Rosén et al. (2014)	Healthy control	25	Healthy elderly, no evidence of cognitive impairment	112.631 (83.709–138.258)	Aβ42, T-tau, p-tau181
Antonell et al. (2014)	Healthy control	43	Normal cognition or SCD, no AD pathology in CSF	260.5 (71.6)	Aβ42, T-tau, p-tau181
Olsson et al. (2013)	Healthy control	65	Healthy elderly volunteers	194.6 (76.3)	Aβ42, T-tau, p-tau181
Schmidt-Morgenroth (2023)	Healthy control	45	MMSE ≥ 29, no neurodegenerative disorder (but with osteoarthritis), aged <55	172.5 (75.31)	Aβ42, T-tau, p-tau181
Wennström et al. (2015)	Healthy control	44	Cognitively healthy after clinical evaluation	NA	T-tau, p-tau181
Alcolea et al. (2015)	Healthy control	80	No neuropsychological impairment	200.37 (47.34)	T-tau, p-tau181
Van Hulle et al. (2021)	Healthy control	616	NA	147.93 (55.89)	Aβ42, T-tau, p-tau181
Bos et al. (2019)	Healthy control	140	Normal cognition on neuropsychological assessment	142.46 (56.60)	T-tau, p-tau181
Nordengen et al. (2019)	SCD	18	SCD-I framework, CSF Aβ-positive	188	T-tau, p-tau181
Bos et al. (2019)	MCI	450	Below 1.5SD on at least one neuropsychological test	174.59 (63.36)	T-tau, p-tau181
Wang et al. (2020)	MCI	63	MMSE ≥ 24; loss of objective memory (1SD), CDR = 0.5; preserved ADL; no dementia	374.2	Aβ42, T-tau, p-tau181
Nordengen et al. (2019)	MCI	40	NIA-AA, CSF Aβ-positive	182	T-tau, p-tau181
Schmidt-Morgenroth (2023)	MCI	32	NIA-AA	233.6 (123.6)	Aβ42, T-tau, p-tau181
Van Hulle et al. (2021)	MCI	54	NIA-AA	212.31 (82.94)	Aβ42, T-tau, p-tau181
Alcolea et al. (2015)	MCI	27	Petersen criteria	240.07 (47.64)	T-tau, p-tau181
Rosén et al. (2014)	AD	25	DSM-IV criteria (probable AD) + NINCDS-ADRDA	199.211 (165.877–25.572)	Aβ42, T-tau, p-tau181
Olsson et al. (2013)a	AD	96	DSM-III-R criteria of dementia; NINCDS-ADRDA	241.6 (100.7)	Aβ42, T-tau, p-tau181
Johnson et al. (2023)	AD	164	NINCDS-ADRDA	191.6 (IQR=103.9)	Aβ42, T-tau, p-tau181
Wang et al. (2020)	AD	11	NINCDS-ADRDA probable AD	467.1	Aβ42, T-tau, p-tau181
Bos et al. (2019)	AD	180	NINCDS-ADRDA	192.40 (68.26)	T-tau, p-tau181
Lane et al. (2024)	AD	45	NIA-AA	NA	Aβ42, p-tau181
Abu-Rumeileh et al. (2019)	AD	40	IWG-2 criteria	240 (IQR = 176–293)	T-tau, p-tau181
Nordengen et al. (2019)	AD	29	NIA-AA	221	T-tau, p-tau181
Olsson et al. (2013)b	AD	52	DSM-IV and NINCDS-ADRDA criteria	NA	Aβ42, T-tau, p-tau181
Dage et al. (2023)	AD	96	NIA-AA for early-onset AD, no genetic mutations (e.g. APP/PSEN/MAPT)	263 (78)	T-tau, p-tau181
Van Hulle et al. (2021)	AD	50	NIA-AA	241.36 (99.08)	Aβ42, T-tau, p-tau181

Supplementary Table 6. Pairwise comparisons of correlation coefficients across CU, MCI and AD groups between sTREM2/YKL-40 and AD pathology

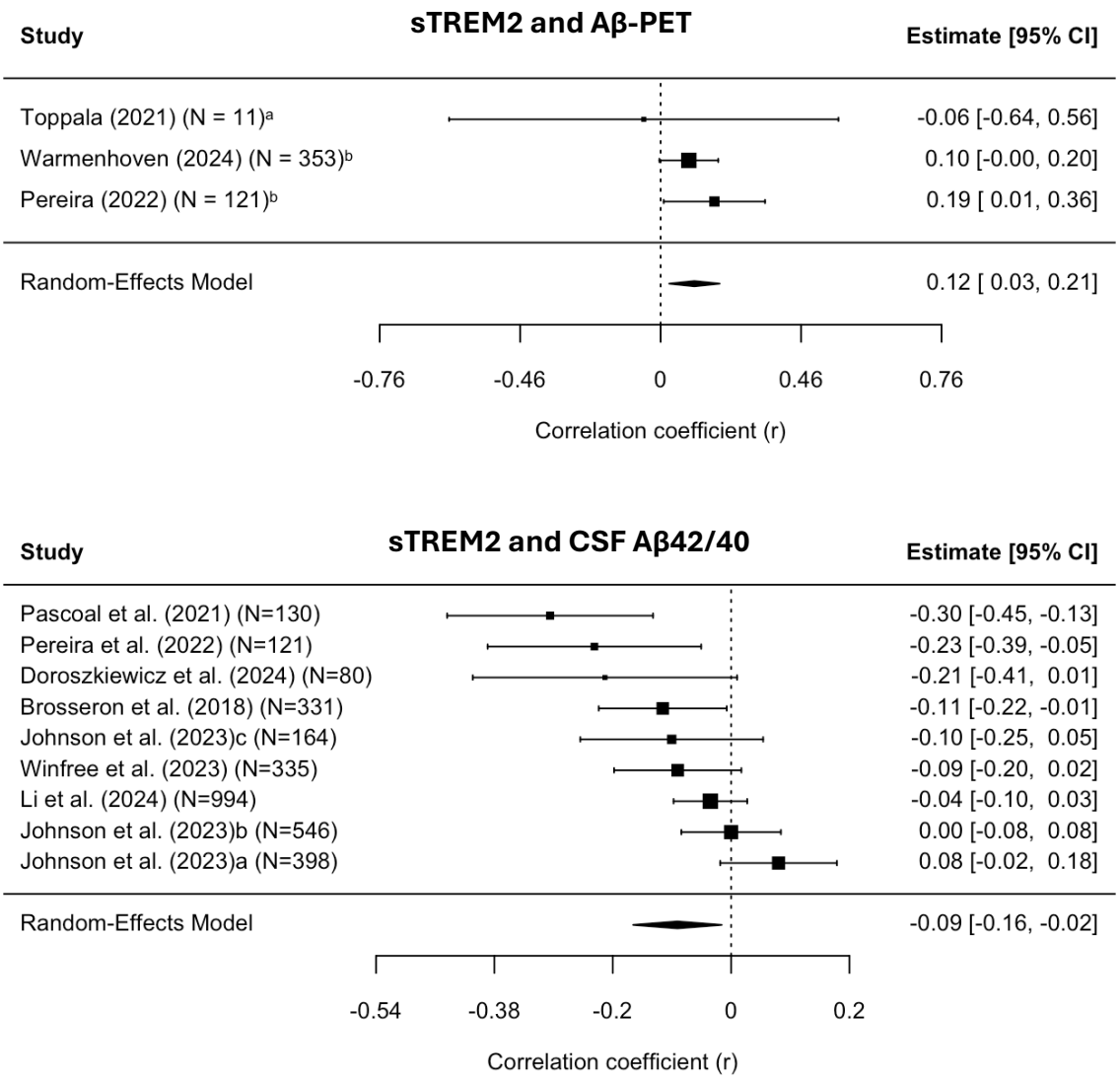
		sTREM2 (unadjusted)		**sTREM2 (adjusted for age)**		**YKL-40 (unadjusted)**		**YKL-40 (adjusted for age)**	
		b (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	b (95% CI)	*p*
Aβ42	CU vs MCI (MCI - CU)	**-0.12 (-0.22, -0.02)**	**.014**	**-0.13 (-0.24, -0.02)**	**.021**	-0.13 (-0.32, 0.07)	.203	0.05 (-0.16, 0.26)	.649
Aβ42	CU vs AD (AD - CU)	0.00 (-0.11, 0.11)	.973	-0.01 (-0.15, 0.13)	.895	0.09 (-0.07, 0.25)	.267	**0.19 (0.03, 0.35)**	**.020**
Aβ42	MCI vs AD (AD - MCI)	**0.13 (0.02, 0.23)**	**.018**	**0.12 (0.01, 0.23)**	**.040**	0.22 (-0.01, 0.45)	.061	0.14 (-0.05, 0.33)	.151
tTau	CU vs MCI (MCI - CU)	**-0.11 (-0.21, -0.01)**	**.032**	**-0.14 (-0.25, -0.03)**	**.010**	-0.09 (-0.21, 0.03)	.135	-0.12 (-0.27, 0.04)	.137
tTau	CU vs AD (AD - CU)	**-0.19 (-0.30, -0.08)**	**< .001**	**-0.24 (-0.38, -0.11)**	**< .001**	**-0.14 (-0.25, -0.02)**	**.021**	**-0.17 (-0.32, -0.01)**	**.034**
tTau	MCI vs AD (AD - MCI)	-0.08 (-0.18, 0.03)	.149	-0.10 (-0.21, 0.01)	.065	-0.05 (-0.17, 0.08)	.444	-0.05 (-0.18, 0.07)	.424
pTau181	CU vs MCI (MCI - CU)	**-0.09 (-0.18, -0.00)**	**.039**	**-0.15 (-0.25, -0.04)**	**.005**	-0.05 (-0.17, 0.06)	.368	0.01 (-0.14, 0.16)	.861
pTau181	CU vs AD (AD - CU)	**-0.18 (-0.28, -0.09)**	**< .001**	**-0.26 (-0.38, -0.14)**	**< .001**	**-0.20 (-0.32, -0.08)**	**< .001**	-0.13 (-0.28, 0.01)	.069
pTau181	MCI vs AD (AD - MCI)	**-0.09 (-0.19, 0.01)**	**.071**	**-0.11 (-0.21, -0.01)**	**.029**	**-0.14 (-0.27, -0.02)**	**.023**	**-0.15 (-0.27, -0.03)**	**.018**

