

Cerebrospinal Fluid Biomarker Ratio Concordance with Amyloid Positron-Emission Tomography: A Diagnostic Test Accuracy Meta-Analysis

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SUPPLEMENTARY DATA

Supplementary Table S1: Analysis dataset (n=35 studies)

The shaded rows correspond to reports that may potentially contain duplicated data. The specific color (green or blue) corresponds to the matched rows, 2 rows per color. For the sensitivity analysis, the darker (green or blue) shaded rows were retained (highest number of participants), and the lighter shaded rows were excluded.

Study	CSF Biomarker ratio	Assay	PET+ method	ROC cutoff method	TP	FN	FP	TN	Calculation
Alcolea 2019	A β 42/A β 40	Lumipulse	Visual	Youden Index	52	7	8	27	Estimated
Alcolea 2019	A β 42/A β 40	Lumipulse	SUVR	Quadratic models	51	8	8	27	Estimated
Alcolea 2019	pTau/A β 42	Lumipulse	Visual	Youden Index	55	4	7	28	Estimated
Alcolea 2019	pTau/A β 42	Lumipulse	SUVR	Quadratic models	52	7	9	26	Estimated
Alcolea 2019	tTau/A β 42	Lumipulse	Visual	Youden Index	48	11	6	29	Estimated
Alcolea 2019	tTau/A β 42	Lumipulse	SUVR	Quadratic models	46	13	7	28	Estimated
Alvarez 2018	tTau/A β 42	Innotest	Visual	Clinical cutoff	22	2	4	21	Reported
Alvarez 2018	tTau/A β 42	Innotest	Visual	Youden Index	22	2	4	21	Estimated
Alvarez 2021	A β 42/A β 40	EUROIMMUN	Visual	Optimally balanced sens / spec	23	0	8	21	Estimated
Alvarez 2021	tTau/A β 42	EUROIMMUN	Visual	Optimally balanced sens / spec	22	1	5	24	Estimated
Amft 2022	A β 42/A β 40	Elecsys	Visual	Youden Index	51	3	9	40	Estimated
Amft 2022	pTau/A β 42	Elecsys	Visual	Youden Index	52	2	12	37	Estimated
Amft 2022	pTau/A β 42	Elecsys	Visual	Predefined	52	2	15	34	Estimated
Amft 2022	tTau/A β 42	Elecsys	Visual	Youden Index	49	5	11	38	Estimated
Amft 2022	tTau/A β 42	Elecsys	Visual	Predefined	50	4	15	34	Estimated
Brendel 2024	A β 42/A β 40	Innotest	Visual	ROC analysis	202	31	22	147	Reported

Campbell 2021	A β 42/A β 40	Lumipulse	SUVr	Youden Index	33	10	2	83	Reported
Campbell 2021	pTau/A β 42	Elecsys	SUVr	Youden Index	33	10	2	83	Reported
Campbell 2021	pTau/A β 42	Lumipulse	SUVr	Youden Index	34	9	1	84	Reported
Cerman 2025	pTau/A β 42	Innotest	Centiloid	Youden	44	9	5	35	Reported
Cerman 2025	tTau/A β 42	Innotest	Centiloid	Youden	40	13	4	36	Reported
Cerman 2025	A β 42/A β 40	EUROIMMUN	Centiloid	Youden	23	5	5	28	Reported
Cerman 2025	pTau/A β 42	EUROIMMUN	Centiloid	Youden	27	3	4	32	Reported
Cerman 2025	tTau/A β 42	EUROIMMUN	Centiloid	Youden	24	6	1	35	Reported
Cerman 2025	A β 42/A β 40	Lumipulse	Centiloid	Youden	56	1	7	34	Reported
Cerman 2025	pTau/A β 42	Lumipulse	Centiloid	Youden	54	3	5	36	Reported
Cerman 2025	tTau/A β 42	Lumipulse	Centiloid	Youden	52	5	5	36	Reported
Doecke 2018	A β 42/A β 40	EUROIMMUN	SUVr	ROC analysis	35	3	4	36	Estimated
Doecke 2018	pTau/A β 42	Innotest	SUVr	ROC analysis	35	3	2	37	Estimated
Doecke 2018	tTau/A β 42	EUROIMMUN	SUVr	ROC analysis	37	1	2	37	Estimated
Doecke 2020	A β 42/A β 40	Elecsys	SUVr	Gaussian mixture models	77	7	14	104	Estimated
Doecke 2020	A β 42/A β 40	Elecsys	SUVr	Youden Index	76	8	12	106	Estimated
Doecke 2020	pTau/A β 42	Elecsys	SUVr	Gaussian mixture models	76	8	20	98	Estimated
Doecke 2020	pTau/A β 42	Elecsys	SUVr	Youden Index	76	8	11	107	Estimated
Doecke 2020	tTau/A β 42	Elecsys	SUVr	Gaussian mixture models	77	7	24	94	Estimated
Doecke 2020	tTau/A β 42	Elecsys	SUVr	Youden Index	70	14	4	114	Estimated
Fagan 2011	pTau/A β 42	Innotest	MCBP	80% specificity	36	2	13	52	Estimated
Fagan 2011	pTau/A β 42	INNO-BIA AlzBio3	MCBP	80% specificity	37	1	13	52	Estimated
Fagan 2011	tTau/A β 42	INNO-BIA AlzBio3	MCBP	80% specificity	35	3	13	52	Estimated
Fagan 2011	tTau/A β 42	Innotest	MCBP	80% specificity	36	2	13	52	Estimated

Guillén 2023	A β 42/A β 40	Mixed (Innotest / Lumipulse)	Visual	Predefined	86	7	15	47	Estimated
Guillén 2023	pTau/A β 42	Mixed (Innotest / Lumipulse)	Visual	Predefined	53	4	7	30	Estimated
Guillén 2023	tTau/A β 42	Mixed (Innotest / Lumipulse)	Visual	Predefined	80	16	13	51	Estimated
Hansson ADNI 2018	pTau/A β 42	Elecsys	Visual	Optimized concordance	306	41	22	277	Estimated
Hansson ADNI 2018	pTau/A β 42	Elecsys	SUVR	Gaussian mixture models	294	53	19	280	Estimated
Hansson ADNI 2018	tTau/A β 42	Elecsys	Visual	Optimized concordance	295	52	18	281	Estimated
Hansson ADNI 2018	tTau/A β 42	Elecsys	SUVR	Gaussian mixture models	280	67	18	281	Estimated
Hansson BioFINDER 2018	pTau/A β 42	Elecsys	Visual	Optimized concordance	100	10	18	149	Estimated
Hansson BioFINDER 2018	pTau/A β 42	Elecsys	SUVR	Gaussian mixture models	94	16	4	163	Estimated
Hansson BioFINDER 2018	tTau/A β 42	Elecsys	Visual	Optimized concordance	100	10	18	149	Estimated
Hansson BioFINDER 2018	tTau/A β 42	Elecsys	SUVR	Gaussian mixture models	94	16	4	163	Estimated
Janelidze 2016	A β 42/A β 40	EUROIMMUN	SUVR	Youden Index	105	3	13	94	Estimated
Janelidze 2016	A β 42/A β 40	Meso Scale Discovery	SUVR	Youden Index	103	5	5	102	Estimated
Janelidze 2016	A β 42/A β 40	Quanterix	SUVR	Youden Index	36	4	3	27	Estimated
Kaplow 2018	tTau/A β 42	Lumipulse	Visual	Youden Index	81	4	5	48	Estimated
Leuzy 2016	A β 42/A β 40	Meso Scale Discovery	Visual	Gaussian mixture models	153	5	15	70	Reported
Leuzy 2016	A β 42/A β 40	Meso Scale Discovery	Centiloid	Gaussian mixture models	143	7	20	73	Reported
Lewczuk 2017	A β 42/A β 40	IBL International	MCBP	Youden Index	93	4	12	89	Estimated

