

Supplementary Table 1. Research strategies

Key-words	Number of full-texts found		
	Pubmed	Web of Science	Cochrane and Embase
(((((parkinson's) OR parkinsons) OR parkinson) OR parkinson's disease) AND cerebrospinal fluid AND α - synuclein	7013	7452	2598
(((((parkinson's) OR parkinsons) OR parkinson) OR parkinson's disease) AND cerebrospinal fluid AND amyloid precursor protein	824	835	302
(((((parkinson's) OR parkinsons) OR parkinson) OR parkinson's disease) AND cerebrospinal fluid AND β - amyloid42	7003	8014	2789
(((((parkinson's) OR parkinsons) OR parkinson) OR parkinson's disease) AND cerebrospinal fluid AND ubiquitin–proteasome system	36	41	20
(((((parkinson's) OR parkinsons) OR parkinson) OR parkinson's disease) AND cerebrospinal fluid AND neuroinflammation	223	238	72
(((((parkinson's) OR parkinsons) OR parkinson) OR parkinson's disease) AND cerebrospinal fluid AND YKL-40	45	59	31
(((((parkinson's) OR parkinsons) OR parkinson) OR parkinson's disease) AND cerebrospinal fluid AND Fms-like tyrosine kinase 3	8	10	4
(((((parkinson's) OR parkinsons) OR parkinson) OR parkinson's disease) AND cerebrospinal fluid AND interleukin-6	79	92	39
(((((parkinson's) OR parkinsons) OR parkinson) OR parkinson's disease) AND cerebrospinal fluid AND oxidative stress	347	361	132
(((((parkinson's) OR parkinsons) OR parkinson) OR parkinson's disease) AND cerebrospinal fluid AND axonal degeneration	61	79	34
(((((parkinson's) OR parkinsons) OR parkinson) OR parkinson's disease) AND cerebrospinal fluid AND tau	1317	1353	398
(((((parkinson's) OR parkinsons) OR parkinson) OR parkinson's disease) AND cerebrospinal fluid AND phospho-tau proteins	79	90	28
(((((parkinson's) OR parkinsons) OR parkinson) OR parkinson's disease) AND cerebrospinal fluid AND neurofilament	271	284	99
(((((parkinson's) OR parkinsons) OR parkinson) OR parkinson's disease) AND cerebrospinal fluid AND copper	104	118	48
(((((parkinson's) OR parkinsons) OR parkinson) OR	62	83	29

parkinson's disease) AND cerebrospinal fluid AND zinc			
(((((parkinson's) OR parkinsons) OR parkinson) OR parkinson's disease) AND cerebrospinal fluid AND iron	221	255	93
(((((parkinson's) OR parkinsons) OR parkinson) OR parkinson's disease) AND cerebrospinal fluid AND manganese	89	104	37
(((((parkinson's) OR parkinsons) OR parkinson) OR parkinson's disease) AND cerebrospinal fluid AND C-reactive response protein	15	19	8
(((((parkinson's) OR parkinsons) OR parkinson) OR parkinson's disease) AND cerebrospinal fluid AND DJ-1	95	119	37
(((((parkinson's) OR parkinsons) OR parkinson) OR parkinson's disease) AND cerebrospinal fluid AND Arginine	39	52	17
(((((parkinson's) OR parkinsons) OR parkinson) OR parkinson's disease) AND cerebrospinal fluid AND Citrulline	15	18	9
Total full-texts after removing duplicates	19326	21319	

Supplementary Notes 2. Extraction form

Listed items:

Title

Author

Year of publication

Institute

Country

Number of patients

Disease duration

Inclusion and exclusion criteria

General characteristics

N of patients

Age and SD

Time since diagnosis and SD (years)

% male

Mean MMSE and SD

Additional information on age across groups

Additional information on gender across groups

Additional information on disease duration across groups

Additional information on UPDRS scores across groups

Additional information on HY scores across groups

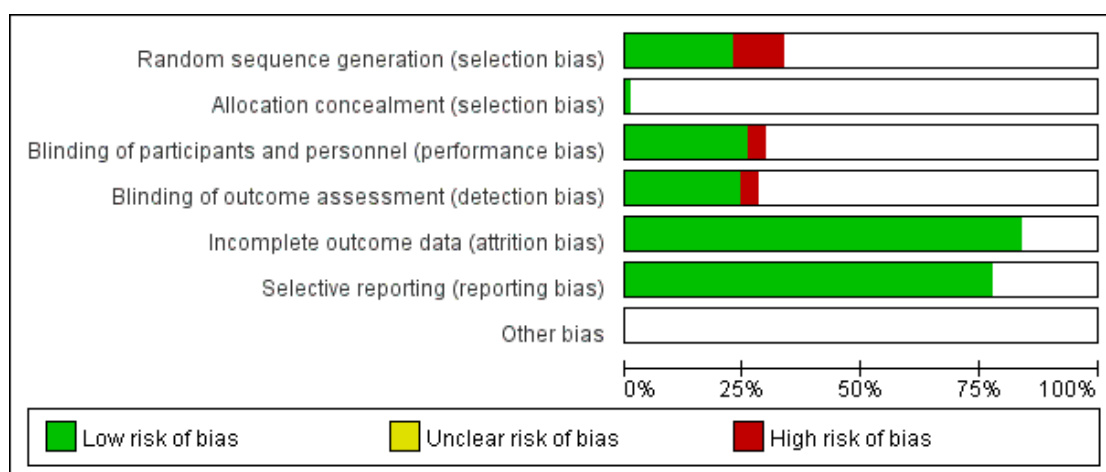
Additional information on MMSE scores across groups