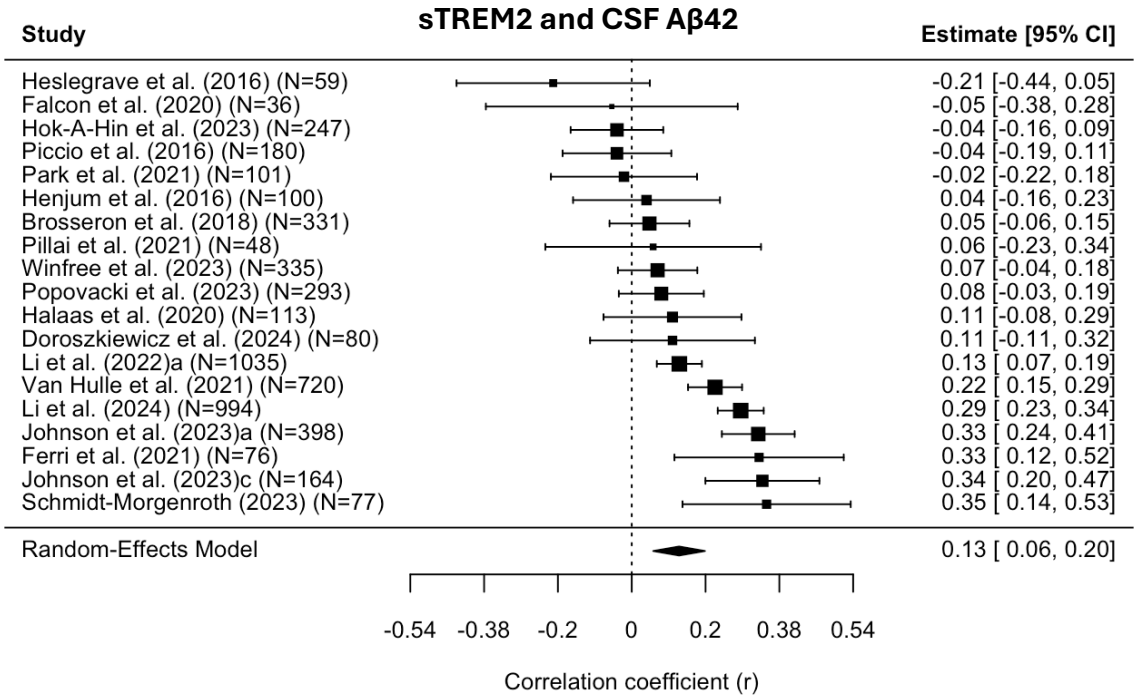
b = difference in correlation strength on Fisher's z scale.

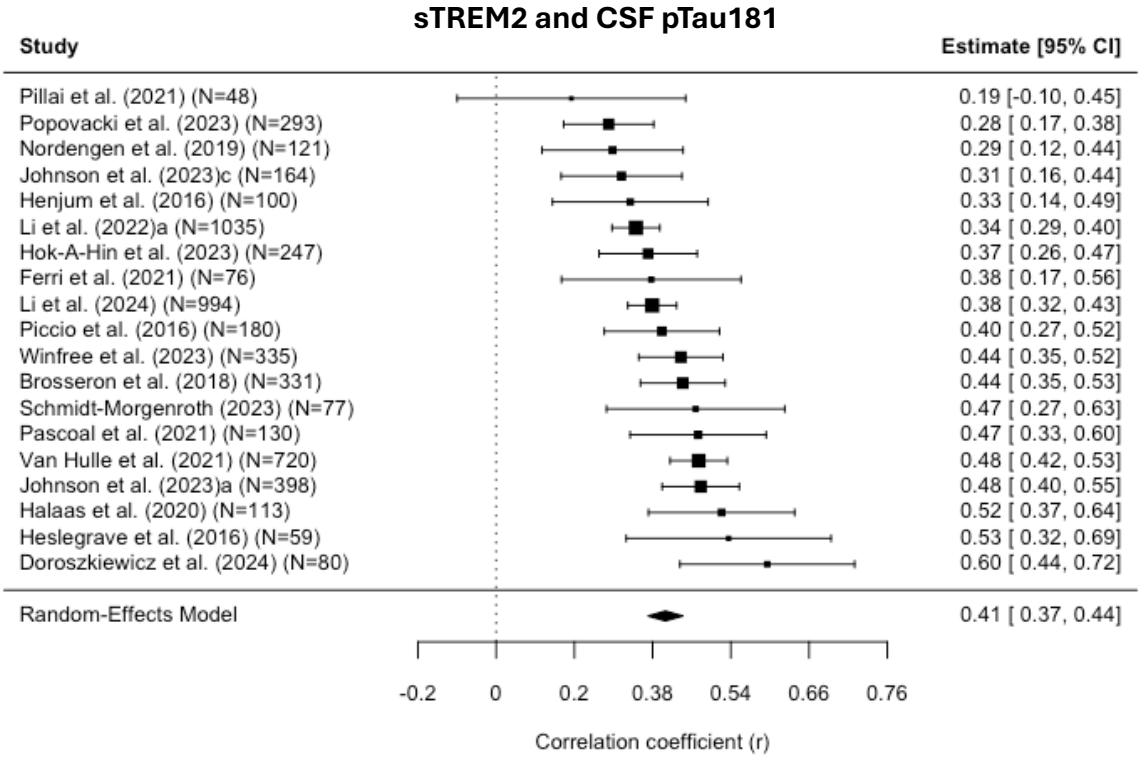
Supplementary Table 7. Cross-sectional associations between blood-derived sTREM2/YKL-40 with AD biomarkers

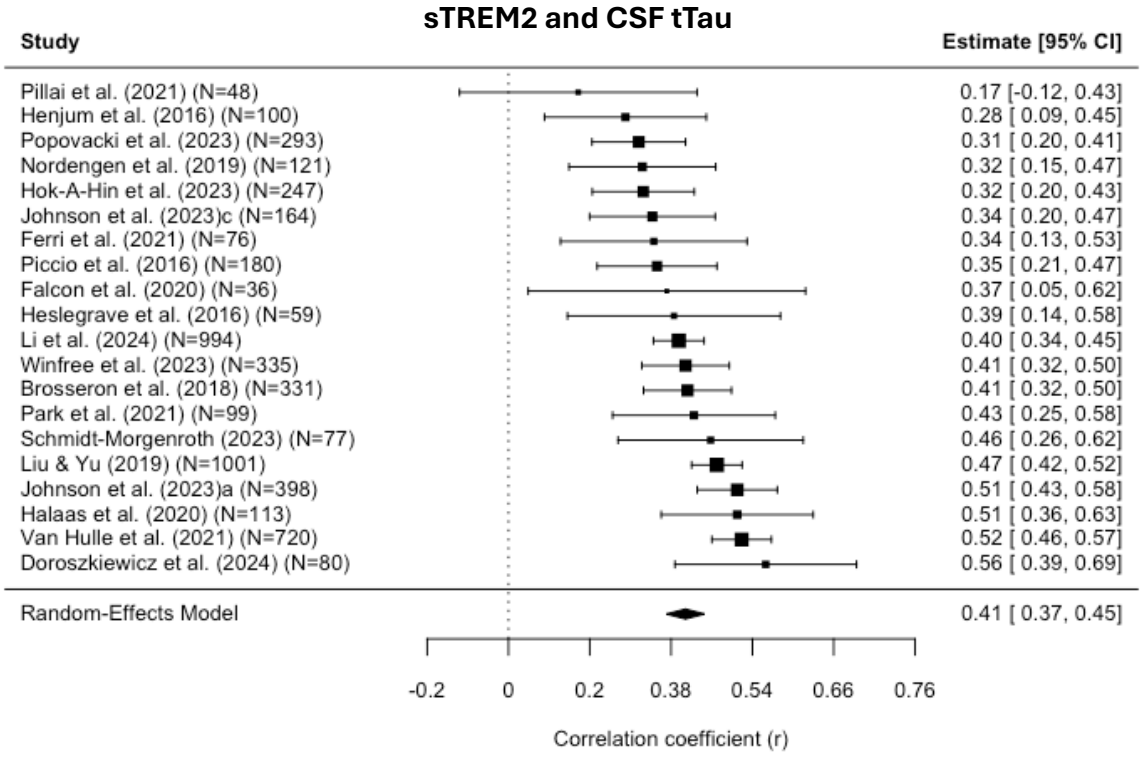
Study	*N*	Cohort	Plasma/ Serum	Assay method	Covariates	PET Aβ	CSF Aβ42/40	CSF Aβ42	CSF pTau181	CSF tTau	NfL
Blood sTREM2											
Ferri et al. (2021)	76	NA (AD-only)	Plasma	ELISA	0	/	/	**r = 0.332, p = .01**	r = 0.199, p = .14	r = 0.085, p = .53	/
Park et al. (2021)	101	Asan Medical Center	Plasma	Solid phase proximity ligation assay	0	/	/	r = 0.104, p = .303	/	**r = -0.248, p = .013 (n = 99)**	**0.359, p < .001**
Zhao et al. (2022)	150	CABLE	Plasma	ELISA	0	/	/	**r = -0.388, p = .013**	/	/	/
Brosseron et al. (2023)	309	DELCODE	Serum	ELISA	Age, sex, BMI, APOE status	/	r = -0.08, p = .21	/	r = 0.01, p = .84	r = 0.1, p = .10	/
Blood YKL-40											
Brosseron et al. (2023)	309	DELCODE	Serum	ELISA	Age, sex, BMI, APOE status	/	r = -0.09, p = .16	/	**r = 0.15, p = .019**	**r = 0.17, p = .005**	/
Craig-Schapiro et al. (2010)	237	WU-ADRC	Plasma	ELISA	0	r = .018, p = .858 ([11C]-PIB)	/	r = -.079, p = .226	r = −.027, p = .675	r = .038, p = .564	/
Prins et al. (2022)	121	Centre for Human Drug Research	Plasma	ELISA	0	/	/	p = .877	/	/	/
Vergallo et al. (2020)	302	INSIGHT-preAD	Plasma	ELISA	Age, sex, APOE status	**b = −0.025, p = 0.036 (**[18F]Florbetapir)	/	/	/	/	/

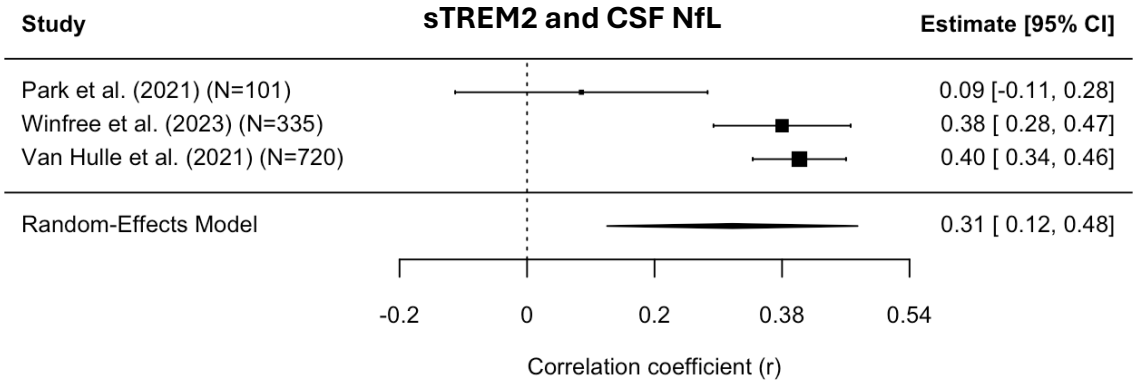
Supplementary Figure 1. Forest plots of cross-sectional correlations between sTREM2 and AD biomarkers