Li 2015	pTau/A β 42	Innotest	SUVR	ROC analysis	48	1	13	95	Estimated
Li 2015	tTau/A β 42	Innotest	SUVR	ROC analysis	44	5	8	100	Estimated
Logan 2022	A β 42/A β 40	Elecsys	Visual	Youden Index	106	4	20	147	Estimated
Logan 2022	pTau/A β 42	Elecsys	Visual	Predefined	101	9	18	149	Estimated
Lombardi 2020	A β 42/A β 40	Lumipulse	Visual	Youden Index	26	2	6	5	Reported
Mao 2025	pTau/A β 42	Elecsys	Visual	ROC analysis	49	1	3	18	Estimated
Mao 2025	tTau/A β 42	Elecsys	Visual	ROC analysis	49	1	3	18	Estimated
Mao 2025	A β 42/A β 40	Innotest	Visual	ROC analysis	44	6	2	19	Estimated
Mao 2025	pTau/A β 42	Innotest	Visual	ROC analysis	47	3	2	19	Estimated
Mao 2025	tTau/A β 42	Innotest	Visual	ROC analysis	47	3	2	19	Estimated
Mao 2025	A β 42/A β 40	Lumipulse	Visual	ROC analysis	49	1	2	19	Estimated
Mao 2025	pTau/A β 42	Lumipulse	Visual	ROC analysis	48	2	2	19	Estimated
Mao 2025	tTau/A β 42	Lumipulse	Visual	ROC analysis	49	1	3	18	Estimated
Moon 2023	pTau/A β 42	INNO-BIA AlzBio3	SUVR	Youden	30	4	11	80	Estimated
Moon 2023	tTau/A β 42	INNO-BIA AlzBio3	SUVR	Youden	27	7	6	84	Estimated
Moon 2023	A β 42/A β 40	Innotest	SUVR	Youden	30	3	15	74	Estimated
Moon 2023	pTau/A β 42	Innotest	SUVR	Youden	24	6	10	70	Estimated
Moon 2023	tTau/A β 42	Innotest	SUVR	Youden	26	5	4	79	Estimated
Moon 2023	A β 42/A β 40	Lumipulse	SUVR	Youden	28	5	7	82	Estimated
Moon 2023	pTau/A β 42	Lumipulse	SUVR	Youden	28	5	6	83	Estimated
Moon 2023	tTau/A β 42	Lumipulse	SUVR	Youden	28	5	11	79	Estimated
Niemantsverdriet 2017	A β 42/A β 40	Innotest	Visual	ROC analysis	39	1	12	15	Reported
Niemantsverdriet 2017	A β 42/A β 40	Innotest	SUVRwm	ROC analysis	49	6	2	10	Reported
Niemantsverdriet 2017	A β 42/A β 40	Innotest	SUVRcb	ROC analysis	47	5	4	11	Reported
Nisenbaum 2023	A β 42/A β 40	Lumipulse	Visual	Youden Index	288	17	5	37	Estimated

Nisenbaum 2023	pTau/A β 42	Lumipulse	Visual	Youden Index	292	14	7	35	Estimated
Nisenbaum 2023	tTau/A β 42	Lumipulse	Visual	Youden Index	277	23	7	31	Estimated
Nojima 2022	A β 42/A β 40	Lumipulse	Visual	Youden Index	68	15	21	95	Estimated
Nojima 2022	pTau/A β 42	Lumipulse	Visual	Youden Index	66	17	16	100	Estimated
Nojima 2022	tTau/A β 42	Lumipulse	Visual	Youden Index	68	15	17	99	Estimated
Park 2025	pTau/A β 42	Elecsys	Visual	Youden	62	2	2	52	Reported
Park 2025	pTau/A β 42	Elecsys	Visual	Gaussian mixture models	64	0	10	44	Reported
Park 2025	pTau/A β 42	Innotest	Visual	Youden	62	2	6	48	Reported
Park 2025	pTau/A β 42	Innotest	Visual	Gaussian mixture models	62	2	6	48	Reported
Park 2025	pTau/A β 42	Elecsys	SUVR	Youden	58	3	5	50	Reported
Park 2025	pTau/A β 42	Elecsys	SUVR	Gaussian mixture models	61	0	12	43	Reported
Park 2025	pTau/A β 42	Innotest	SUVR	Youden	57	4	10	45	Reported
Park 2025	pTau/A β 42	Innotest	SUVR	Gaussian mixture models	57	4	10	45	Reported
Park 2025	tTau/A β 42	Elecsys	Visual	Youden	64	0	5	49	Reported
Park 2025	tTau/A β 42	Elecsys	Visual	Gaussian mixture models	64	0	13	41	Reported
Park 2025	tTau/A β 42	Innotest	Visual	Youden	60	4	8	46	Reported
Park 2025	tTau/A β 42	Innotest	Visual	Gaussian mixture models	62	2	9	45	Reported
Park 2025	tTau/A β 42	Elecsys	SUVR	Youden	59	2	9	46	Reported
Park 2025	tTau/A β 42	Elecsys	SUVR	Gaussian mixture models	60	1	15	40	Reported
Park 2025	tTau/A β 42	Innotest	SUVR	Youden	56	5	10	45	Reported
Park 2025	tTau/A β 42	Innotest	SUVR	Gaussian mixture models	58	3	11	45	Reported
Salvado 2019	pTau/A β 42	Elecsys	Centiloid	Youden Index	234	15	15	252	Estimated
Salvado 2019	pTau/A β 42	Elecsys	Centiloid	Maximize OPA	234	15	15	252	Estimated
Salvado 2019	tTau/A β 42	Elecsys	Centiloid	Youden Index	236	13	23	244	Estimated
Salvado 2019	tTau/A β 42	Elecsys	Centiloid	Maximize OPA	236	13	23	244	Estimated

Sanchez-Soblechero 2024	A β 42/A β 40	Lumipulse	Visual	Predefined	66	0	4	40	Estimated
Sanchez-Soblechero 2024	A β 42/A β 40	Lumipulse	Visual	Youden	66	0	4	40	Estimated
Sanchez-Soblechero 2024	A β 42/A β 40	Lumipulse	Visual	Gaussian mixture models	66	0	6	38	Estimated
Schindler 2018	A β 42/A β 40	Elecsys	SUVR	ROC analysis	48	2	26	122	Reported
Schindler 2018	pTau/A β 42	Elecsys	SUVR	ROC analysis	46	4	15	133	Reported
Schindler 2018	tTau/A β 42	Elecsys	SUVR	ROC analysis	46	4	22	126	Reported
Therriault 2021	A β 42/A β 40	Lumipulse	Visual	Youden Index	65	8	9	94	Estimated
Troike 2024	pTau/AB42	Elecsys	Centiloid	Not reported	21	3	1	10	Estimated
Troike 2024	tTau/AB42	Elecsys	Centiloid	Not reported	20	4	1	10	Estimated
van Harten 2022	pTau/A β 42	Elecsys	SUVR	Gaussian mixture models	142	4	53	325	Estimated
van Harten 2022	pTau/A β 42	Elecsys	SUVR	Cut point resulting in 90% PPA	131	15	26	352	Estimated
van Harten 2022	pTau/A β 42	Elecsys	SUVR	Youden Index	134	12	30	348	Estimated
van Harten 2022	pTau/A β 42	Elecsys	SUVR	ADNI	130	16	23	355	Estimated
van Harten 2022	pTau/A β 42	Elecsys	SUVR	AIBL	142	4	64	314	Estimated
van Harten 2022	pTau/A β 42	Elecsys	SUVR	BioFINDER	136	10	38	340	Estimated
van Harten 2022	pTau/A β 42	Elecsys	SUVR	Knight ADRC	142	4	49	329	Estimated
van Harten 2022	tTau/A β 42	Elecsys	SUVR	Gaussian mixture models	142	4	53	325	Estimated
van Harten 2022	tTau/A β 42	Elecsys	SUVR	Cut point resulting in 90% PPA	133	13	26	352	Estimated
van Harten 2022	tTau/A β 42	Elecsys	SUVR	Youden Index	137	9	34	344	Estimated
van Harten 2022	tTau/A β 42	Elecsys	SUVR	ADNI	137	9	30	348	Estimated
van Harten 2022	tTau/A β 42	Elecsys	SUVR	AIBL	137	9	34	344	Estimated
van Harten 2022	tTau/A β 42	Elecsys	SUVR	BioFINDER	137	9	34	344	Estimated
van Harten 2022	tTau/A β 42	Elecsys	SUVR	Knight ADRC	142	4	72	306	Estimated

Vandijck 2019	A β 42/A β 40	Lumipulse	SUVR	Youden Index	34	5	7	80	Estimated
Vandijck 2019	pTau/A β 42	Lumipulse	SUVR	Youden Index	34	5	6	81	Estimated
Vandijck 2019	tTau/A β 42	Lumipulse	SUVR	Youden Index	29	5	9	67	Estimated
Weston 2015	tTau/A β 42	Innotest	Visual	Not reported	17	0	0	6	Estimated
Weston 2015	tTau/A β 42	Innotest	SUVR	Not reported	11	3	0	9	Estimated
Willemse 2021	A β 42/A β 40	Lumipulse	Visual	Youden Index	177	2	19	90	Reported
Willemse 2021	pTau/A β 42	Elecsys	Visual	Youden Index	172	7	12	97	Reported
Willemse 2021	pTau/A β 42	Lumipulse	Visual	Youden Index	173	6	10	99	Reported
Willemse 2021	tTau/A β 42	Elecsys	Visual	Youden Index	162	17	11	98	Reported
Willemse 2021	tTau/A β 42	Lumipulse	Visual	Youden Index	162	17	11	98	Reported

A β , amyloid- β ; ADNI, Alzheimer's Disease Neuroimaging Initiative; BioFINDER, Biomarkers For Identifying NeuroDegenerative Disorders Early and Reliably ; cb, cerebellum; CSF, cerebrospinal fluid; FN, false negative; FP, false positive; MCBP, mean cortical binding potential; OPA, overall percent agreement; PET, positron-emission tomography; PPA, positive percent agreement; pTau, phosphorylated Tau 181P; ROC, receiver operating characteristic; sens, sensitivity; spec, specificity; SUVR, standardized uptake value ratio; TN, true negative; TP, true positive; tTau, total Tau; wm, white matter.