Additional information on BMI across groups

Additional information on follow-up years across groups

Additional information on assay methods across groups

Supplementary Figure 3. Quality analysis chart



	Performance (points)	Adaptation (points)	Learning (points)	Transfer (points)	Knowledge (points)	Skills (points)	Other (points)
Aasly 2014							
Abbasi 2018							
Abdo 2007							
Aerts 2010	●						
Aerts 2012	●						
Akhtar 2018	●						
Alimonti 2007	●						
Alves 2010	●						
Anzari 2016	●						
Archer 2020	●	●					
Bargar 2021	●						
Bench 2012							
Bibi 2007	●						
Blennow 1996							
Bob 2013							
Bacca 2006	●						
Bell 1999	●						
Borroni 2008							
Bougea 2020							
Brockmann 2021							
Brosseau 2020							
Brosseron 2019	●						
Buddhala 2015							
Campbell 2019	●						
Chahinea 2019	●						
Chiasserini 2017	●						
Compta 2022							
Constantinescu 2010							
Daniela 2013	●						
Delgado-Alvarado 2017							
Dij 2013							
Dijk 2014							
Edina 2014							
Forte 2004	●						
Ferland 2019							
Gaetani 2021	●						
Gao 2016	●						
Gazzariga 1992							
Gelman 2018							
Gool 1994							
Halbgebauer 2016	●						
Hall 2016							
Hall 2018	●						
Hansson 2017							
Herbert 2014							
Herbert 2016	●						
Haywood 2016							
Holmberg 1998							
Holmberg 2001							
Holmberg 2003							
Hong 2010							
Hong 2021							
Hozumi 2011							
Ibanez 2017							
Isabel 2021	●						
Jabbari 2018							
Jeppsson 2019							
Jiménez-Jiménez 1998	●						
Kang 2013							
Kasuhira 2020							
Kuiper 2000							
Lee 2022							
Leko 2018							
Lerche 2021	●						
Liguori 2022							
Lins 2004							
Llorens 2016	●						
Llorens 2018							
Masas 2018	●						
Maibour 2018							
Marques 2019							
Marthe 2020							
Min 2021	●						
Molina-1 1997							
Molina 1993	●						
Molina-2 1997							
Mollenhauer 2006	●						
Mollenhauer 2008							
Mollenhauer 2011							
Mollenhauer 2013							
Mollenhauer 2018							
Mondello 2014							
Nielsen 2014	●						
Ning 2019							
Pagano 2016							
Papuc 2020							
Park 2011	●						
Parnetti 2008							
Parnetti 2011	●						
Parnetti 2014							
Peng 2018							
Poggiolini 2022							
Quadalti 2021							
Qureshi 2006							
Sampedro 2018	●						
Sampardo 2020							
Sanyal 2016	●						
Schirinz-1 2018							
Schirinz 2020							
Schirinz-2 2018							
Schulz 2022							
Sezal 2021	●						
Shahsawaz 2020							
Sherbat 2018	●						
Shi 2011	●						
Shi 2016							
Shrag 2017							
Sjogren 2000							
Starhor 2018							
Stav 2015							
Steenhoven 2018							
Tadayon 2020							
Tateno 2012	●						
Tokuda 2010	●						
Van 2019							
Wang, H 2012							
Wang, Y 2012	●						
Wang 2016							
Wennstrom 2013	●						
Yang 2017							
Youn 2018							
Yu 2014							
Yu 2017							

Supplementary Table 5. Summary of meta-analytic results

Table S1 Characteristics of studies included in the meta-analysis for PD vs HC/OND groups.

Biomarker	Group	study	n.PD	n.cotrol	Main effect				Heterogeneity				Publication bias
					Measure	ES	95%CI	P value	I ²	χ ²	df	P value	Egger intercept
1.t-α-syn	1.PD&HC+OND*	44	7004	3380	SMD	-0.419	-0.542~-0.295	0.000	86.2%	369.65	51	0.000	0.116
	2.PD&HC*	36	6334	2974	SMD	-0.368	-0.509~-0.227	0.000	88.3%	342.47	40	0.000	0.438
	3.PD&OND*	8	608	364	SMD	-0.582	-0.807~-0.356	0.000	54.2%	17.48	8	0.025	0.175
2.p-tau	1.PD&HC+OND*	45	6636	3464	SMD	-0.297	-0.373~-0.221	0.000	60.0%	124.92	50	0.000	0.188
	2.PD&HC*	34	5359	2795	SMD	-0.386	-0.492~-0.281	0.000	76.2%	155.36	37	0.000	0.841
	3.PD&OND	11	572	440	SMD	-0.100	-0.256~-0.056	0.207	30.2%	14.32	10	0.000	NA
3.t-tau	1.PD&HC+OND*	57	7368	3958	SMD	-0.274	-0.349~-0.200	0.000	64.4%	171.18	61	0.000	0.032
	2.PD&HC*	42	6585	3267	SMD	-0.313	-0.396~-0.231	0.000	66.2%	136.18	46	0.000	0.035
	3.PD&OND	15	892	705	SMD	-0.129	-0.269~-0.012	0.072	36.9%	23.77	15	0.069	NA
4.Aβ42	1.PD&HC+OND*	52	6926	3564	SMD	-0.239	-0.309~-0.169	0.000	57.0%	127.74	55	0.000	0.023
	2.PD&HC*	42	6238	3078	SMD	-0.262	-0.341~-0.183	0.000	61.4%	116.45	45	0.000	0.009
	3.PD&OND*	10	758	440	SMD	-0.143	-0.273~-0.013	0.031	0.0%	5.67	9	0.772	0.365
5.Zn	1.PD&HC*	5	191	172	SMD	-0.398	-0.623~-0.173	0.001	9.6%	4.42	4	0.152	0.706
6.DJ-1	1.PD&HC*	2	203	224	SMD	-0.791	-1.380~-0.202	0.008	88.2%	8.48	1	0.004	NA
7.YKL-40	1.PD&HC*	2	257	92	SMD	-0.322	-0.561~-0.082	0.009	0.0%	0.83	2	0.660	NA
8.NFL	1.PD&HC*	9	927	462	SMD	0.157	-0.047~-0.360	0.131	60.9%	28.16	11	0.000	0.078
9.o-α-syn	1.PD&HC+OND*	8	428	277	SMD	1.616	0.888~2.344	0.000	93.2%	117.10	8	0.000	0.122
	2.PD&HC*	3	122	145	SMD	2.436	0.950~3.921	0.001	94.6%	55.50	3	0.000	0.908
	3.PD&OND*	5	306	116	SMD	0.997	0.556~1.439	0.000	70.5%	13.56	4	0.009	0.682
10.p-α-syn	1. PD&HC+OND*	2	255	252	SMD	0.439	0.259~0.619	0.000	94.5%	36.41	2	0.000	NA

The bolded portion indicates that the biomarker has a higher level in the PD group than in the control group (HC or OND). The * mark indicates positive results. CI confidence interval, Df degrees of freedom.