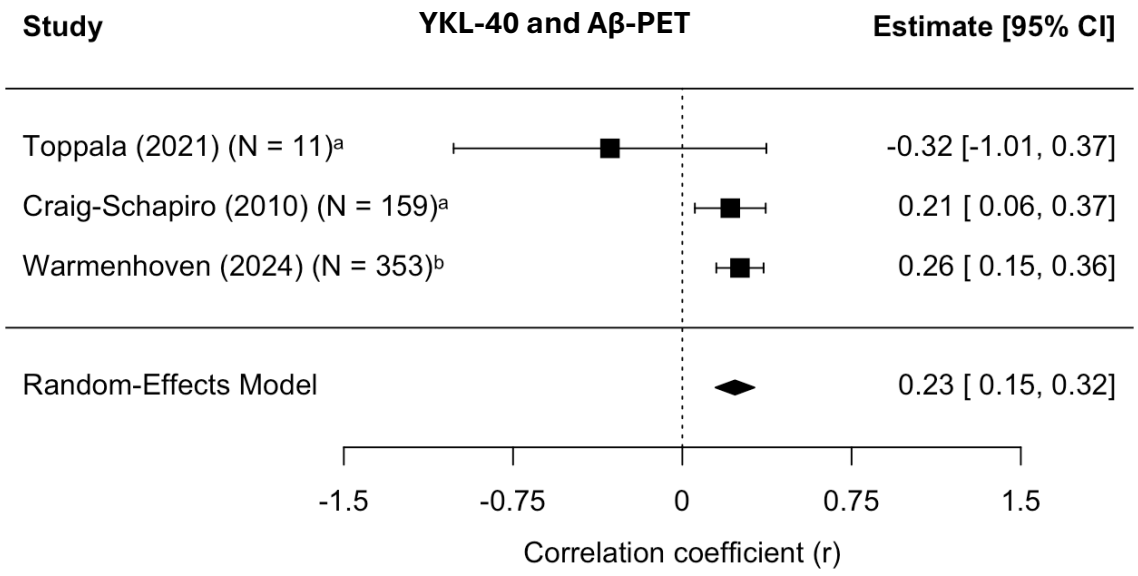

sTREM2 and CSF Aβ42
Study
Estimate [95% CI]
Heslegrave et al. (2016) (N=59) -0.21 [-0.44, 0.05]
Falcon et al. (2020) (N=36) -0.05 [-0.38, 0.28]
Hok-A-Hin et al. (2023) (N=247) -0.04 [-0.16, 0.09]
Piccio et al. (2016) (N=180) -0.04 [-0.19, 0.11]
Park et al. (2021) (N=101) -0.02 [-0.22, 0.18]
Henjum et al. (2016) (N=100) 0.04 [-0.16, 0.23]
Brosseron et al. (2018) (N=331) 0.05 [-0.06, 0.15]
Pillai et al. (2021) (N=48) 0.06 [-0.23, 0.34]
Winfree et al. (2023) (N=335) 0.07 [-0.04, 0.18]
Popovacki et al. (2023) (N=293) 0.08 [-0.03, 0.19]
Halaas et al. (2020) (N=113) 0.11 [-0.08, 0.29]
Doroszkiewicz et al. (2024) (N=80) 0.11 [-0.11, 0.32]
Li et al. (2022)a (N=1035) 0.13 [0.07, 0.19]
Van Hulle et al. (2021) (N=720) 0.22 [0.15, 0.29]
Li et al. (2024) (N=994) 0.29 [0.23, 0.34]
Johnson et al. (2023)a (N=398) 0.33 [0.24, 0.41]
Ferri et al. (2021) (N=76) 0.33 [0.12, 0.52]
Johnson et al. (2023)c (N=164) 0.34 [0.20, 0.47]
Schmidt-Morgenroth (2023) (N=77) 0.35 [0.14, 0.53]
Random-Effects Model 0.13 [0.06, 0.20]
-0.54 -0.38 -0.2 0 0.2 0.38 0.54
Correlation coefficient (r)

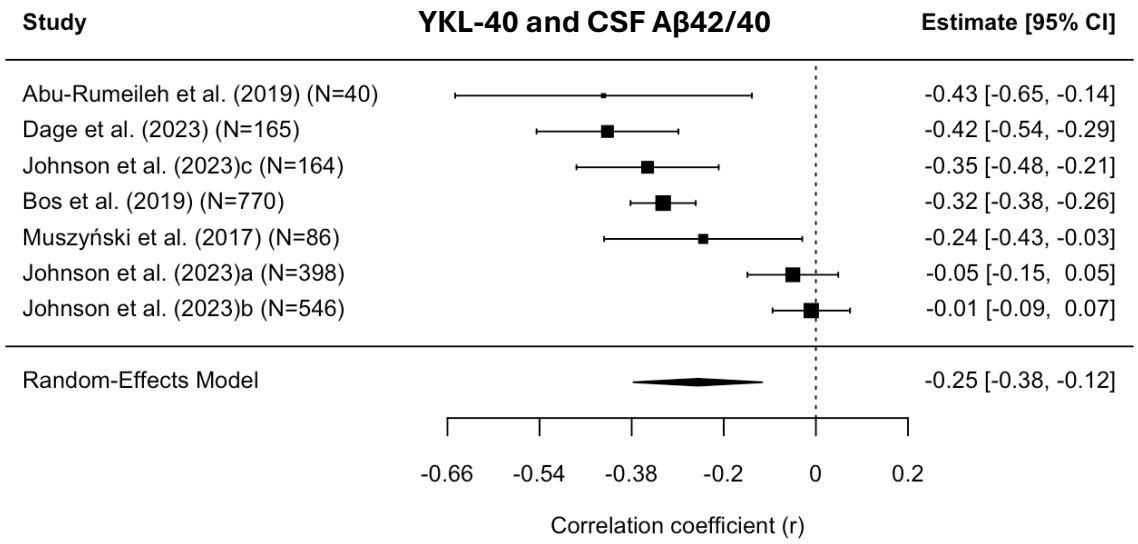

sTREM2 and CSF pTau181
Study
Estimate [95% CI]
Pillai et al. (2021) (N=48) 0.19 [-0.10, 0.45]
Popovacki et al. (2023) (N=293) 0.28 [0.17, 0.38]
Nordengen et al. (2019) (N=121) 0.29 [0.12, 0.44]
Johnson et al. (2023)c (N=164) 0.31 [0.16, 0.44]
Henjum et al. (2016) (N=100) 0.33 [0.14, 0.49]
Li et al. (2022)a (N=1035) 0.34 [0.29, 0.40]
Hok-A-Hin et al. (2023) (N=247) 0.37 [0.26, 0.47]
Ferri et al. (2021) (N=76) 0.38 [0.17, 0.56]
Li et al. (2024) (N=994) 0.38 [0.32, 0.43]
Piccio et al. (2016) (N=180) 0.40 [0.27, 0.52]
Winfree et al. (2023) (N=335) 0.44 [0.35, 0.52]
Brosseron et al. (2018) (N=331) 0.44 [0.35, 0.53]
Schmidt-Morgenroth (2023) (N=77) 0.47 [0.27, 0.63]
Pascoal et al. (2021) (N=130) 0.47 [0.33, 0.60]
Van Hulle et al. (2021) (N=720) 0.48 [0.42, 0.53]
Johnson et al. (2023)a (N=398) 0.48 [0.40, 0.55]
Halaas et al. (2020) (N=113) 0.52 [0.37, 0.64]
Heslegrave et al. (2016) (N=59) 0.53 [0.32, 0.69]
Doroszkiewicz et al. (2024) (N=80) 0.60 [0.44, 0.72]
Random-Effects Model 0.41 [0.37, 0.44]
-0.2 0 0.2 0.38 0.54 0.66 0.76
Correlation coefficient (r)

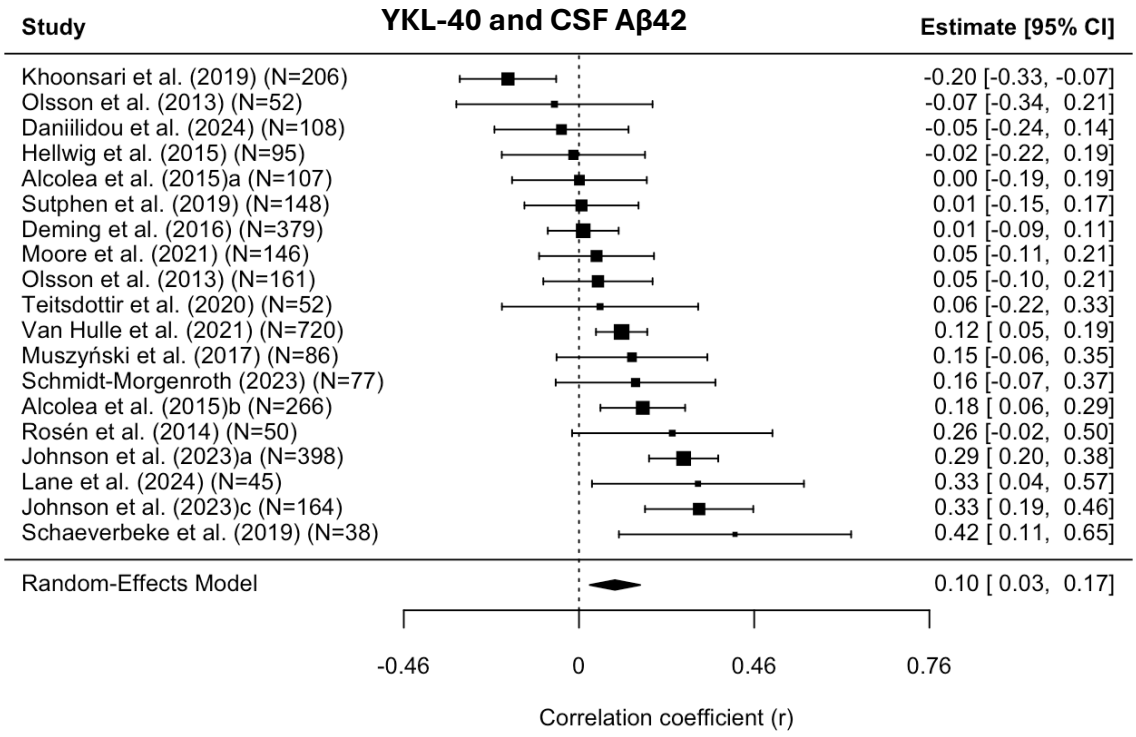

sTREM2 and CSF tTau
Study
Estimate [95% CI]
Pillai et al. (2021) (N=48) 0.17 [-0.12, 0.43]
Henjum et al. (2016) (N=100) 0.28 [0.09, 0.45]
Popovacki et al. (2023) (N=293) 0.31 [0.20, 0.41]
Nordengen et al. (2019) (N=121) 0.32 [0.15, 0.47]
Hok-A-Hin et al. (2023) (N=247) 0.32 [0.20, 0.43]
Johnson et al. (2023)c (N=164) 0.34 [0.20, 0.47]
Ferri et al. (2021) (N=76) 0.34 [0.13, 0.53]
Piccio et al. (2016) (N=180) 0.35 [0.21, 0.47]
Falcon et al. (2020) (N=36) 0.37 [0.05, 0.62]
Heslegrave et al. (2016) (N=59) 0.39 [0.14, 0.58]
Li et al. (2024) (N=994) 0.40 [0.34, 0.45]
Winfree et al. (2023) (N=335) 0.41 [0.32, 0.50]
Brosseron et al. (2018) (N=331) 0.41 [0.32, 0.50]
Park et al. (2021) (N=99) 0.43 [0.25, 0.58]
Schmidt-Morgenroth (2023) (N=77) 0.46 [0.26, 0.62]
Liu & Yu (2019) (N=1001) 0.47 [0.42, 0.52]
Johnson et al. (2023)a (N=398) 0.51 [0.43, 0.58]
Halaas et al. (2020) (N=113) 0.51 [0.36, 0.63]
Van Hulle et al. (2021) (N=720) 0.52 [0.46, 0.57]
Doroszkiewicz et al. (2024) (N=80) 0.56 [0.39, 0.69]
Random-Effects Model 0.41 [0.37, 0.45]
-0.2
0
0.2
0.38
0.54
0.66
0.76
Correlation coefficient (r)