Supplementary Table S2: Bivariate meta-regression by assay type (n=35 studies)

Diagnostic measure	Covariate	Estimate (95% CI)	P-value
Sensitivity	Elecsys	0.9262 (0.9137, 0.9371)	<0.0001
	Lumipulse	0.8957 (0.8726, 0.9151)	<0.0001
	Innotest	0.9038 (0.8779, 0.9247)	<0.0001
	Other	0.9143 (0.8858, 0.9362)	<0.0001
Sensitivity difference	Lumipulse vs. Elecsys	−0.0305 (−0.0547, −0.0064)	0.0087
	Innotest vs. Elecsys	−0.0224 (−0.0485, 0.0036)	0.0732
	Other vs. Elecsys	−0.0119 (−0.0395, 0.0156)	0.3767
	Innotest vs. Lumipulse	0.0081 (−0.0234, 0.0395)	0.6170
	Other vs. Lumipulse	0.0186 (−0.0141, 0.0513)	0.2773
	Other vs. Innotest	0.0105 (−0.0236, 0.0446)	0.5490
FPR	Elecsys	0.1118 (0.0989, 0.1261)	<0.0001
	Lumipulse	0.1380 (0.1159, 0.1635)	<0.0001
	Innotest	0.1513 (0.1244, 0.1827)	<0.0001
	Other	0.1481 (0.1183, 0.1837)	<0.0001
FPR difference	Lumipulse vs. Elecsys	0.0262 (−0.0012, 0.0536)	0.0518
	Innotest vs. Elecsys	0.0395 (0.0074, 0.0716)	0.0100
	Other vs. Elecsys	0.0363 (0.0009, 0.0716)	0.0308
	Innotest vs. Lumipulse	0.0133 (−0.0243, 0.0508)	0.4861
	Other vs. Lumipulse	0.0101 (−0.0303, 0.0505)	0.6222
	Other vs. Innotest	−0.0032 (−0.0469, 0.0405)	0.8860

CI, confidence interval; FPR, false positive rate.

Significant values at $p < 0.05$ for **p-value differences** are shown in bold.

Supplementary Table S3: Bivariate meta-regression by study design (n=35 studies)

Diagnostic measure	Covariate	Estimate (95% CI)	P-value
Sensitivity	Observational - prospective	0.9155 (0.9044, 0.9255)	<0.0001
	Observational - retrospective	0.9166 (0.8951, 0.9340)	<0.0001
	Clinical trial	0.8984 (0.8500, 0.9325)	<0.0001
Sensitivity difference	Observational - retrospective vs. Observational - prospective	0.0011 (−0.0209, 0.0231)	0.9236
	Clinical trial vs. Observational - prospective	−0.0171 (−0.0591, 0.0249)	0.3919
	Clinical trial vs. Observational - retrospective	−0.0182 (−0.0632, 0.0268)	0.4052
FPR	Observational - prospective	0.1198 (0.1086, 0.1321)	<0.0001
	Observational - retrospective	0.1513 (0.1258, 0.1809)	<0.0001
	Clinical trial	0.1590 (0.1102, 0.2241)	<0.0001
FPR difference	Observational - retrospective vs. Observational - prospective	0.0314 (0.0015, 0.0614)	0.0287
	Clinical trial vs. Observational - prospective	0.0392 (−0.0186, 0.0971)	0.1411
	Clinical trial vs. Observational - retrospective	0.0078 (−0.0552, 0.0707)	0.8065

CI, confidence interval; FPR, false positive rate.

Significant values at $p < 0.05$ for **p-value differences** are shown in bold.

Supplementary Table S4: Bivariate meta-regression by region (n=35 studies)

Diagnostic measure	Covariate	Estimate (95% CI)	P-value
Sensitivity	Europe	0.9156 (0.9003, 0.9288)	<0.0001
	Multinational	0.8920 (0.8374, 0.9298)	<0.0001
	North America	0.9134 (0.8935, 0.9298)	<0.0001
	East Asia	0.9453 (0.9059, 0.9688)	<0.0001
	South-East Asia	0.9141 (0.8878, 0.9347)	<0.0001
	Western Pacific	0.9050 (0.8629, 0.9351)	<0.0001
	Unknown	0.9477 (0.8160, 0.9867)	<0.0001
Sensitivity difference	Multinational vs. Europe	-0.0236 (-0.0713, 0.0241)	<0.0001
	North America vs. Europe	-0.0023 (-0.0253, 0.0207)	<0.0001
	East Asia vs. Europe	0.0297 (-0.0038, 0.0632)	0.1371
	South-East Asia vs. Europe	-0.0015 (-0.0288, 0.0258)	0.9146
	Western Pacific vs. Europe	-0.0106 (-0.0490, 0.0277)	0.5727
	Unknown vs. Europe	0.0320 (-0.0392, 0.1032)	0.4794
	North America vs. Multinational	0.0214 (-0.0276, 0.0703)	0.3620
	East Asia vs. Multinational	0.0533 (-0.0013, 0.1080)	0.0543
	South-East Asia vs. Multinational	0.0221 (-0.0290, 0.0732)	0.3725
	Western Pacific vs. Multinational	0.0130 (-0.0448, 0.0708)	0.6569
	Unknown vs. Multinational	0.0557 (-0.0276, 0.1389)	0.2999
	East Asia vs. North America	0.0320 (-0.0033, 0.0672)	0.1230
	South-East Asia vs. North America	0.0008 (-0.0287, 0.0302)	0.9591
	Western Pacific vs. North America	-0.0084 (-0.0483, 0.0316)	0.6738
	Unknown vs. North America	0.0343 (-0.0378, 0.1064)	0.4569
	South-East Asia vs. East Asia	-0.0312 (-0.0694, 0.0070)	0.1478
	Western Pacific vs. East Asia	-0.0403 (-0.0871, 0.0064)	0.1033

	Unknown vs. East Asia	0.0023 (−0.0737, 0.0784)	0.9527
	Western Pacific vs. South-East Asia	−0.0092 (−0.0517, 0.0334)	0.6683
	Unknown vs. South-East Asia	0.0335 (−0.0400, 0.1071)	0.4690
	Unknown vs. Western Pacific	0.0427 (−0.0357, 0.1210)	0.3905
FPR	Europe	0.1442 (0.1261, 0.1645)	<0.0001
	Multinational	0.1673 (0.1139, 0.2389)	<0.0001
	North America	0.1015 (0.0861, 0.1194)	<0.0001
	East Asia	0.1305 (0.0805, 0.2047)	<0.0001
	South-East Asia	0.1367 (0.1128, 0.1647)	<0.0001
	Western Pacific	0.1091 (0.0799, 0.1471)	<0.0001
	Unknown	0.1019 (0.0316, 0.2827)	0.0006
FPR difference	Multinational vs. Europe	0.0231 (−0.0420, 0.0881)	0.4662
	North America vs. Europe	−0.0427 (−0.0681, −0.0173)	0.0011
	East Asia vs. Europe	−0.0137 (−0.0779, 0.0504)	0.6855
	South-East Asia vs. Europe	−0.0075 (−0.0398, 0.0247)	0.6497
	Western Pacific vs. Europe	−0.0351 (−0.0736, 0.0033)	0.0962
	Unknown vs. Europe	−0.0424 (−0.1579, 0.0732)	0.5362
	North America vs. Multinational	−0.0658 (−0.1301, −0.0015)	0.0192
	East Asia vs. Multinational	−0.0368 (−0.1240, 0.0504)	0.4141
	South-East Asia vs. Multinational	−0.0306 (−0.0979, 0.0367)	0.3482
	Western Pacific vs. Multinational	−0.0582 (−0.1287, 0.0123)	0.0845
	Unknown vs. Multinational	−0.0654 (−0.1952, 0.0643)	0.3969
	East Asia vs. North America	0.0290 (−0.0344, 0.0924)	0.3281
	South-East Asia vs. North America	0.0352 (0.0044, 0.0660)	0.0204
	Western Pacific vs. North America	0.0076 (−0.0297, 0.0448)	0.6847
	Unknown vs. North America	0.0004 (−0.1148, 0.1155)	0.9952
	South-East Asia vs. East Asia	0.0062 (−0.0602, 0.0727)	0.8567

Western Pacific vs. East Asia	−0.0214 (−0.0911, 0.0483)	0.5324
Unknown vs. East Asia	−0.0286 (−0.1580, 0.1007)	0.6857
Western Pacific vs. South-East Asia	−0.0276 (−0.0698, 0.0146)	0.2157
Unknown vs. South-East Asia	−0.0348 (−0.1517, 0.0820)	0.6049
Unknown vs. Western Pacific	−0.0072 (−0.1259, 0.1115)	0.9075

CI, confidence interval; FPR, false positive rate.

Significant values at $p < 0.05$ for **p-value differences** are shown in bold.