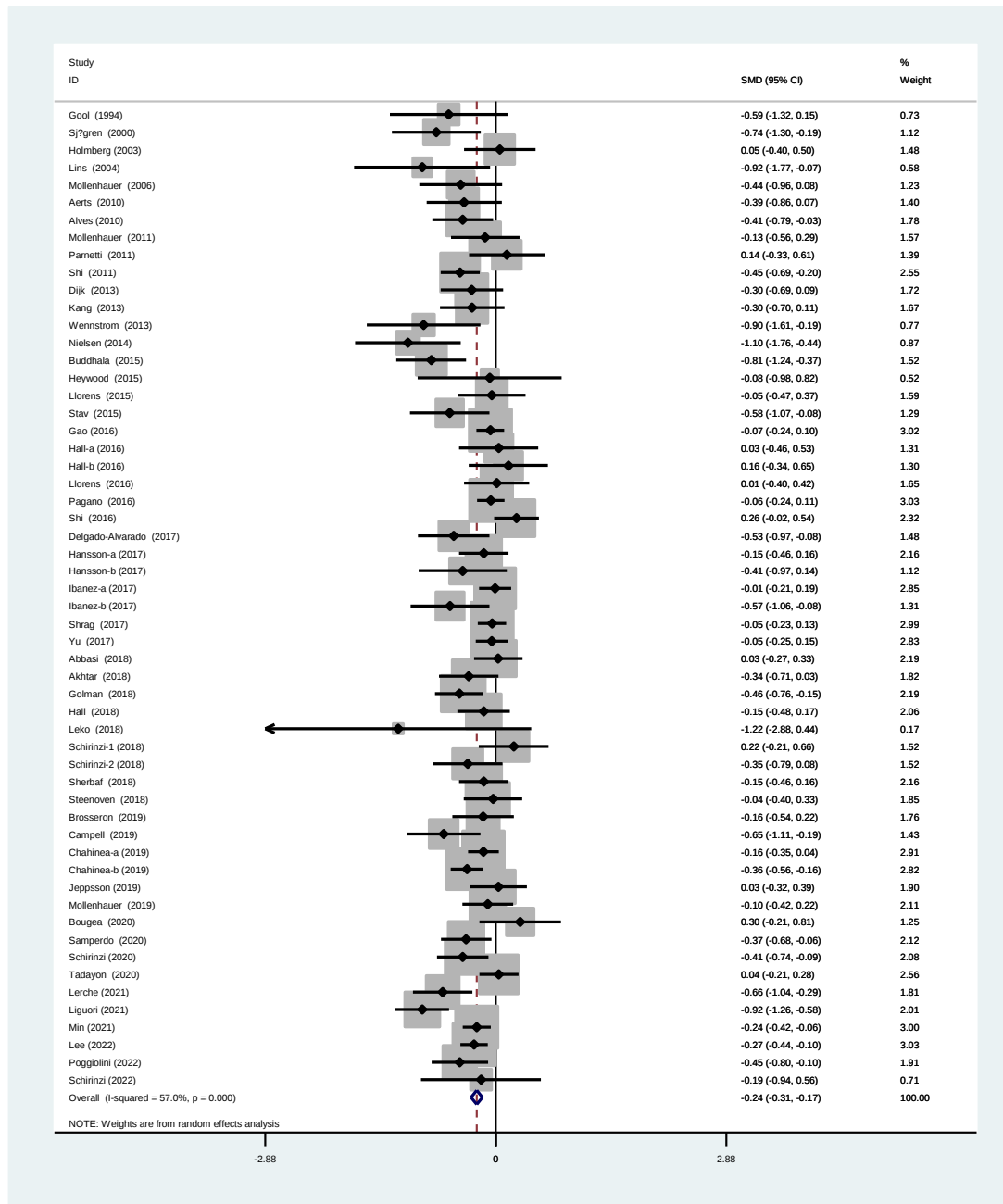
Table S2 Characteristics of studies included in the meta-analysis for PD vs Parkinsonism and AD groups.

Group	Biomarker	study	n.PD	n.cotrol	Main effect				Heterogeneity				Publication bias
					Measure	ES	95%CI	P value	I ²	χ^2	df	P value	Egger intercept
1.PD&MSA	1.t-a-syn	11	1114	318	SMD	0.257	0.055~0.459	0.013	54.4%	26.33	12	0.010	0.542
	2.NFL	7	295	146	SMD	-3.069	-4.545~-1.594	0.000	95.5%	133.68	6	0.000	0.011
	3.t-tau	5	281	144	SMD	-0.977	-1.520~-0.434	0.000	82.7%	23.13	4	0.000	1.000
	4.Aβ42*	2	257	56	SMD	0.284	-0.006~0.575	0.055	0.0%	0.82	1	0.365	NA
	5.YKL-40	2	181	61	SMD	-0.973	-1.292~-0.655	0.000	0.0%	0.28	1	0.596	NA
	6.CRP	2	177	59	SMD	-0.556	-0.871~-0.242	0.001	0.0%	0.47	1	0.493	NA
2.PD&PSP	1.Aβ42	4	521	91	SMD	0.561	0.103~1.018	0.016	68.4%	12.66	4	0.013	0.045
	2.NFL	6	634	195	SMD	-1.509	-2.222~-0.796	0.000	92.4%	91.89	7	0.000	0.097
3.PD&DLB	1.Aβ42	10	839	346	SMD	0.775	0.498~1.052	0.000	70.6%	30.58	9	0.000	0.592
	2.p-tau	10	591	283	SMD	-0.495	-0.689~-0.301	0.000	28.0%	12.50	9	0.187	0.592
	3.t-tau	14	1023	519	SMD	-0.812	-1.131~-0.493	0.000	83.4%	84.53	14	0.000	0.235
4.PD&CBD	1.NFL	3	195	24	SMD	-1.421	-1.928~-0.914	0.000	0.0%	1.65	2	0.438	0.035