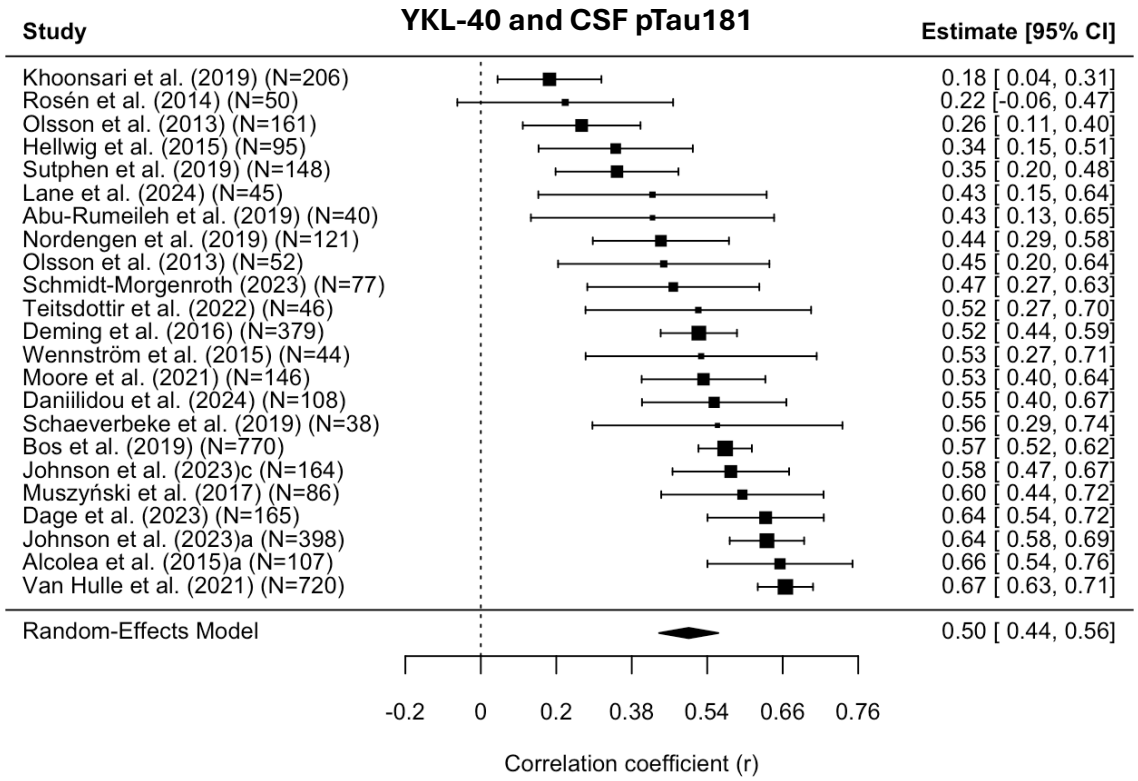

Study
sTREM2 and CSF NfL
Estimate [95% CI]
Park et al. (2021) (N=101) 0.09 [-0.11, 0.28]
Winfree et al. (2023) (N=335) 0.38 [0.28, 0.47]
Van Hulle et al. (2021) (N=720) 0.40 [0.34, 0.46]
Random-Effects Model 0.31 [0.12, 0.48]
-0.2
0
0.2
0.38
0.54
Correlation coefficient (r)

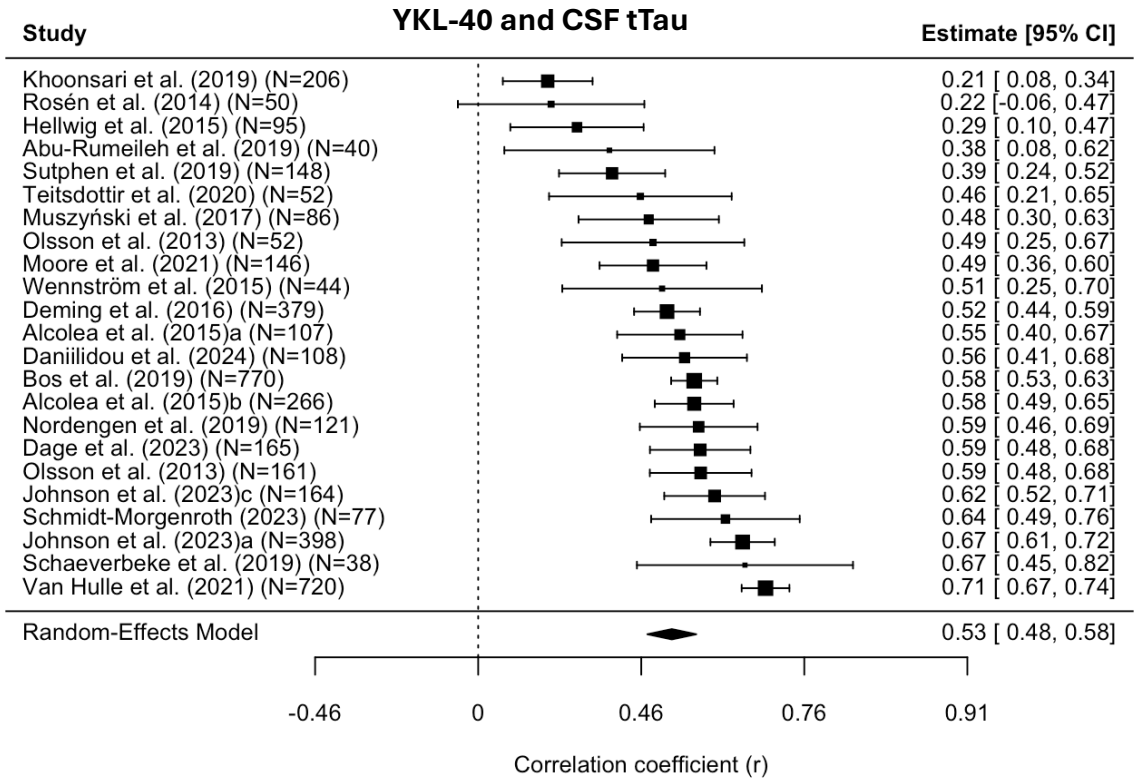
Supplementary Figure 2. Forest plots of cross-sectional correlations between YKL-40 and AD biomarkers