Supplementary Table S5: Bivariate meta-regression by percent PET positive, by percent cognitively impaired and by percent cognitively impaired controlling for percent PET positive

Diagnostic measure	Covariate	Estimate (95% CI)	P-value
By percent PET positive (n = 35 studies)			
Sensitivity	Percent PET positive < 50	0.9078 (0.8935, 0.9203)	<0.0001
	Percent PET positive ≥ 50	0.9198 (0.9068, 0.9311)	<0.0001
Sensitivity difference	Percent PET positive ≥ 50 vs. < 50	0.0120 (−0.0066, 0.0274)	0.1912
FPR	Percent PET positive < 50	0.1103 (0.0983, 0.1234)	<0.0001
	Percent PET positive ≥ 50	0.1510 (0.1342, 0.1696)	<0.0001
FPR difference	Percent PET positive ≥ 50 vs. < 50	0.0408 (0.0183, 0.0665)	0.0002
By percent cognitively impaired (n = 34 studies)			
Sensitivity	Percent cognitively impaired < 50	0.9197 (0.9038, 0.9332)	<0.0001
	Percent cognitively impaired ≥ 50	0.9118 (0.9001, 0.9223)	<0.0001
Sensitivity difference	Percent cognitively impaired ≥ 50 vs. < 50	−0.0079 (−0.0294, 0.0097)	0.4045
FPR	Percent cognitively impaired < 50	0.0961 (0.0833, 0.1107)	<0.0001
	Percent cognitively impaired ≥ 50	0.1476 (0.1340, 0.1624)	<0.0001
FPR difference	Percent cognitively impaired ≥ 50 vs. < 50	0.0515 (0.0288, 0.0775)	<0.0001
By percent cognitively impaired controlling for percent PET positive (n = 34 studies)			
Sensitivity	Percent cognitively impaired < 50	0.9321 (0.9164, 0.9449)	<0.0001
	Percent cognitively impaired ≥ 50	0.9046 (0.8916, 0.9161)	<0.0001
	Percent PET positive (per 1-unit increase)	0.0009 (0.0004, 0.0014)	0.0021
Sensitivity difference	Percent cognitively impaired ≥ 50 vs. < 50	−0.0275 (−0.0478, −0.0072)	0.0111
FPR	Percent cognitively impaired < 50	0.1031 (0.0865, 0.1224)	<0.0001
	Percent cognitively impaired ≥ 50	0.1444 (0.1305, 0.1595)	<0.0001
	Percent PET positive (per 1-unit increase)	0.0005 (−0.0003, 0.0013)	0.1672
FPR difference	Percent cognitively impaired ≥ 50 vs. < 50	0.0413 (0.0165, 0.0660)	0.0019

CI, confidence interval; FPR, false positive rate.

Significant values at $p < 0.05$ for **p-value differences** are shown in bold.

Supplementary Table S6: Bivariate meta-regression by biomarker controlling for percent cognitively impaired (n = 34 studies)

Diagnostic measure	Covariate	Estimate (95% CI)	P-value
Sensitivity	A β 42/A β 40	0.9188 (0.8996, 0.9347)	<0.0001
	pTau/A β 42	0.9195 (0.9043, 0.9325)	<0.0001
	tTau/A β 42	0.9064 (0.8897, 0.9207)	<0.0001
	Percent cognitively impaired (per 1-unit increase)	-0.0001 (-0.0003, 0.0002)	0.6238
Sensitivity difference	pTau/A β 42 vs A β 42/A β 40	0.0007 (-0.0217, 0.0231)	0.9531
	tTau/A β 42 vs A β 42/A β 40	-0.0125 (-0.0358, 0.0109)	0.3007
	tTau/A β 42 vs pTau/A β 42	-0.0132 (-0.0340, 0.0077)	0.2160
FPR	A β 42/A β 40	0.1508 (0.1284, 0.1764)	<0.0001
	pTau/A β 42	0.1209 (0.1056, 0.1381)	<0.0001
	tTau/A β 42	0.1278 (0.1120, 0.1455)	<0.0001
	Percent cognitively impaired (per 1-unit increase)	0.0008 (0.0004, 0.0011)	<0.0001
FPR difference	pTau/A β 42 vs A β 42/A β 40	-0.0299 (-0.0589, -0.0009)	0.0387
	tTau/A β 42 vs A β 42/A β 40	-0.0230 (-0.0523, 0.0063)	0.1169
	tTau/A β 42 vs pTau/A β 42	0.0069 (-0.0163, 0.0300)	0.5610

A β , amyloid- β ; CI, confidence interval; FPR, false positive rate; pTau, phosphorylated Tau 181P; tTau, total Tau.

Significant values at $p < 0.05$ for **p-value differences** are shown in bold.

Supplementary Table S7: Bivariate meta-regression by assay type controlling for percent cognitively impaired (n = 34 studies)

Diagnostic measure	Covariate	Estimate (95% CI)	P-value
Sensitivity	Elecsys	0.9292 (0.9162, 0.9404)	<0.0001
	Lumipulse	0.8944 (0.8710, 0.9140)	<0.0001
	Innotest	0.9027 (0.8764, 0.9239)	<0.0001
	Other	0.9132 (0.8843, 0.9354)	<0.0001
	Percent cognitively impaired (per 1-unit increase)	0.0001 (−0.0002, 0.0003)	0.5392
Sensitivity difference	Lumipulse vs. Elecsys	−0.0348 (−0.0599, −0.0097)	0.0041
	Innotest vs. Elecsys	−0.0265 (−0.0536, 0.0006)	0.0414
	Other vs. Elecsys	−0.0161 (−0.0446, 0.0125)	0.2464
	Innotest vs. Lumipulse	0.0083 (−0.0233, 0.0398)	0.6102
	Other vs. Lumipulse	0.0187 (−0.0142, 0.0516)	0.2763
	Other vs. Innotest	0.0104 (−0.0239, 0.0448)	0.5532
FPR	Elecsys	0.1231 (0.1082, 0.1398)	<0.0001
	Lumipulse	0.1320 (0.1109, 0.1564)	<0.0001
	Innotest	0.1451 (0.1195, 0.1751)	<0.0001
	Other	0.1413 (0.1131, 0.1752)	<0.0001
	Percent cognitively impaired (per 1-unit increase)	0.0006 (0.0002, 0.0009)	0.0005
FPR difference	Lumipulse vs. Elecsys	0.0089 (−0.0195, 0.0373)	0.5366
	Innotest vs. Elecsys	0.0220 (−0.0106, 0.0546)	0.1737
	Other vs. Elecsys	0.0182 (−0.0173, 0.0536)	0.3005
	Innotest vs. Lumipulse	0.0131 (−0.0224, 0.0486)	0.4670
	Other vs. Lumipulse	0.0093 (−0.0288, 0.0474)	0.6292
	Other vs. Innotest	−0.0038 (−0.0451, 0.0375)	0.8570

CI, confidence interval; FPR, false positive rate.
Significant values at $p < 0.05$ for **p-value differences** are shown in bold.

Supplementary Table S8: Bivariate meta-regression by age, sample size and STARD score controlling for percent cognitively impaired

Diagnostic measure	Covariate	Estimate (95% CI)	P-value
By age controlling for percent cognitively impaired (n = 33 studies)			
Sensitivity	Age < 68 years	0.9172 (0.9035, 0.9291)	<0.0001
	Age ≥ 68 years	0.9101 (0.8957, 0.9228)	<0.0001
	Percent cognitively impaired (per 1-unit increase)	−0.0001 (−0.0004, 0.0002)	0.4290
Sensitivity difference	Age ≥ 68 years vs. < 68 years	−0.0071 (−0.0260, 0.0119)	0.4648
FPR	Age < 68 years	0.1417 (0.1267, 0.1582)	<0.0001
	Age ≥ 68 years	0.1190 (0.1051, 0.1346)	<0.0001
	Percent cognitively impaired (per 1-unit increase)	0.0006 (0.0003, 0.0010)	0.0006
FPR difference	Age ≥ 68 years vs. < 68 years	−0.0227 (−0.0450, −0.0004)	0.0469
By sample size controlling for percent cognitively impaired (n = 34 studies)			
Sensitivity	Sample size < 200	0.9007 (0.8843, 0.9150)	<0.0001
	Sample size ≥ 200	0.9220 (0.9104, 0.9323)	<0.0001
	Percent cognitively impaired (per 1-unit increase)	−0.0000 (−0.0003, 0.0003)	0.8403
Sensitivity difference	Sample size ≥ 200 vs. < 200	0.0213 (0.0023, 0.0403)	0.0246
FPR	Sample size < 200	0.1461 (0.1300, 0.1639)	<0.0001
	Sample size ≥ 200	0.1195 (0.1066, 0.1338)	<0.0001
	Percent cognitively impaired (per 1-unit increase)	0.0006 (0.0003, 0.0010)	0.0006
FPR difference	Sample size ≥ 200 vs. < 200	−0.0266 (−0.0489, −0.0043)	0.0184
By STARD score controlling for percent cognitively impaired (n = 34 studies)			
Sensitivity	STARD score ≥ 67%	0.9126 (0.8994, 0.9243)	<0.0001
	STARD score < 67%	0.9165 (0.9018, 0.9291)	<0.0001
	Percent cognitively impaired (per 1-unit increase)	−0.0001 (−0.0004, 0.0002)	0.6683
Sensitivity difference	STARD score < 67% vs. ≥ 67%	0.0038 (−0.0150, 0.0226)	0.6895
FPR	STARD score ≥ 67%	0.1508 (0.1360, 0.1668)	<0.0001
	STARD score < 67%	0.1091 (0.0965, 0.1232)	<0.0001
	Percent cognitively impaired (per 1-unit increase)	0.0005 (0.0002, 0.0009)	0.0044
FPR difference	STARD score < 67% vs. ≥ 67%	−0.0417 (−0.0627, −0.0207)	0.0001

CI, confidence interval; FPR, false positive rate.