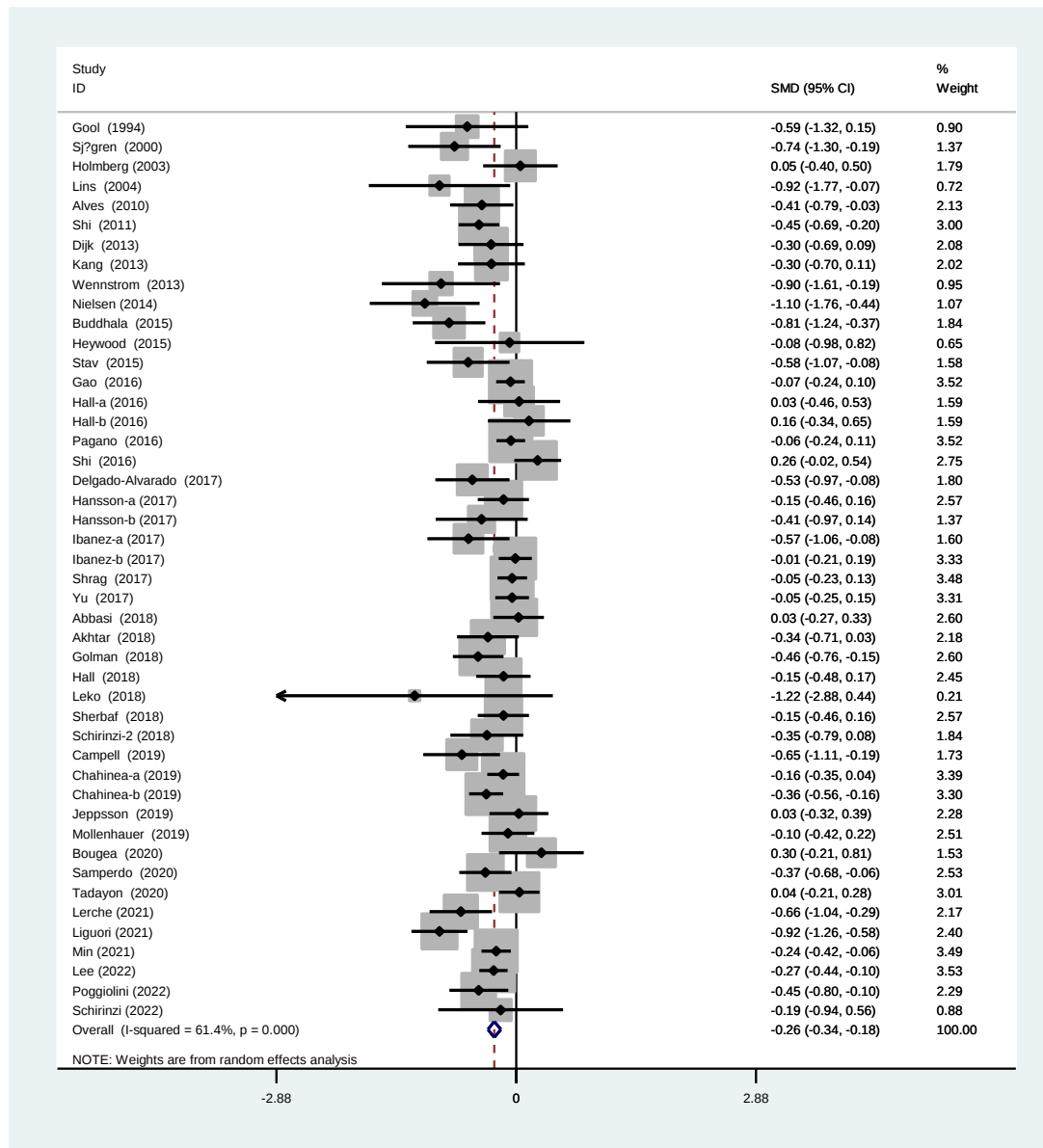
The bolded portion indicates that the biomarker has a higher level in the PD group than in the control group (MSA, PSP, DLB or AD). CI confidence interval, Df degrees of freedom.

Supplementary material 6. Forest plot for A β 42 in PD& Control group (A), PD&HC group (B), PD&OND group (C), PD&MSA group(D), PD&PSP(E), PD&DLB group(F) displaying effect size (risk ratio) calculated using a random effect model. ES, effective size; CI, confidence intervals; SMD, standardized mean difference.