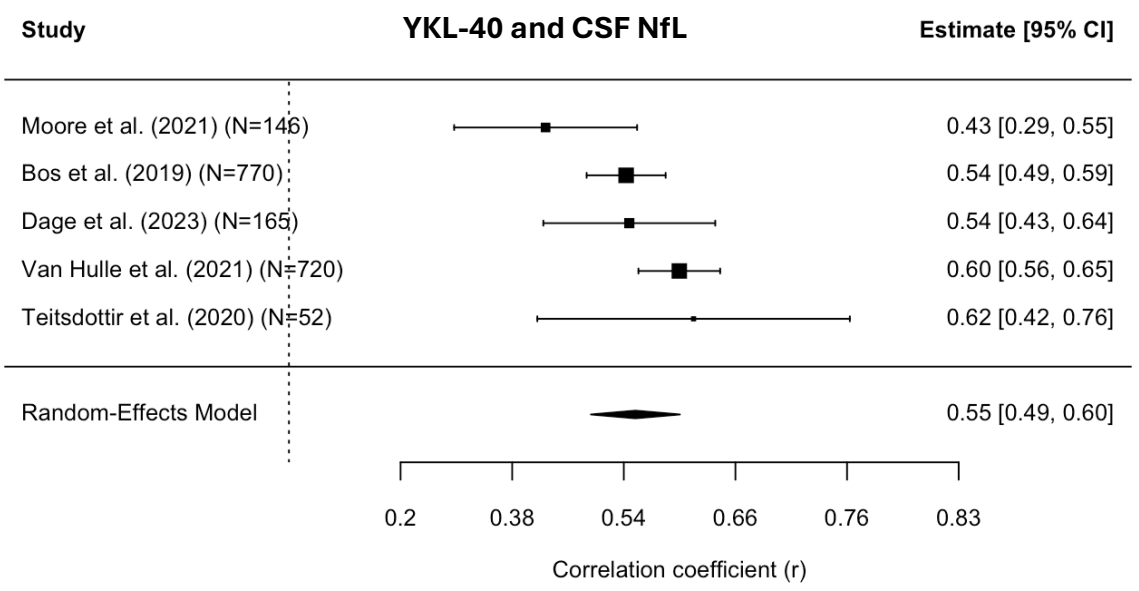




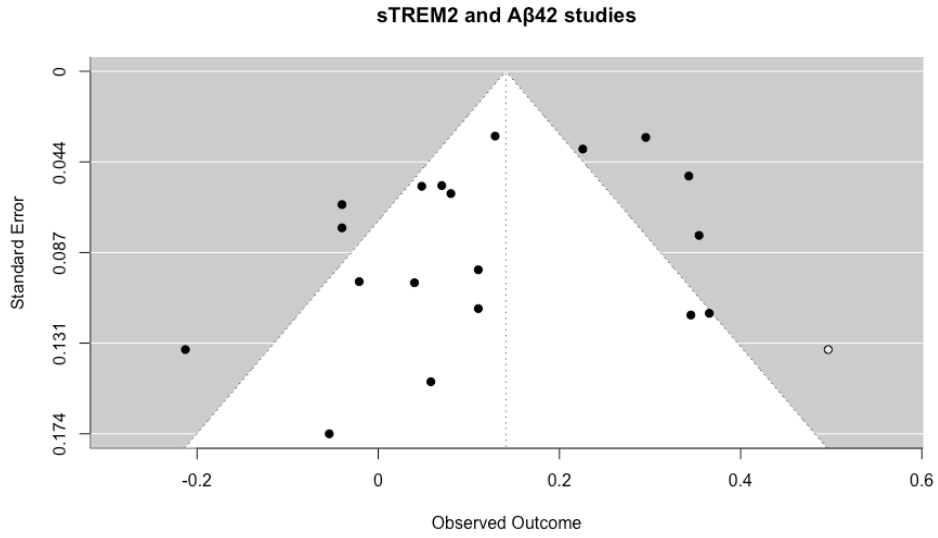

YKL-40 and CSF Aβ42
Study
Estimate [95% CI]
Khoonsari et al. (2019) (N=206) -0.20 [-0.33, -0.07]
Olsson et al. (2013) (N=52) -0.07 [-0.34, 0.21]
Daniilidou et al. (2024) (N=108) -0.05 [-0.24, 0.14]
Hellwig et al. (2015) (N=95) -0.02 [-0.22, 0.19]
Alcolea et al. (2015)a (N=107) 0.00 [-0.19, 0.19]
Sutphen et al. (2019) (N=148) 0.01 [-0.15, 0.17]
Deming et al. (2016) (N=379) 0.01 [-0.09, 0.11]
Moore et al. (2021) (N=146) 0.05 [-0.11, 0.21]
Olsson et al. (2013) (N=161) 0.05 [-0.10, 0.21]
Teitsdottir et al. (2020) (N=52) 0.06 [-0.22, 0.33]
Van Hulle et al. (2021) (N=720) 0.12 [0.05, 0.19]
Muszyński et al. (2017) (N=86) 0.15 [-0.06, 0.35]
Schmidt-Morgenroth (2023) (N=77) 0.16 [-0.07, 0.37]
Alcolea et al. (2015)b (N=266) 0.18 [0.06, 0.29]
Rosén et al. (2014) (N=50) 0.26 [-0.02, 0.50]
Johnson et al. (2023)a (N=398) 0.29 [0.20, 0.38]
Lane et al. (2024) (N=45) 0.33 [0.04, 0.57]
Johnson et al. (2023)c (N=164) 0.33 [0.19, 0.46]
Schaeverbeke et al. (2019) (N=38) 0.42 [0.11, 0.65]
Random-Effects Model 0.10 [0.03, 0.17]
-0.46
0
0.46
0.76
Correlation coefficient (r)

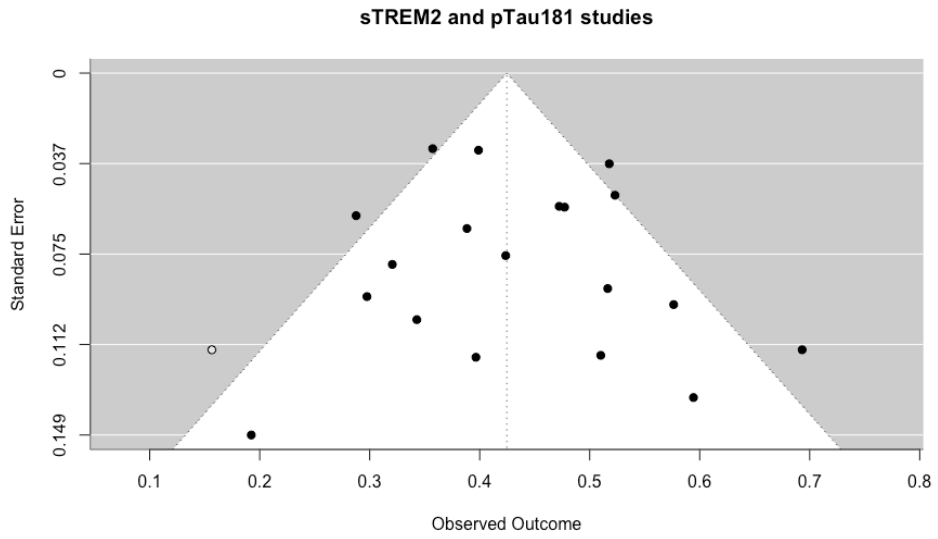

YKL-40 and CSF pTau181
Study
Estimate [95% CI]
Khoonsari et al. (2019) (N=206) 0.18 [0.04, 0.31]
Rosén et al. (2014) (N=50) 0.22 [-0.06, 0.47]
Olsson et al. (2013) (N=161) 0.26 [0.11, 0.40]
Hellwig et al. (2015) (N=95) 0.34 [0.15, 0.51]
Sutphen et al. (2019) (N=148) 0.35 [0.20, 0.48]
Lane et al. (2024) (N=45) 0.43 [0.15, 0.64]
Abu-Rumeileh et al. (2019) (N=40) 0.43 [0.13, 0.65]
Nordengen et al. (2019) (N=121) 0.44 [0.29, 0.58]
Olsson et al. (2013) (N=52) 0.45 [0.20, 0.64]
Schmidt-Morgenroth (2023) (N=77) 0.47 [0.27, 0.63]
Teitsdottir et al. (2022) (N=46) 0.52 [0.27, 0.70]
Deming et al. (2016) (N=379) 0.52 [0.44, 0.59]
Wennström et al. (2015) (N=44) 0.53 [0.27, 0.71]
Moore et al. (2021) (N=146) 0.53 [0.40, 0.64]
Daniilidou et al. (2024) (N=108) 0.55 [0.40, 0.67]
Schaeverbeke et al. (2019) (N=38) 0.56 [0.29, 0.74]
Bos et al. (2019) (N=770) 0.57 [0.52, 0.62]
Johnson et al. (2023)c (N=164) 0.58 [0.47, 0.67]
Muszyński et al. (2017) (N=86) 0.60 [0.44, 0.72]
Dage et al. (2023) (N=165) 0.64 [0.54, 0.72]
Johnson et al. (2023)a (N=398) 0.64 [0.58, 0.69]
Alcolea et al. (2015)a (N=107) 0.66 [0.54, 0.76]
Van Hulle et al. (2021) (N=720) 0.67 [0.63, 0.71]
Random-Effects Model 0.50 [0.44, 0.56]
-0.2
0
0.2
0.38
0.54
0.66
0.76
Correlation coefficient (r)

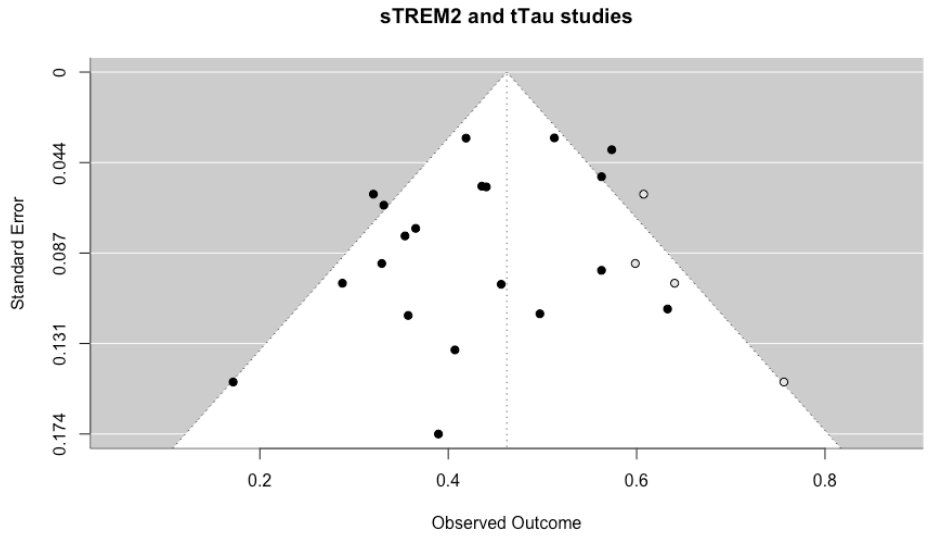

YKL-40 and CSF tTau
Study
Estimate [95% CI]
Khoonsari et al. (2019) (N=206) 0.21 [0.08, 0.34]
Rosén et al. (2014) (N=50) 0.22 [-0.06, 0.47]
Hellwig et al. (2015) (N=95) 0.29 [0.10, 0.47]
Abu-Rumeileh et al. (2019) (N=40) 0.38 [0.08, 0.62]
Sutphen et al. (2019) (N=148) 0.39 [0.24, 0.52]
Teitsdottir et al. (2020) (N=52) 0.46 [0.21, 0.65]
Muszyński et al. (2017) (N=86) 0.48 [0.30, 0.63]
Olsson et al. (2013) (N=52) 0.49 [0.25, 0.67]
Moore et al. (2021) (N=146) 0.49 [0.36, 0.60]
Wennström et al. (2015) (N=44) 0.51 [0.25, 0.70]
Deming et al. (2016) (N=379) 0.52 [0.44, 0.59]
Alcolea et al. (2015)a (N=107) 0.55 [0.40, 0.67]
Daniilidou et al. (2024) (N=108) 0.56 [0.41, 0.68]
Bos et al. (2019) (N=770) 0.58 [0.53, 0.63]
Alcolea et al. (2015)b (N=266) 0.58 [0.49, 0.65]
Nordengen et al. (2019) (N=121) 0.59 [0.46, 0.69]
Dage et al. (2023) (N=165) 0.59 [0.48, 0.68]
Olsson et al. (2013) (N=161) 0.59 [0.48, 0.68]
Johnson et al. (2023)c (N=164) 0.62 [0.52, 0.71]
Schmidt-Morgenroth (2023) (N=77) 0.64 [0.49, 0.76]
Johnson et al. (2023)a (N=398) 0.67 [0.61, 0.72]
Schaeverbeke et al. (2019) (N=38) 0.67 [0.45, 0.82]
Van Hulle et al. (2021) (N=720) 0.71 [0.67, 0.74]
Random-Effects Model 0.53 [0.48, 0.58]
-0.46
0
0.46
0.76
0.91
Correlation coefficient (r)


YKL-40 and CSF NfL
Study
Estimate [95% CI]
Moore et al. (2021) (N=146) 0.43 [0.29, 0.55]
Bos et al. (2019) (N=770) 0.54 [0.49, 0.59]
Dage et al. (2023) (N=165) 0.54 [0.43, 0.64]
Van Hulle et al. (2021) (N=720) 0.60 [0.56, 0.65]
Teitsdottir et al. (2020) (N=52) 0.62 [0.42, 0.76]
Random-Effects Model 0.55 [0.49, 0.60]
0.2
0.38
0.54
0.66
0.76
0.83
Correlation coefficient (r)