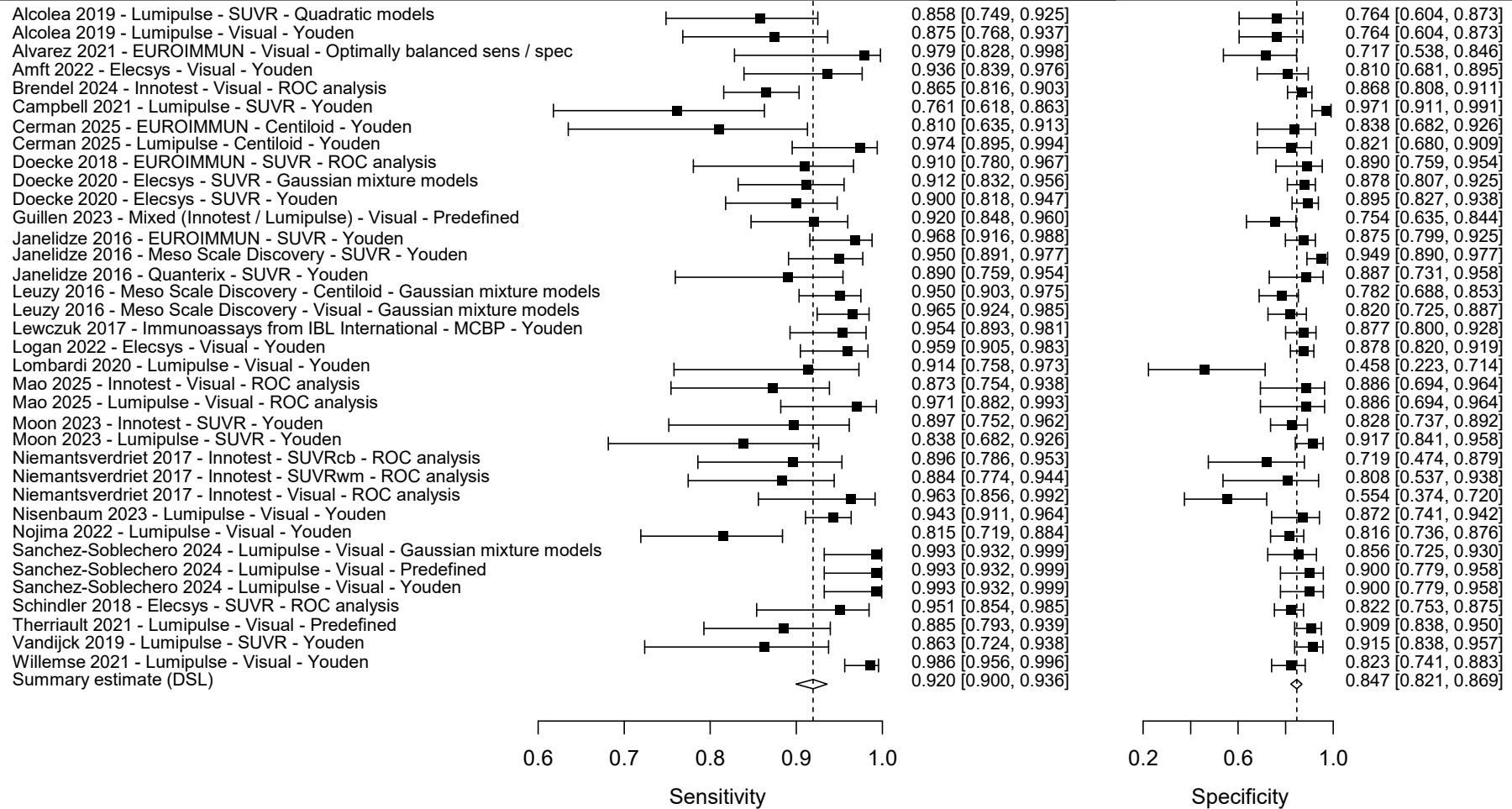
Significant values at $p < 0.05$ for **p-value differences** are shown in bold.

Supplementary Figure S1: Univariate Forest Plot A β 42/A β 40 (n=24 studies)

A β , amyloid- β ; DSL, DerSimonian–Laird (DSL) random effects estimation; MCBP, mean cortical binding potential; OPA, overall percent agreement; PET, positron-emission tomography; PPA, positive percent agreement; ROC, receiver operating characteristic; SUVR, standardized uptake value ratio.

Aβ42/Aβ40

Study - Assay - PET+ method - ROC cut-off method

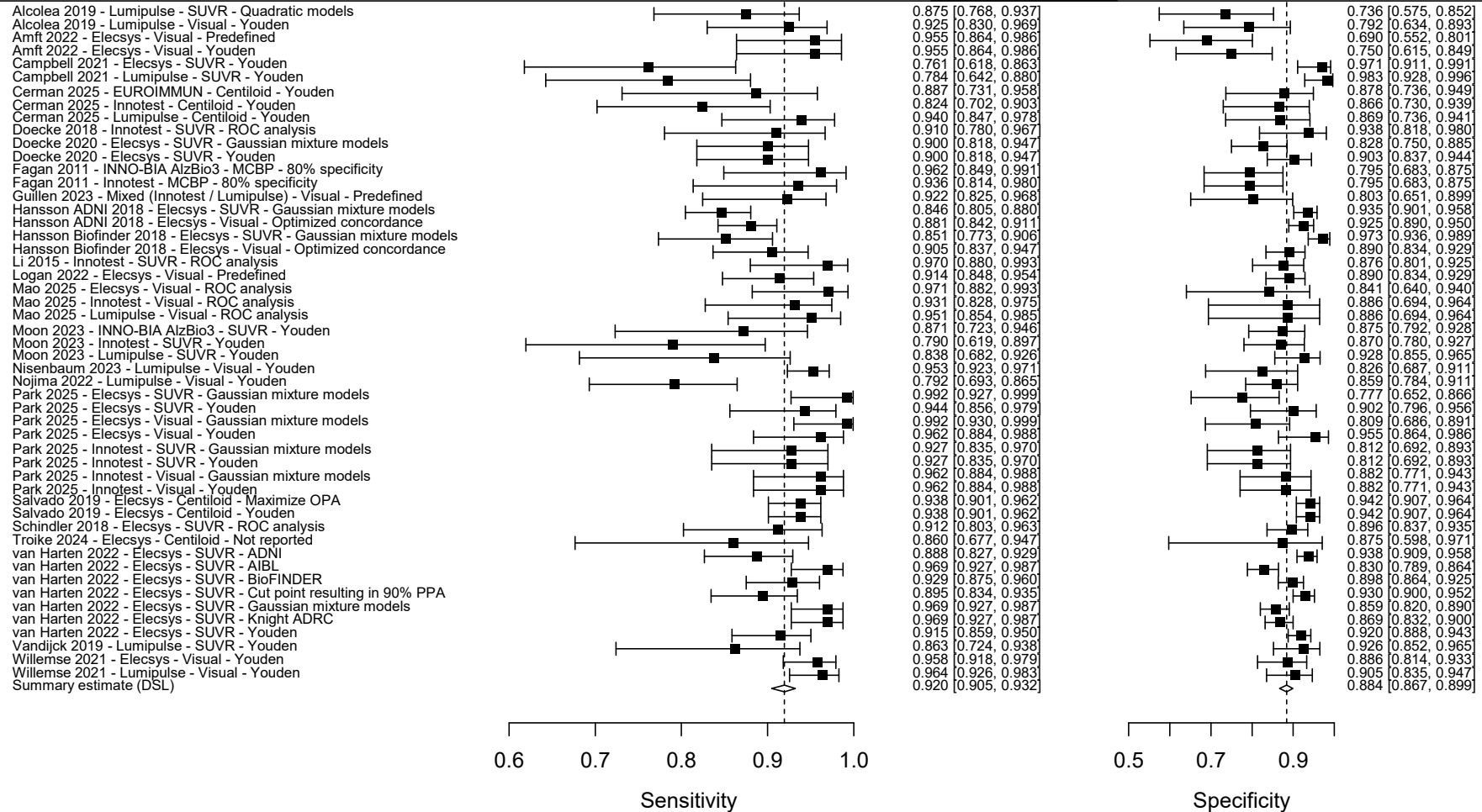


Supplementary Figure S2: Univariate Forest Plot pTau/A β 42 (n=23 studies)

A β , amyloid- β ; DSL, DerSimonian-Laird (DSL) random effects estimation; OPA, overall percent agreement; PET, positron-emission tomography; PPA, positive percent agreement; pTau, phosphorylated Tau 181P; ROC, receiver operating characteristic; SUVR, standardized uptake value ratio.