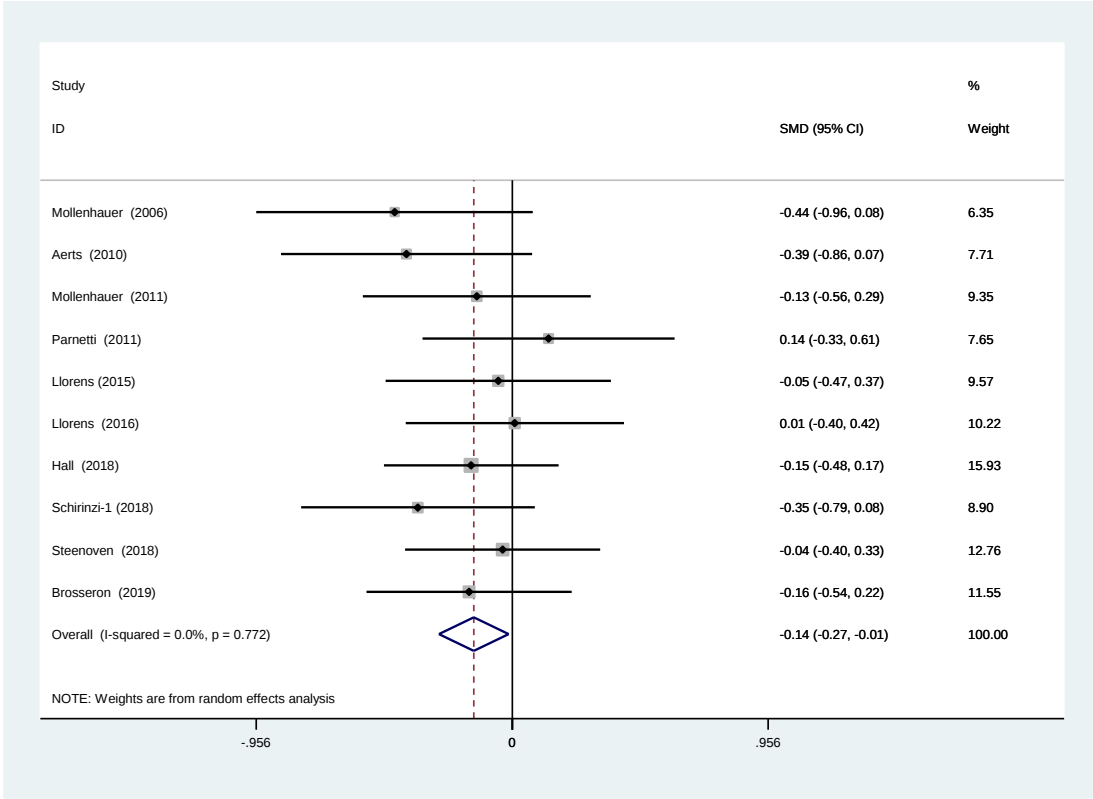
(A) PD& Control group



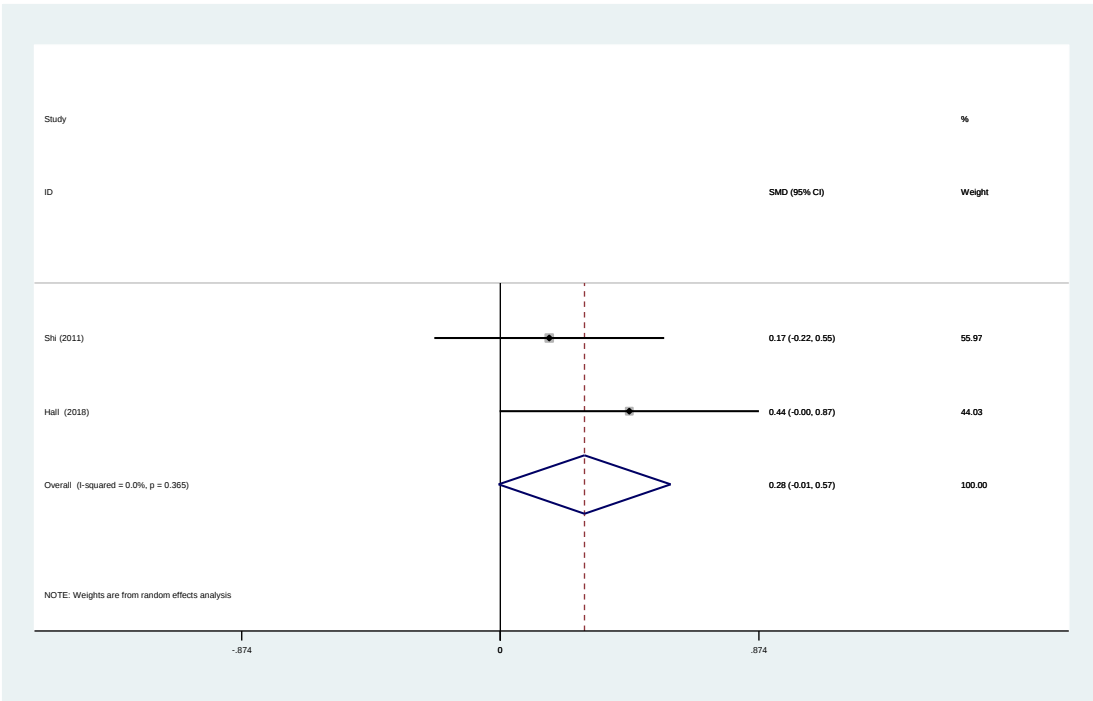
(B) PD&HC group



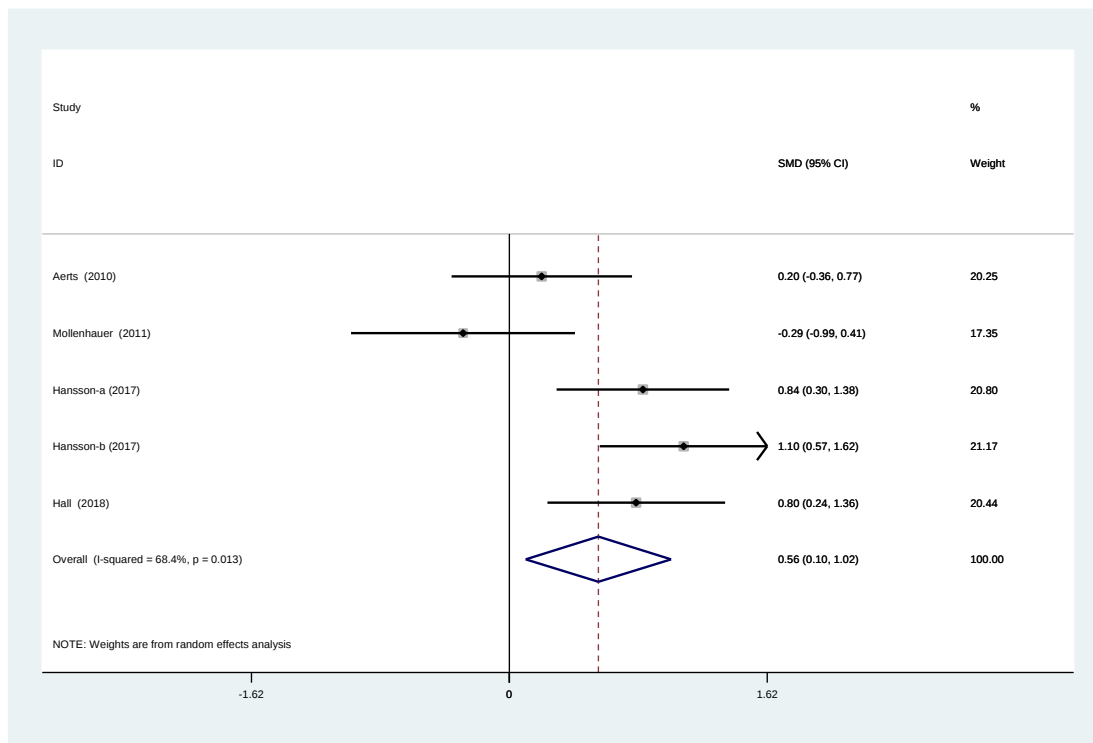
(C) PD&OND group



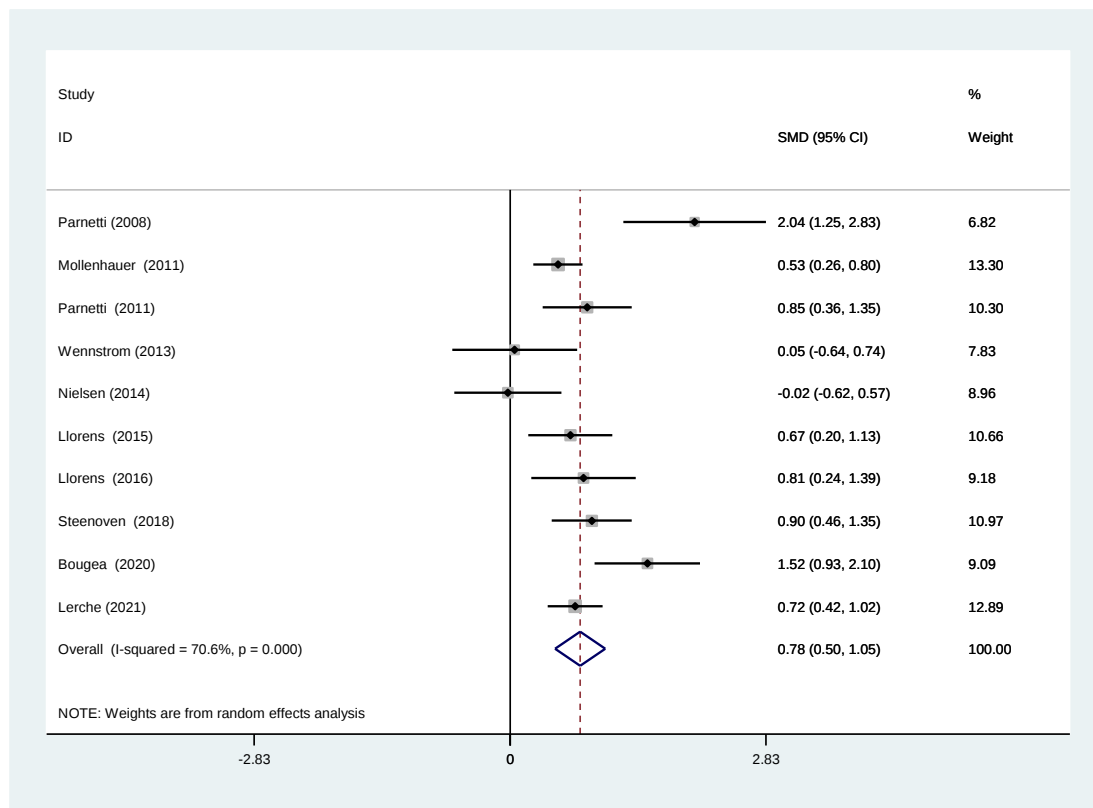