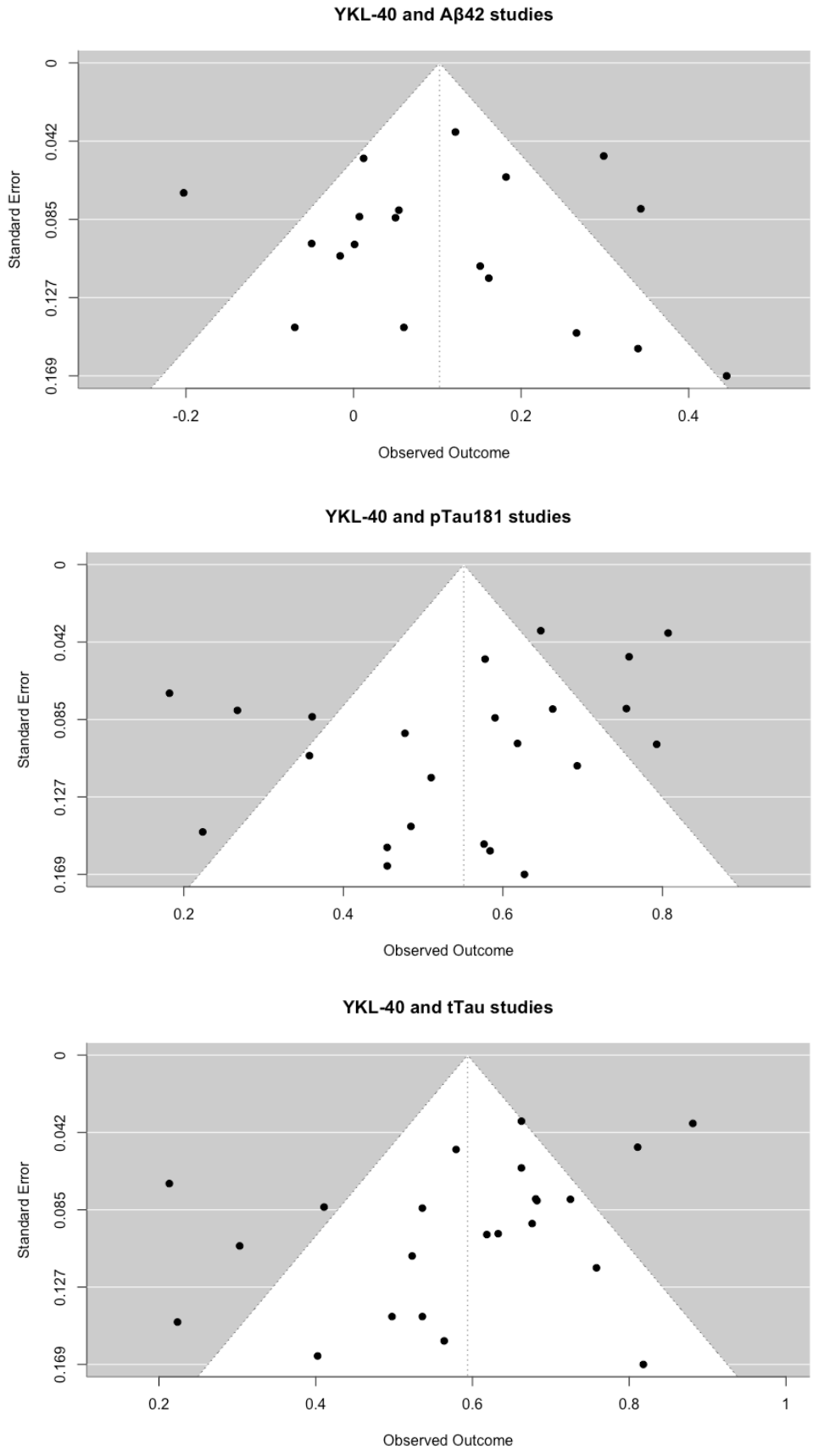
Supplementary Figure 3a. Funnel plots (with Trim-and-Fill, where applicable) for publication bias of sTREM2 studies





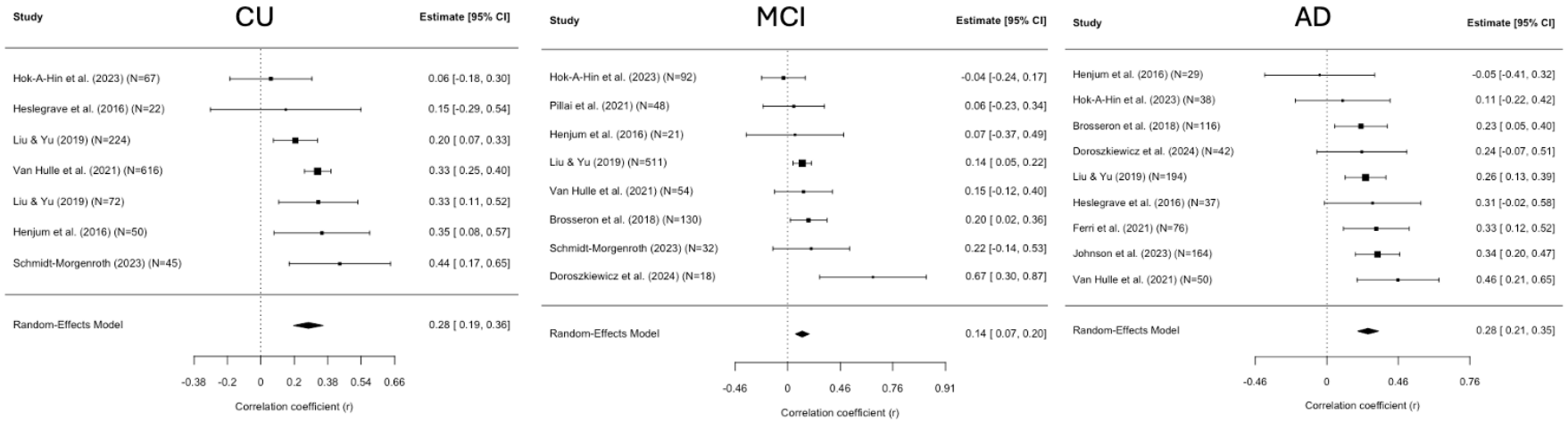


Supplementary Figure 3b. Funnel plots (with Trim-and-Fill, where applicable) for publication bias of YKL-40 studies

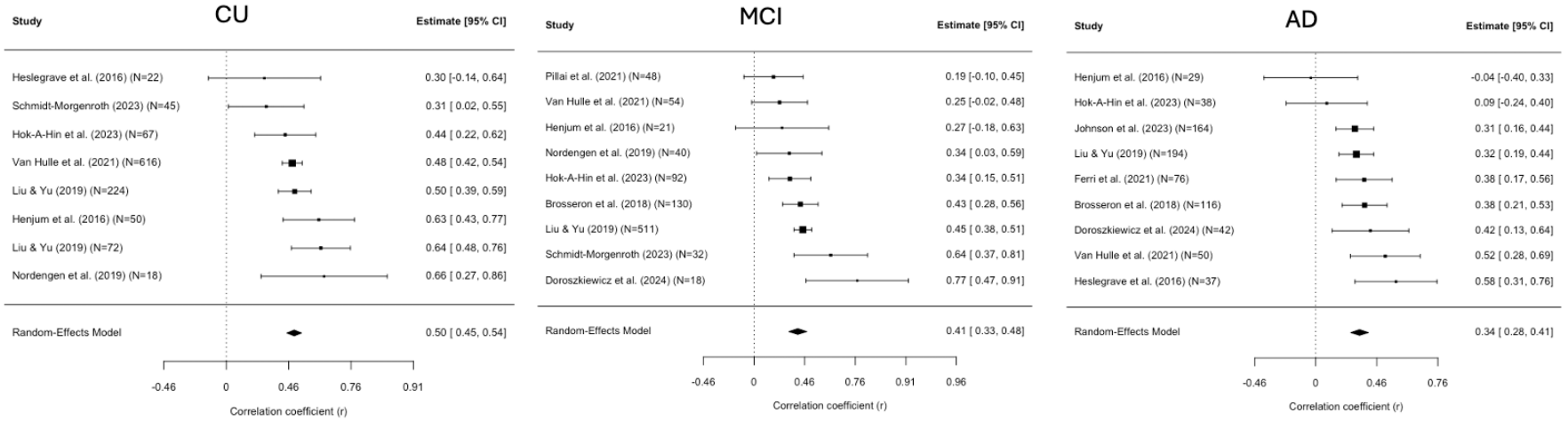


Supplementary Figure 4. Forest plots of associations between sTREM2 and AD biomarkers across diagnostic groups (CU, MCI, AD)

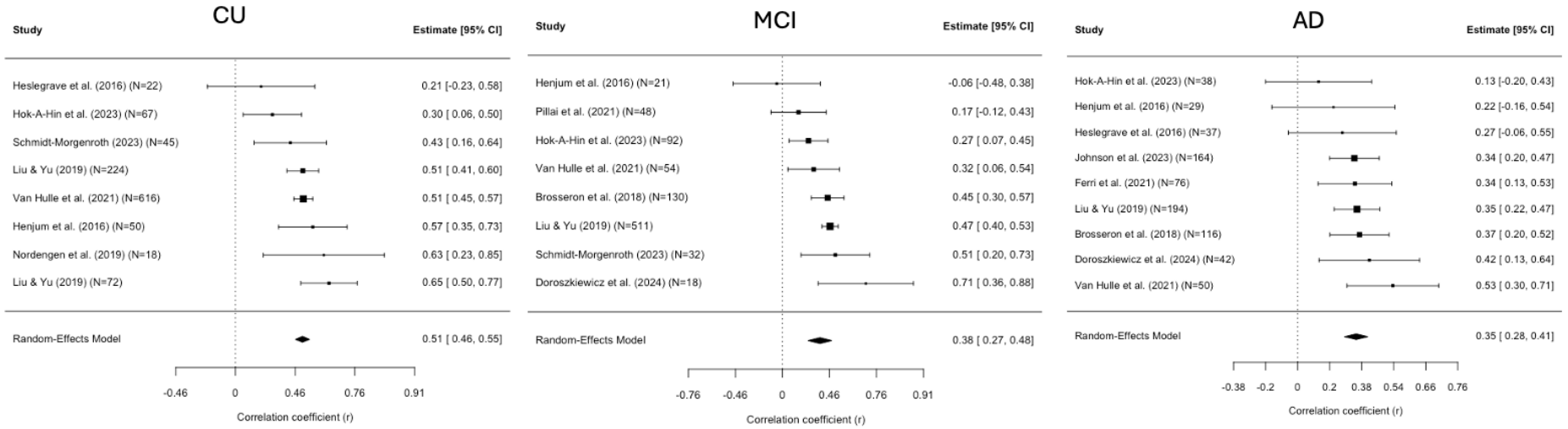
A) sTREM2 and Aβ42 across CU, MCI and AD groups