pTau/Aβ42

Study - Assay - PET+ method - ROC cut-off method

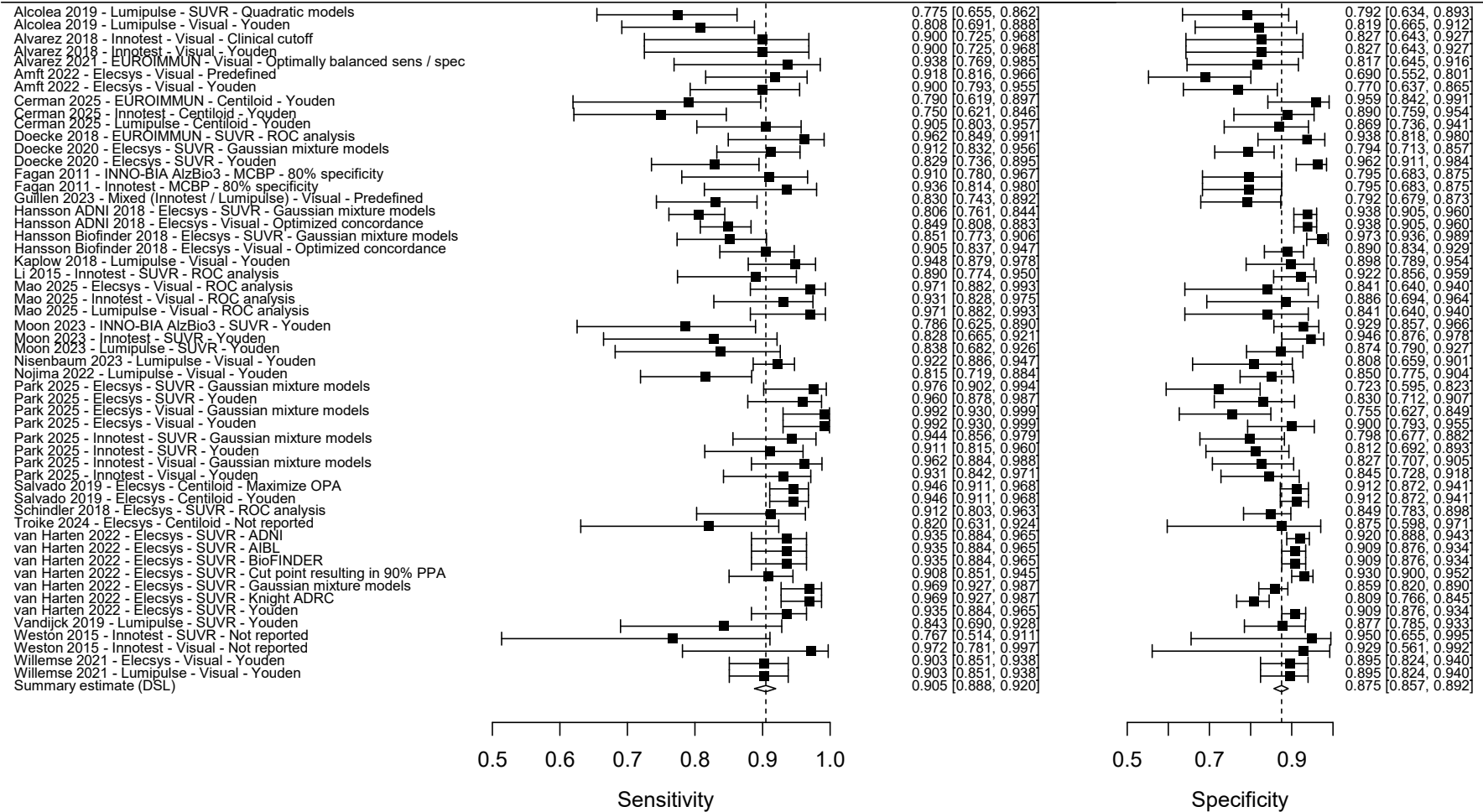


Supplementary Figure S3: Univariate Forest Plot tTau/A β 42 (25 studies)

A β , amyloid- β ; DSL, DerSimonian-Laird (DSL) random effects estimation; OPA, overall percent agreement; PET, positron-emission tomography; PPA, positive percent agreement; ROC, receiver operating characteristic; sens, sensitivity; spec, specificity; SUVR, standardized uptake value ratio; tTau, total Tau.

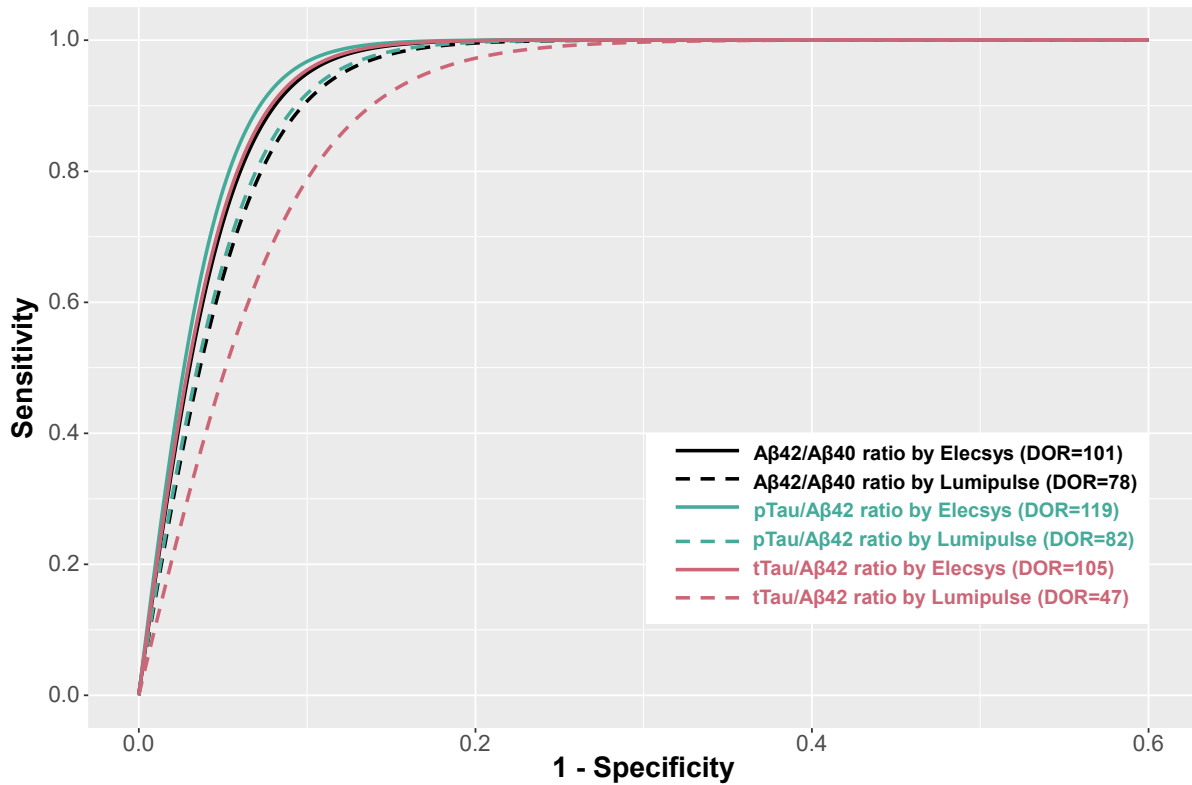
tTau/Aβ42

Study - Assay - PET+ method - ROC cut-off method



Supplementary Figure S4: Univariate model DOR ROC curves by CSF biomarker ratios and assays (n=35 studies)

A β , amyloid- β ; CSF, cerebrospinal fluid; DOR, diagnostic odds ratio; pTau, phosphorylated Tau 181P; ROC, receiver operating characteristic; tTau, total Tau.



The most accurate biomarker assay was Elecsys pTau/A β 42: DOR=119, ROC AUC=0.968

The least accurate biomarker assay was Lumipulse tTau/A β 42: DOR=47, ROC AUC=0.936

Other assay by biomarker combinations were intermediate:

Elecsys tTau/A β 42: DOR=105, ROC AUC=0.964

Elecsys A β 42/A β 40: DOR=101, ROC AUC=0.964

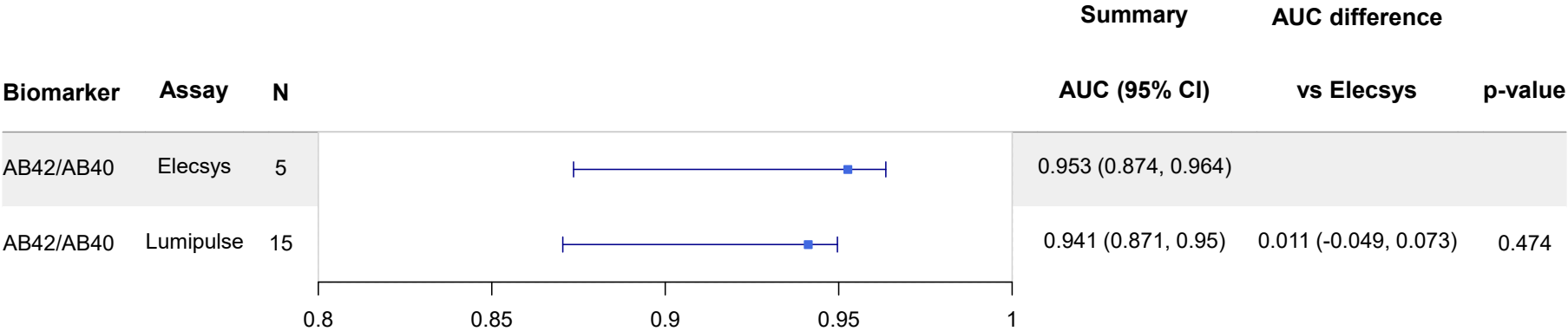
Lumipulse pTau/A β 42: DOR=82, ROC AUC=0.957

Lumipulse A β 42/A β 40: DOR=78, ROC AUC=0.936

Nevertheless, all represent outstanding tests.