(D) PD&MSA group



(E) PD&PSP

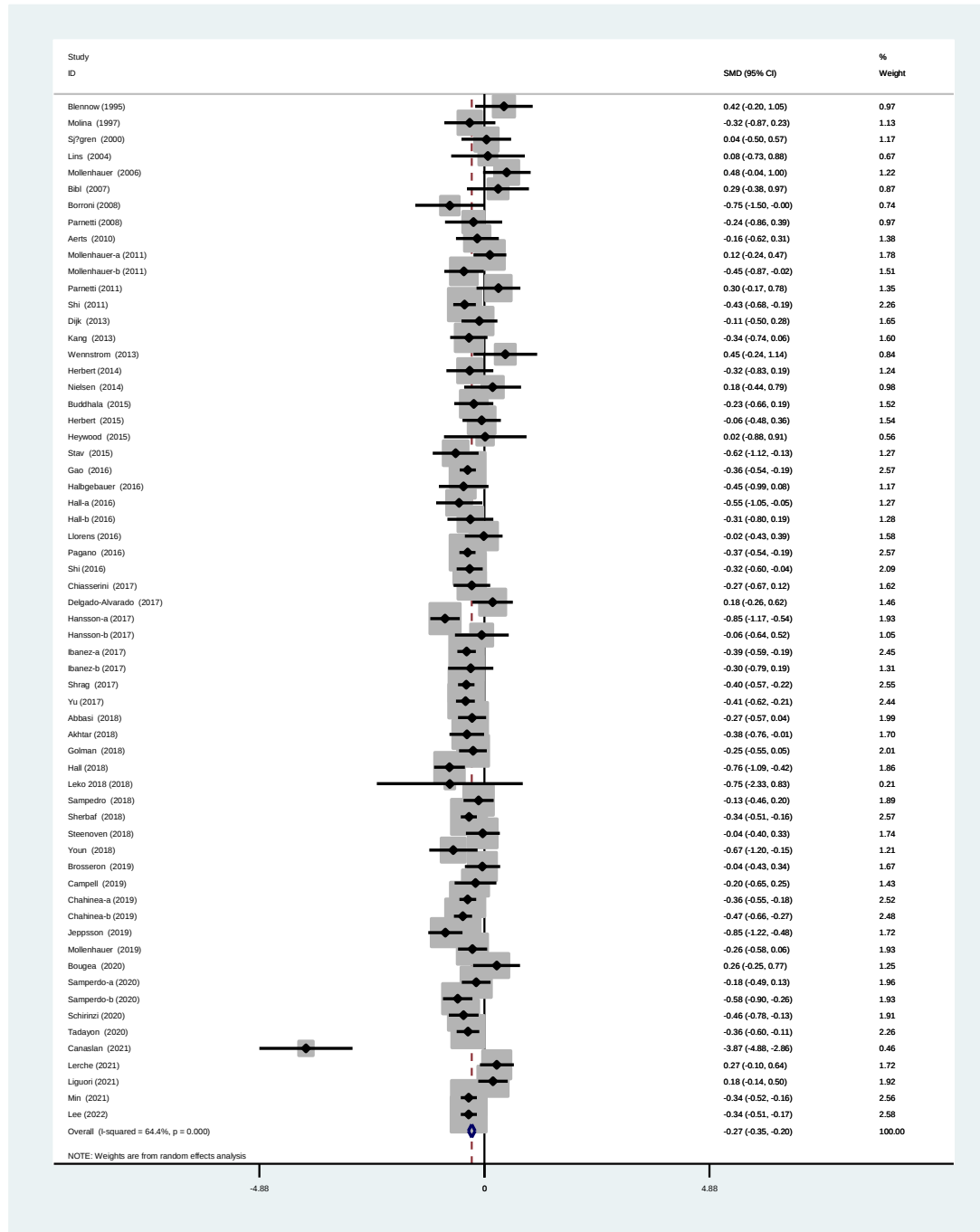


(F) PD&DLB

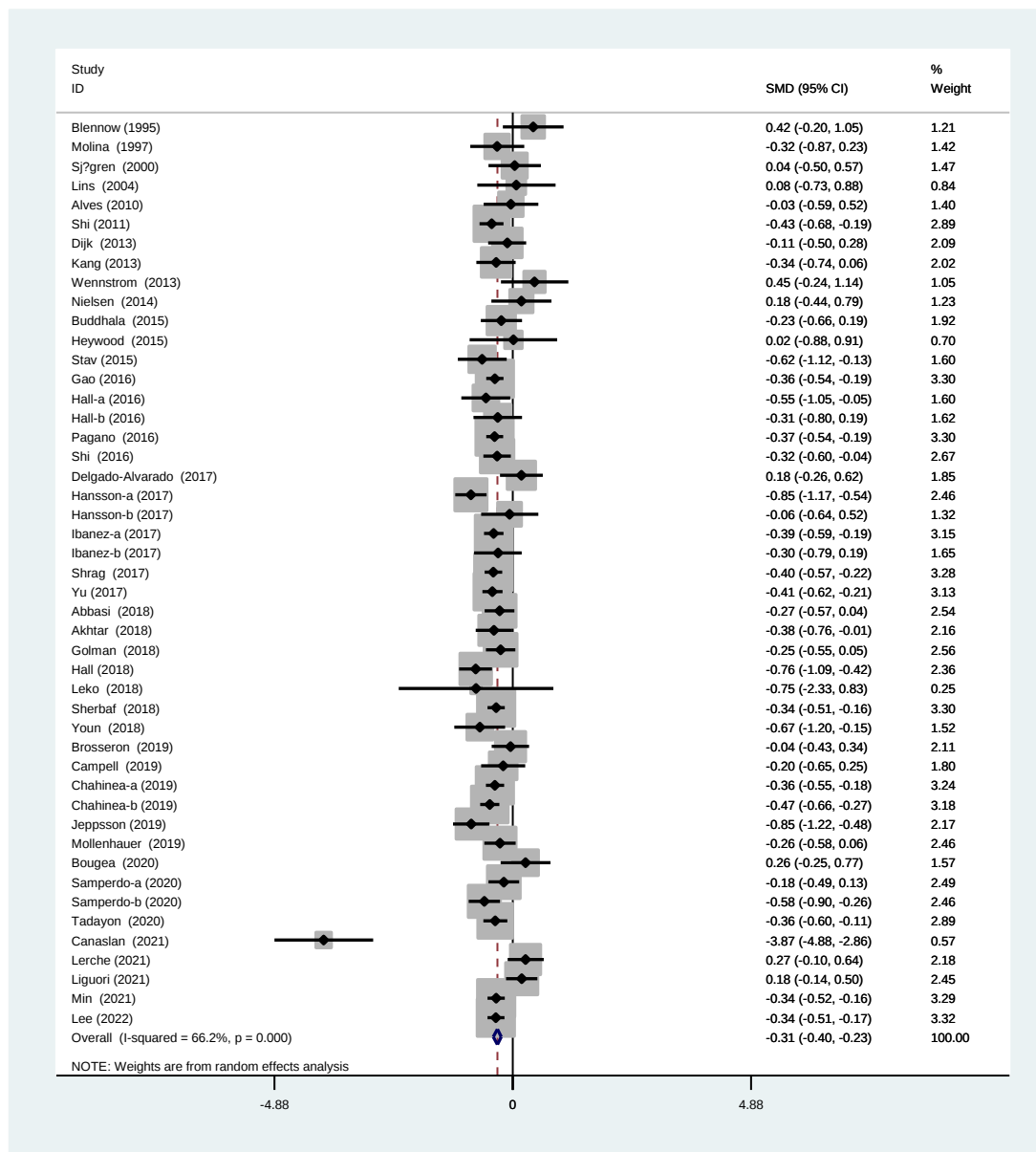


Supplementary material 7. Forest plot for t-tau in PD& Control group (A), PD&HC group (B), PD&OND group (C), PD&MSA group(D), PD&PSP(E), PD&DLB group(F) displaying effect size (risk ratio) calculated using a random effect model. ES, effective size; CI, confidence intervals; SMD, standardized mean difference.