B) sTREM2 and pTau181 across CU, MCI and AD groups

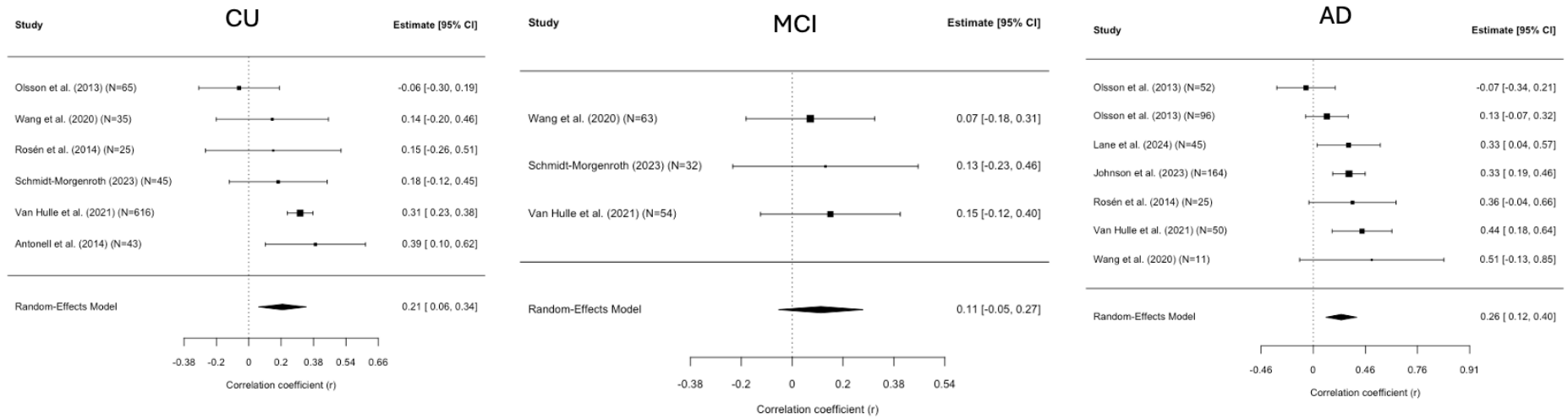


C) sTREM2 and tTau across CU, MCI and AD groups

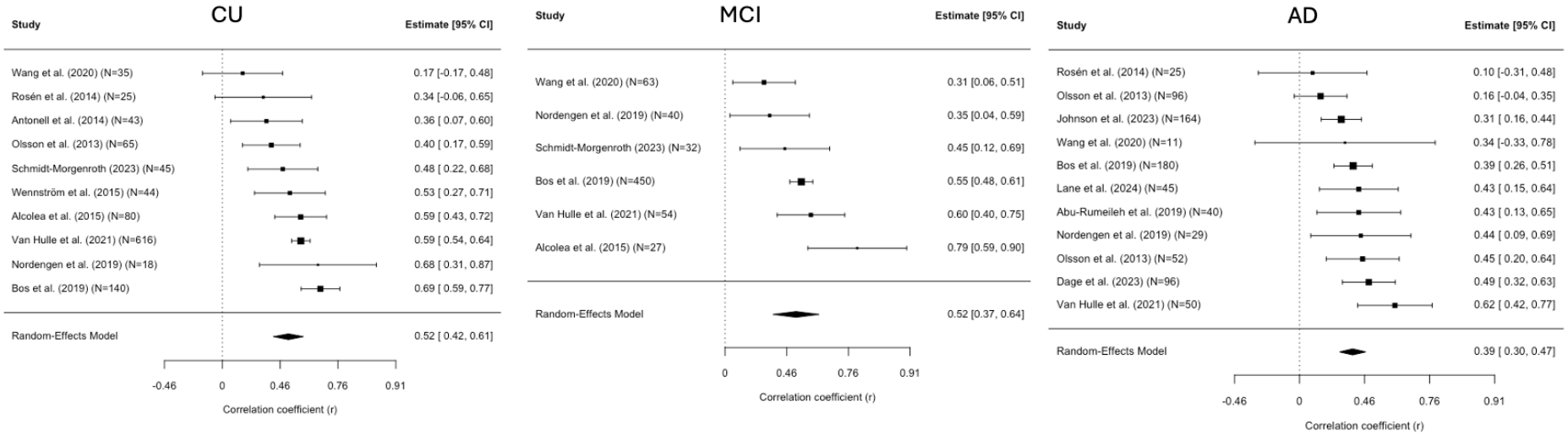


Supplementary Figure 5. Forest plots of associations between YKL-40 and AD biomarkers across diagnostic groups (CU, MCI, AD)

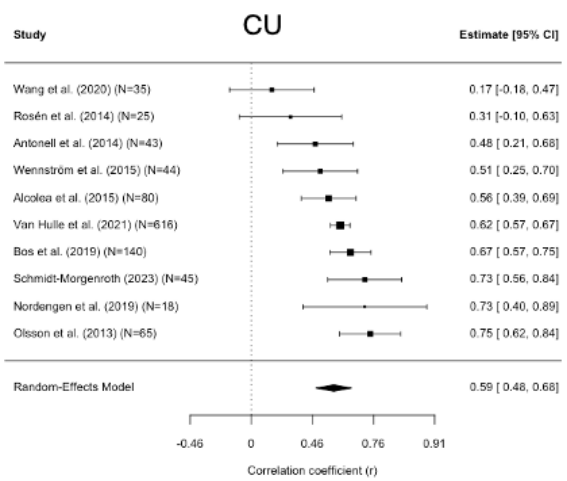
A) YKL-40 and Aβ42 across CU, MCI and AD groups

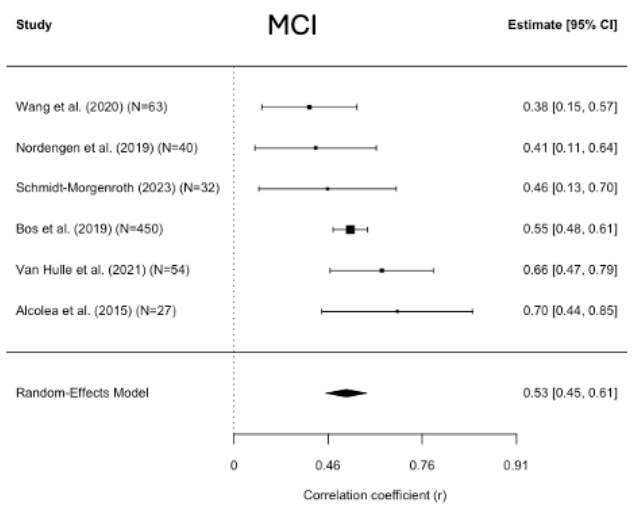


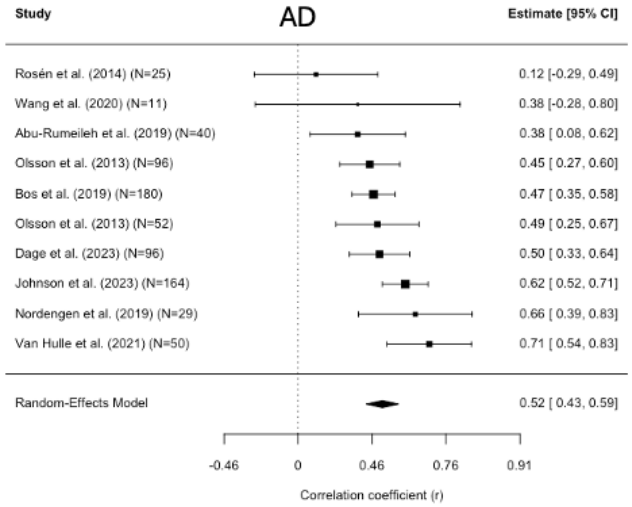
B) YKL-40 and pTau181 across CU, MCI and AD groups



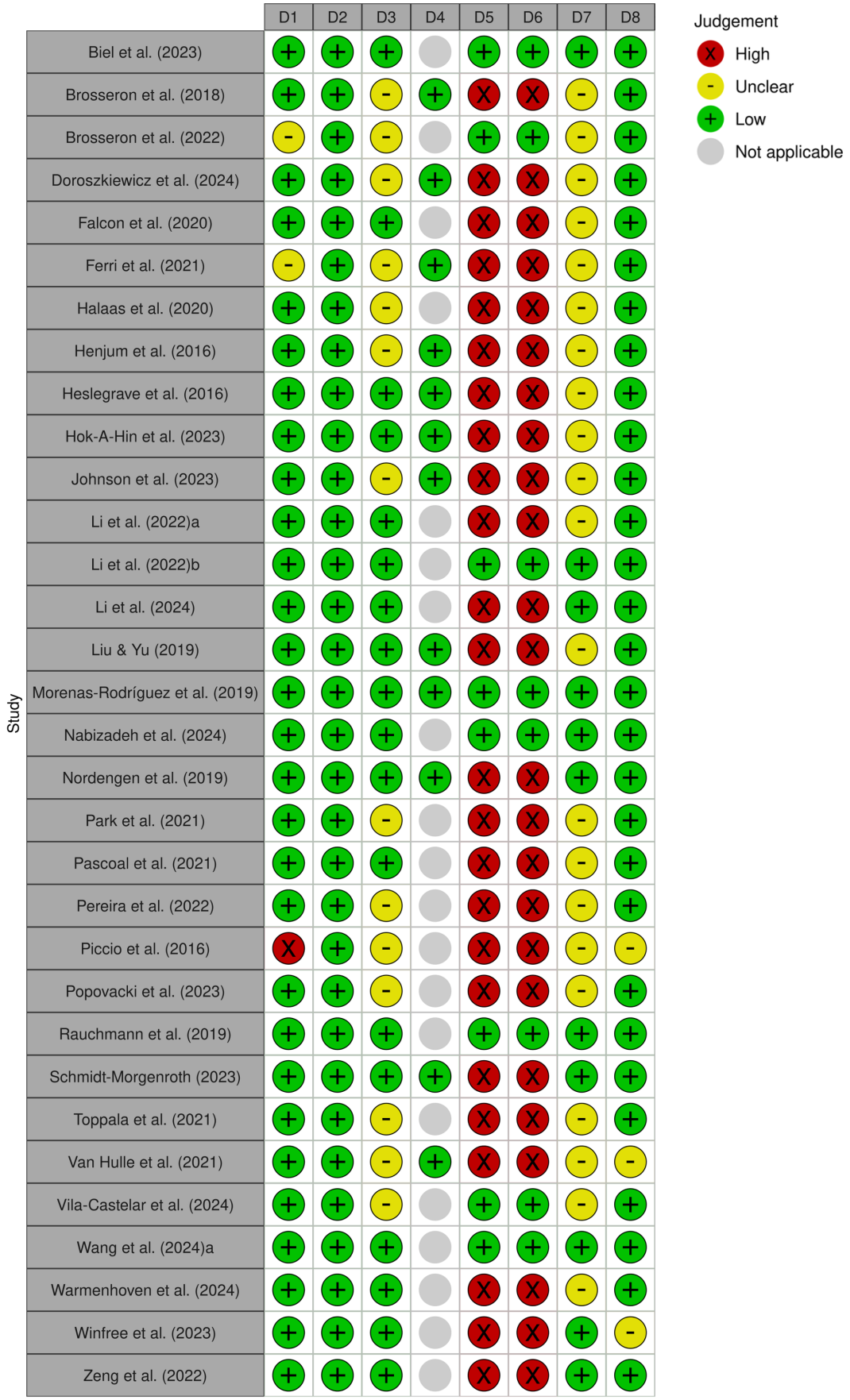
C) YKL-40 and tTau across CU, MCI and AD groups