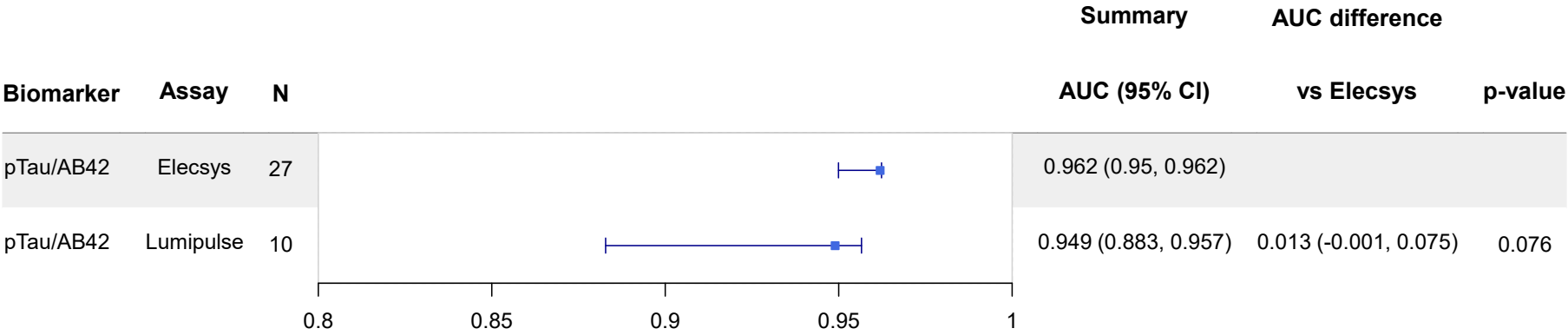
Supplementary Figure S5: Bivariate model SROC AUC values for the CSF biomarker ratio Aβ42/Aβ40 by assay (n=16 studies)

Aβ, amyloid-β; AUC, area under the curve; CI, confidence interval; CSF, cerebrospinal fluid; N, number of assay observations; SROC, summary receiver operating characteristic.



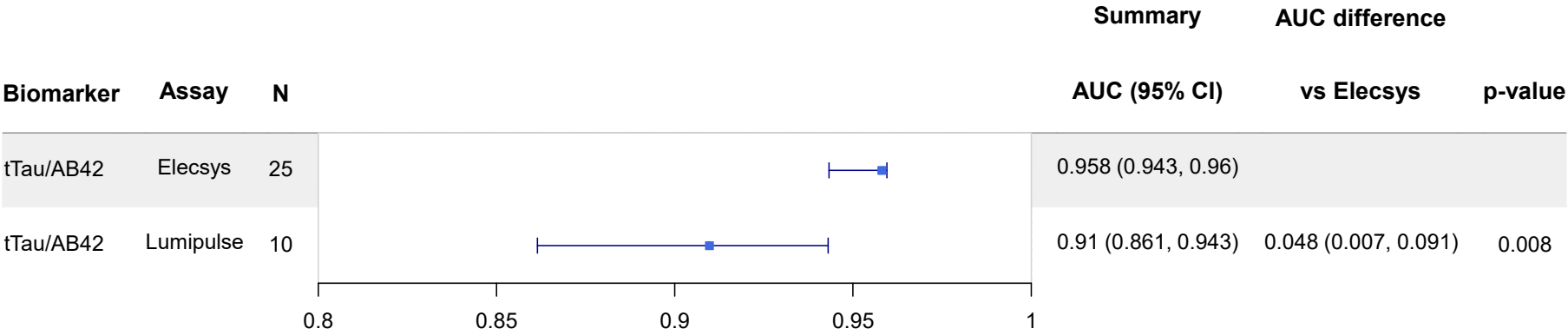
Supplementary Figure S6: Bivariate model SROC AUC values for the CSF biomarker ratio pTau/Aβ42 by assay (n=20 studies)

Aβ, amyloid-β; AUC, area under the curve; CI, confidence interval; CSF, cerebrospinal fluid; N, number of assay observations; pTau, phosphorylated Tau 181P; SROC, summary receiver operating characteristic.



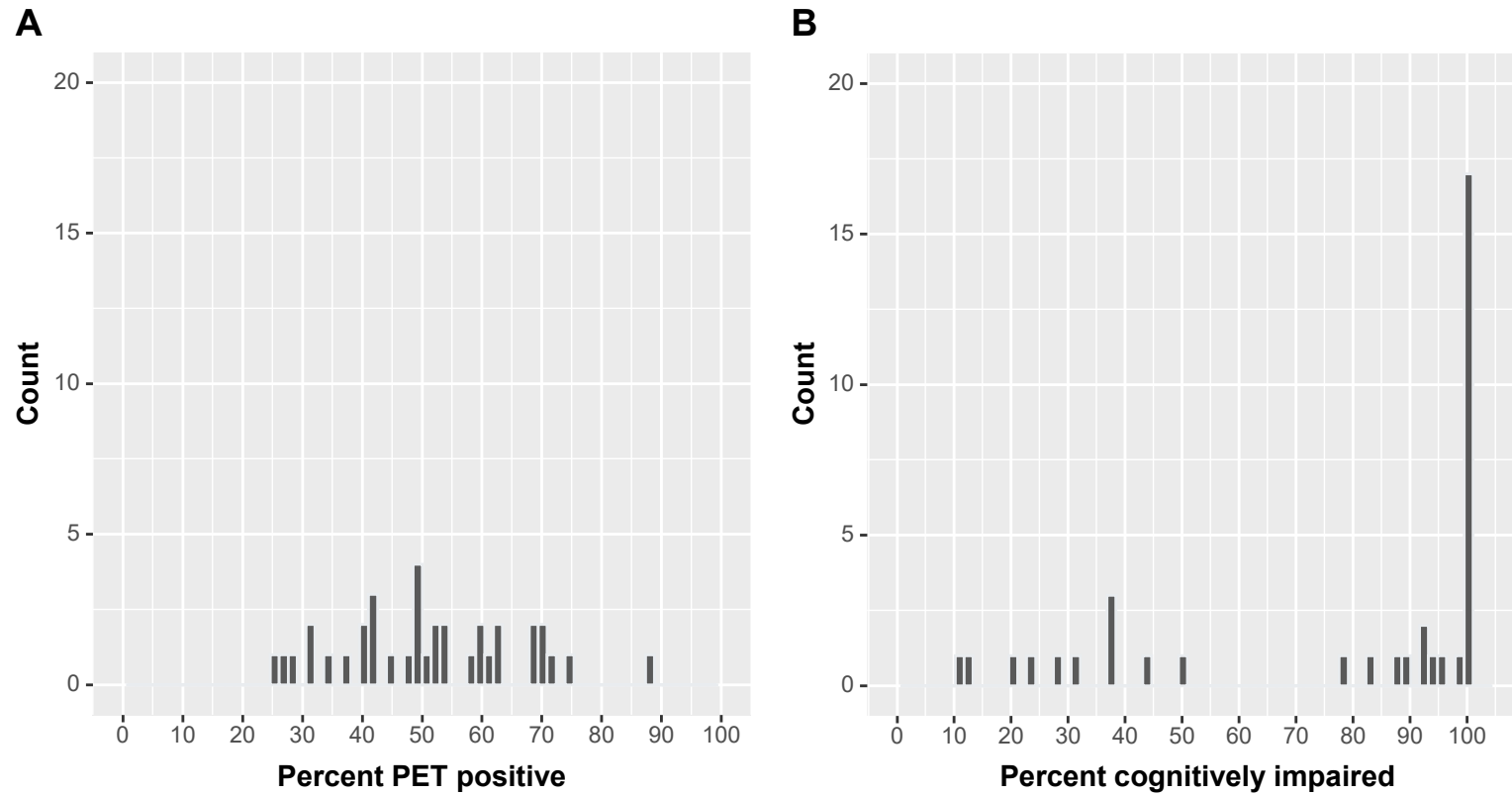
Supplementary Figure S7: Bivariate model SROC AUC values for the CSF biomarker ratio tTau/Aβ42 by assay (n=19 studies)

Aβ, amyloid-β; AUC, area under the curve; CI, confidence interval; CSF, cerebrospinal fluid; N, number of assay observations; SROC, summary receiver operating characteristic; tTau, total Tau.