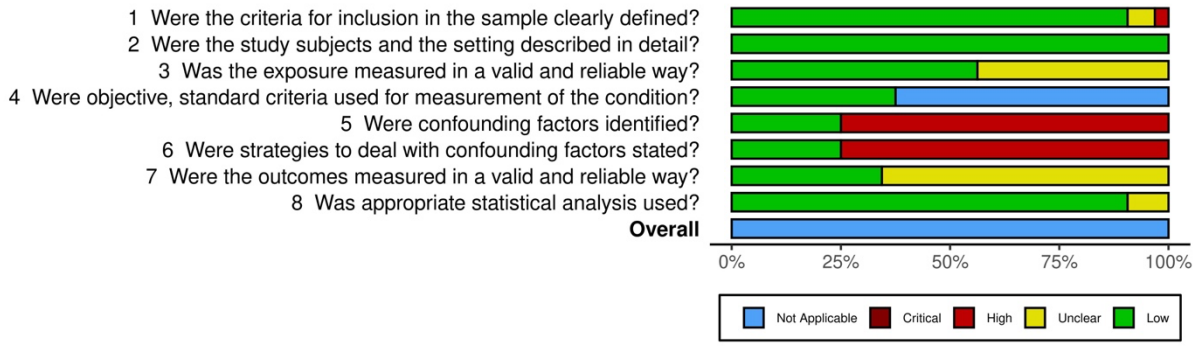




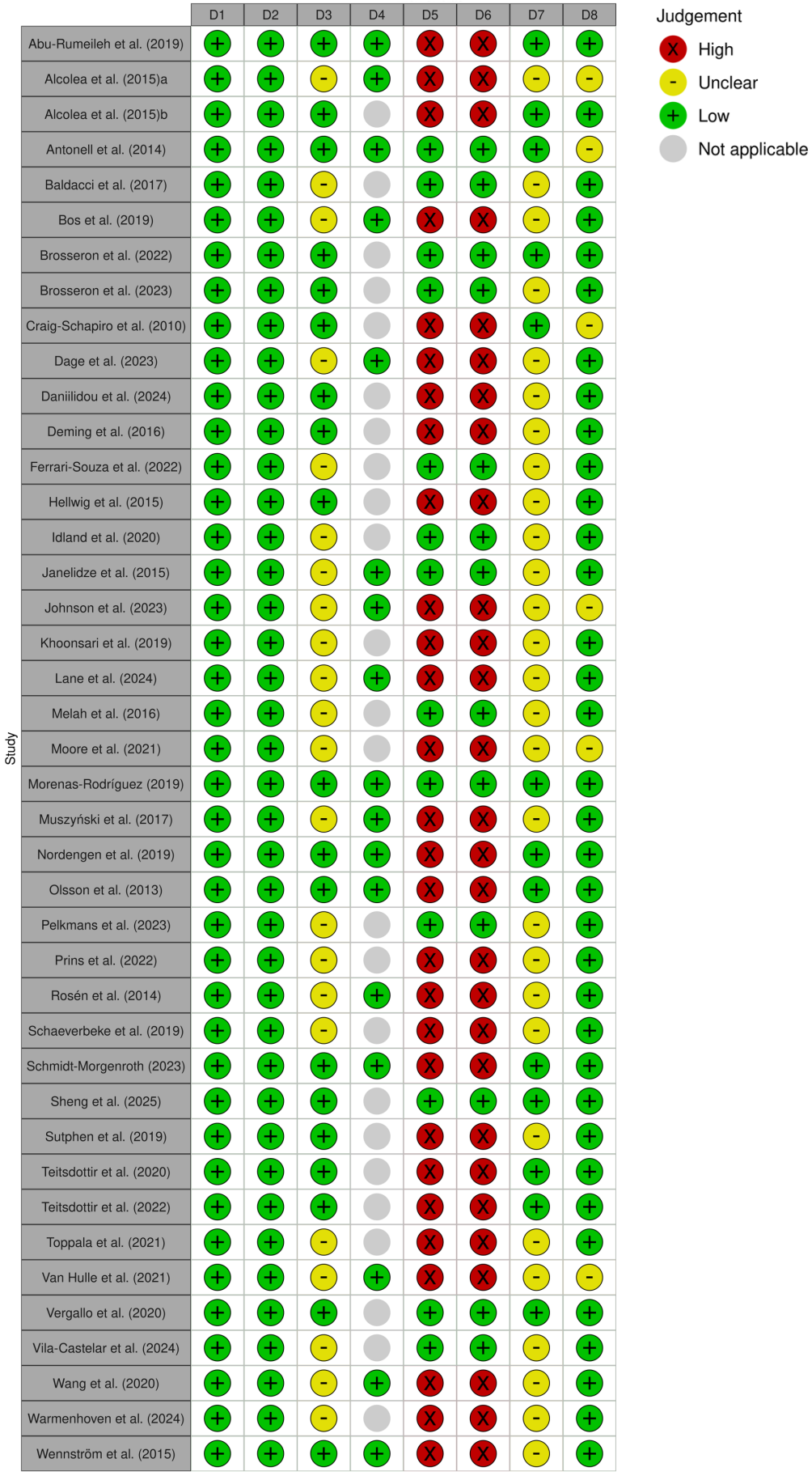


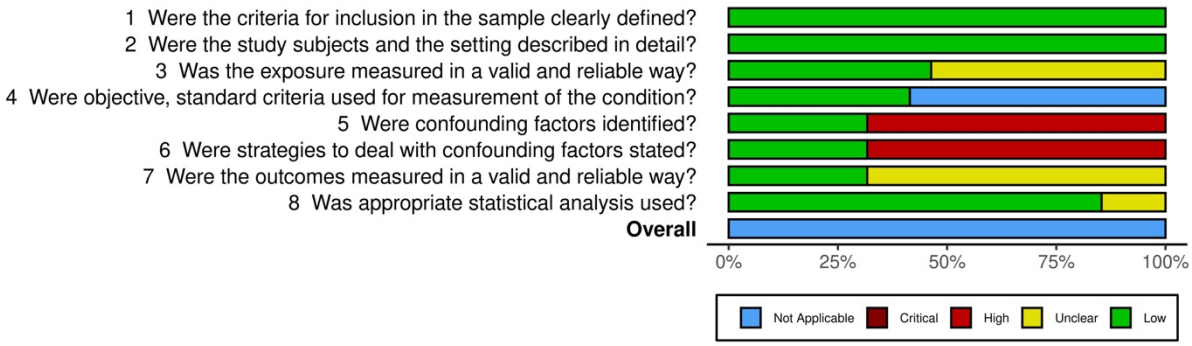
Supplementary Figure 6a. Risk of Bias plots for cross-sectional sTREM2 studies



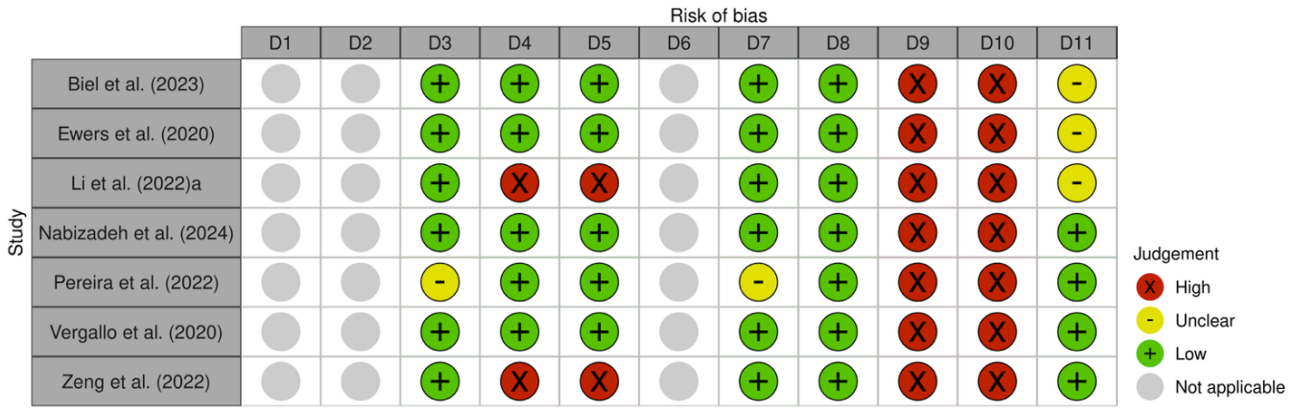

1 Were the criteria for inclusion in the sample clearly defined?
2 Were the study subjects and the setting described in detail?
3 Was the exposure measured in a valid and reliable way?
4 Were objective, standard criteria used for measurement of the condition?
5 Were confounding factors identified?
6 Were strategies to deal with confounding factors stated?
7 Were the outcomes measured in a valid and reliable way?
8 Was appropriate statistical analysis used?
Overall
0%
25%
50%
75%
100%
Not Applicable
Critical
High
Unclear
Low

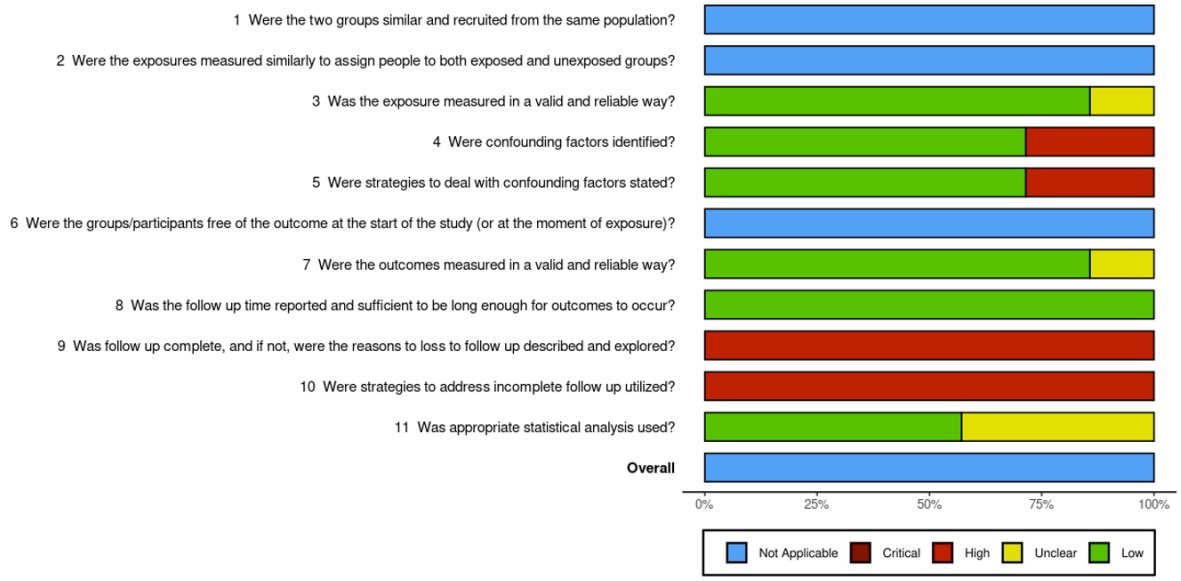
Supplementary Figure 6b. Risk of Bias for cross-sectional YKL-40 studies




1 Were the criteria for inclusion in the sample clearly defined?
2 Were the study subjects and the setting described in detail?
3 Was the exposure measured in a valid and reliable way?
4 Were objective, standard criteria used for measurement of the condition?
5 Were confounding factors identified?
6 Were strategies to deal with confounding factors stated?
7 Were the outcomes measured in a valid and reliable way?
8 Was appropriate statistical analysis used?
Overall
0%
25%
50%
75%
100%
Not Applicable
Critical
High
Unclear
Low

Supplementary Figure 7. Risk of Bias for longitudinal studies





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