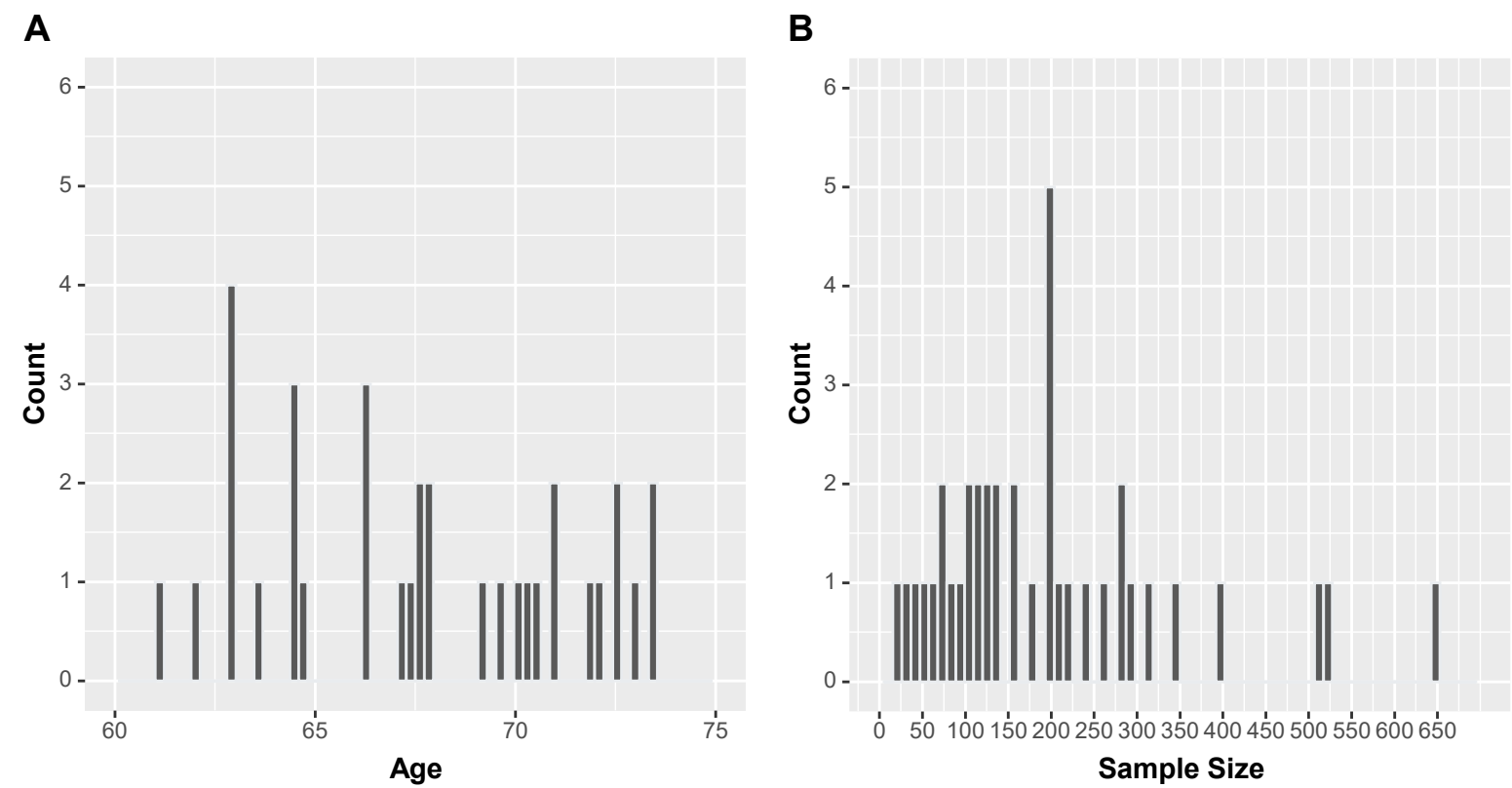


Supplementary Figure S8: Study distributions of (A) percentage PET positive and (B) percentage with any cognitive impairment*

* Includes subjective cognitive decline, mild cognitive impairment, Alzheimer's disease and other causes of dementia

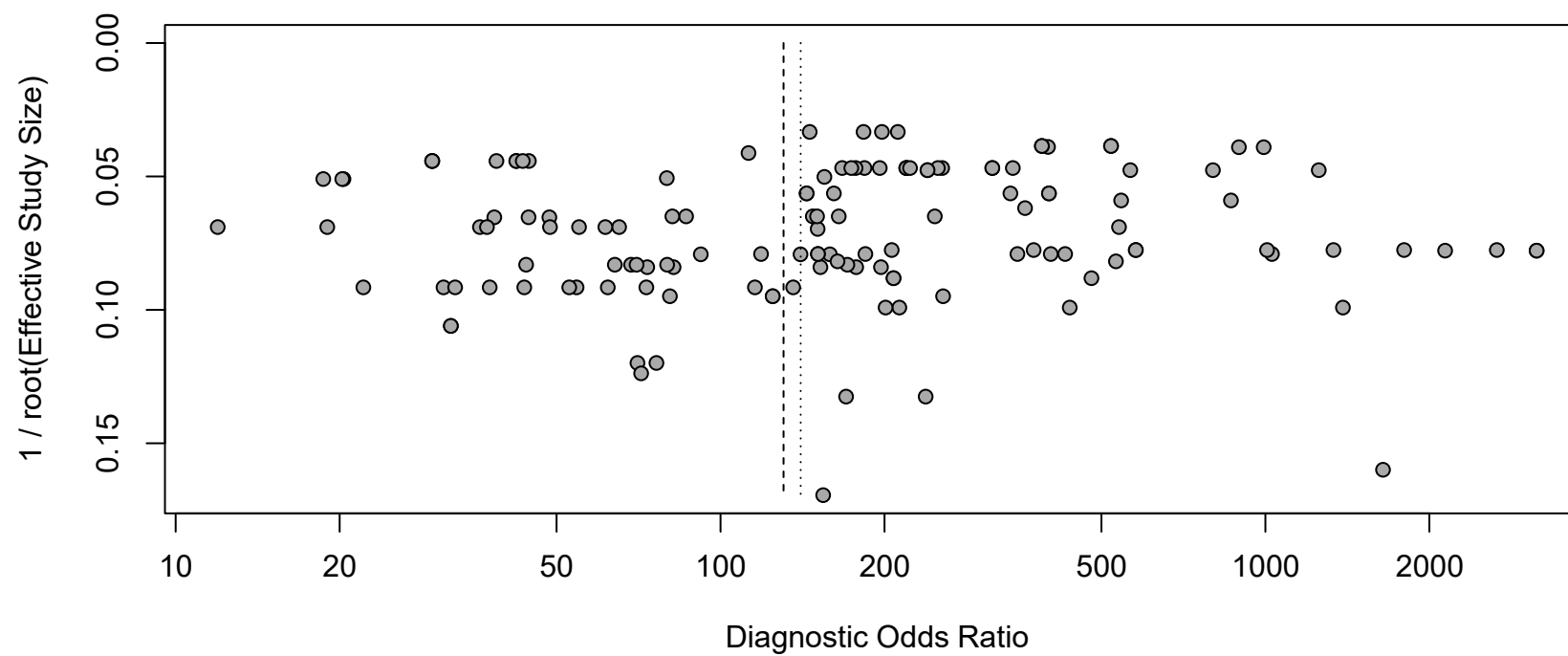


Supplementary Figure S9: Study distributions of (A) mean age and (B) sample size

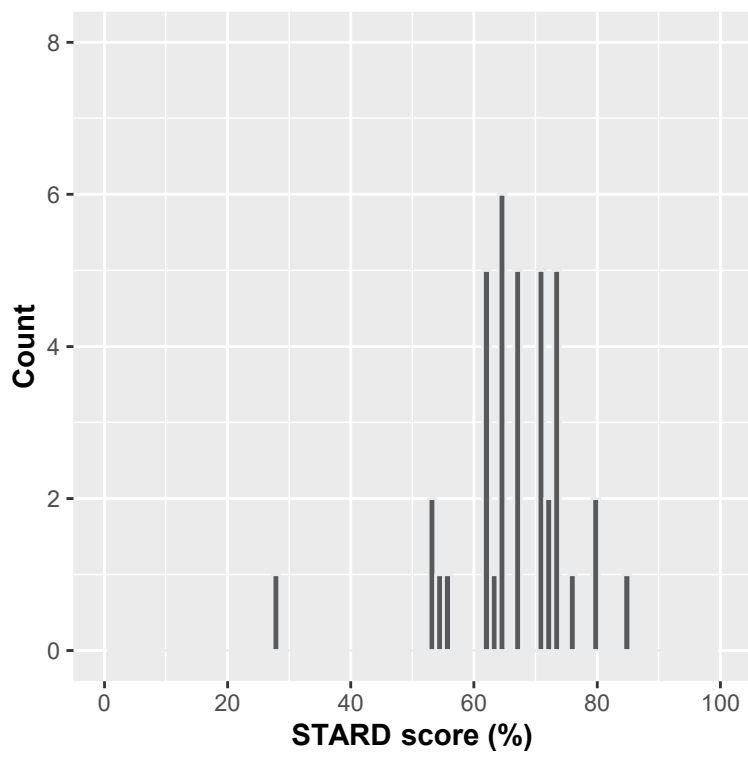


Supplementary Figure S10: Plot for publication bias using DOR (34 studies)

DOR, diagnostic odds ratio. Test result: $t = -1.01$, $p\text{-value} = 0.3150$.



Supplementary Figure S11: Study distributions of STARD scores



**Supplementary Figure S12: Bivariate model SROC curves by CSF biomarker ratios
(potential duplicate data excluded, n=32 studies)**

Each circle represents a study with the circle size proportional to the number of participants in that study. Model-fitted SROC curves are shown by colored solid lines. Summary sensitivity and specificity points are shown by colored squares; these correspond to the data shown in the inset table. The dotted area corresponds to the 95% prediction region.

A β , amyloid- β ; CI, confidence interval; CSF, cerebrospinal fluid; FPR, false positive rate; pTau, phosphorylated Tau 181P; SROC, summary receiver operating characteristic; tTau, total Tau.