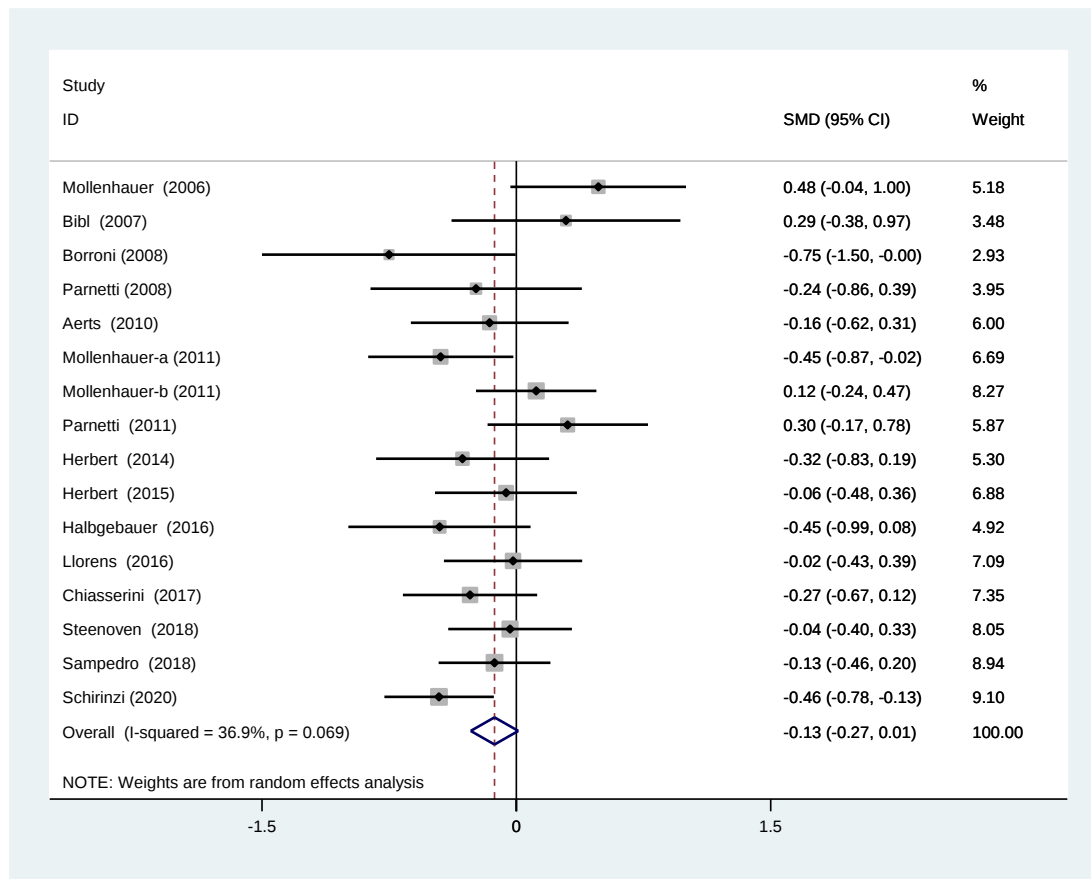
(A) PD& Control group



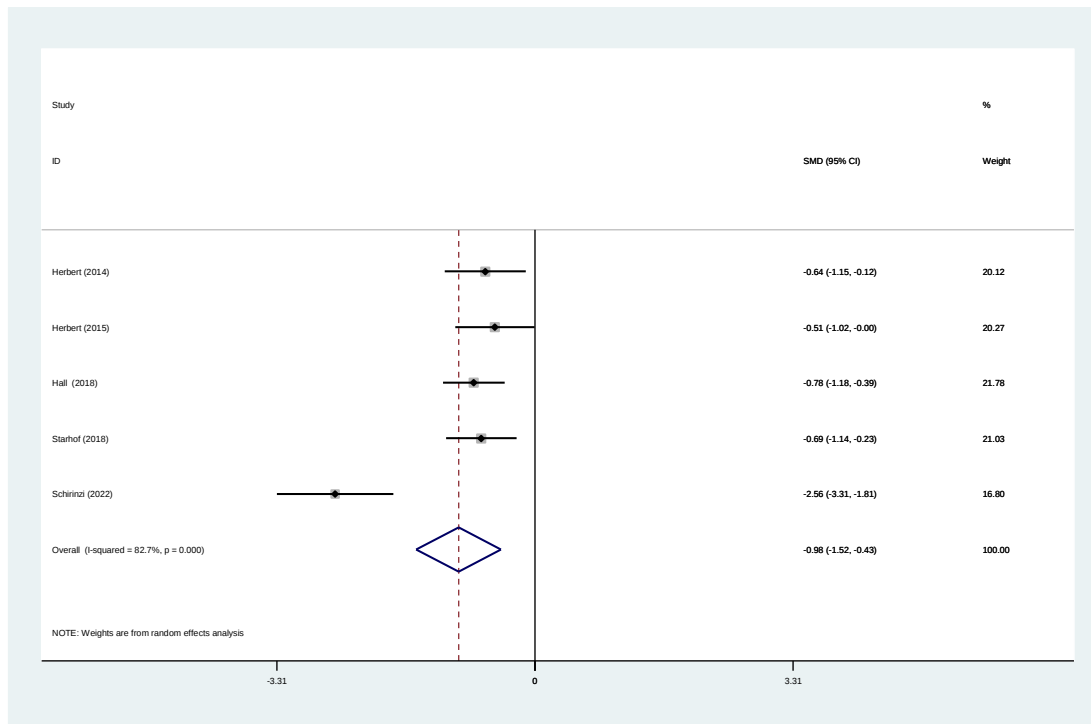
(B) PD&HC group



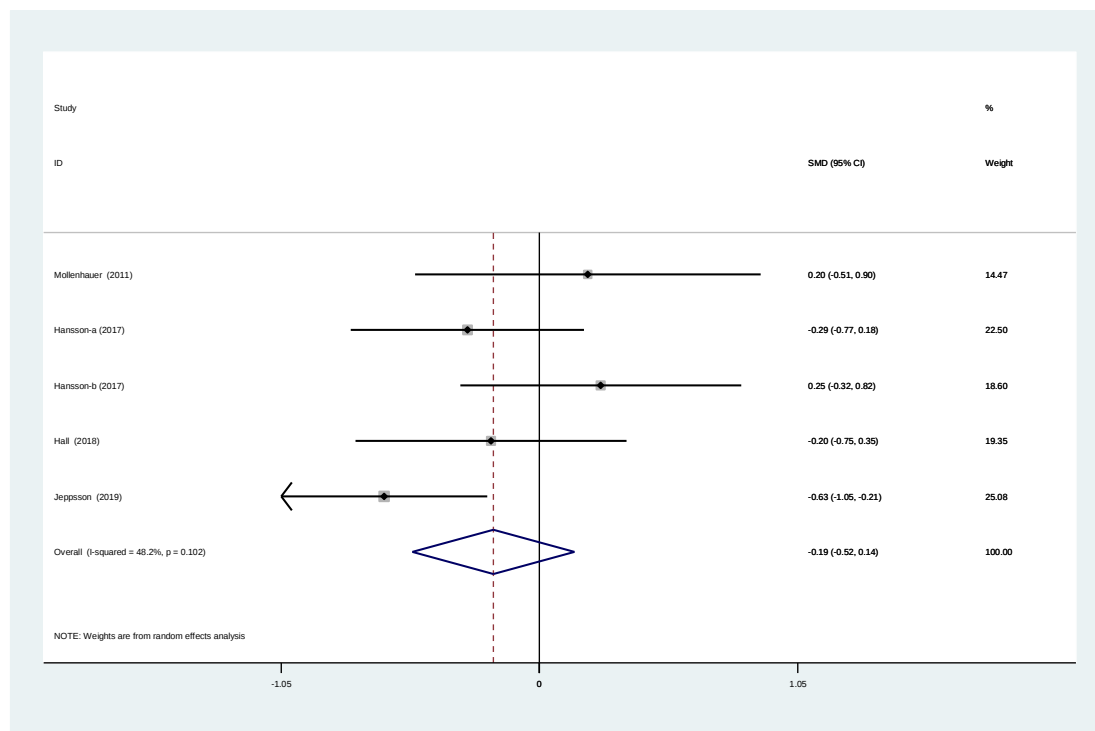
(C) PD&OND group



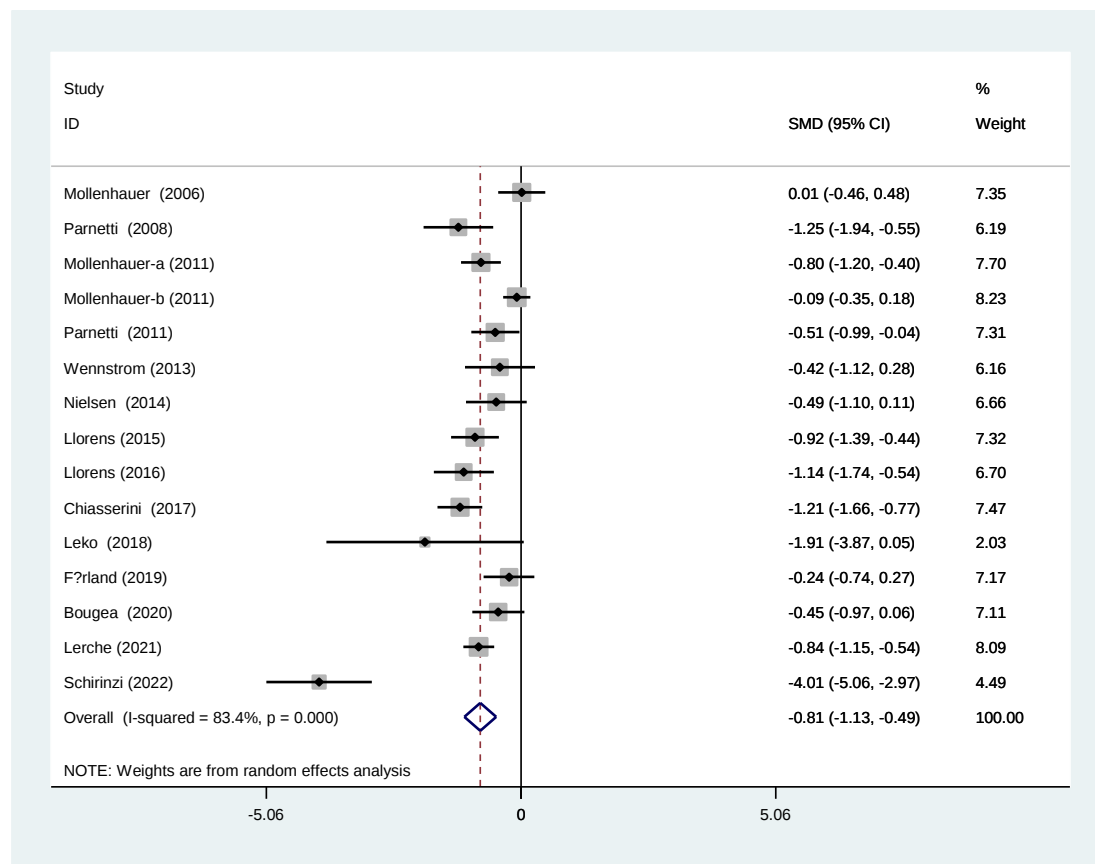
(D) PD&MSA group



(E) PD&PSP

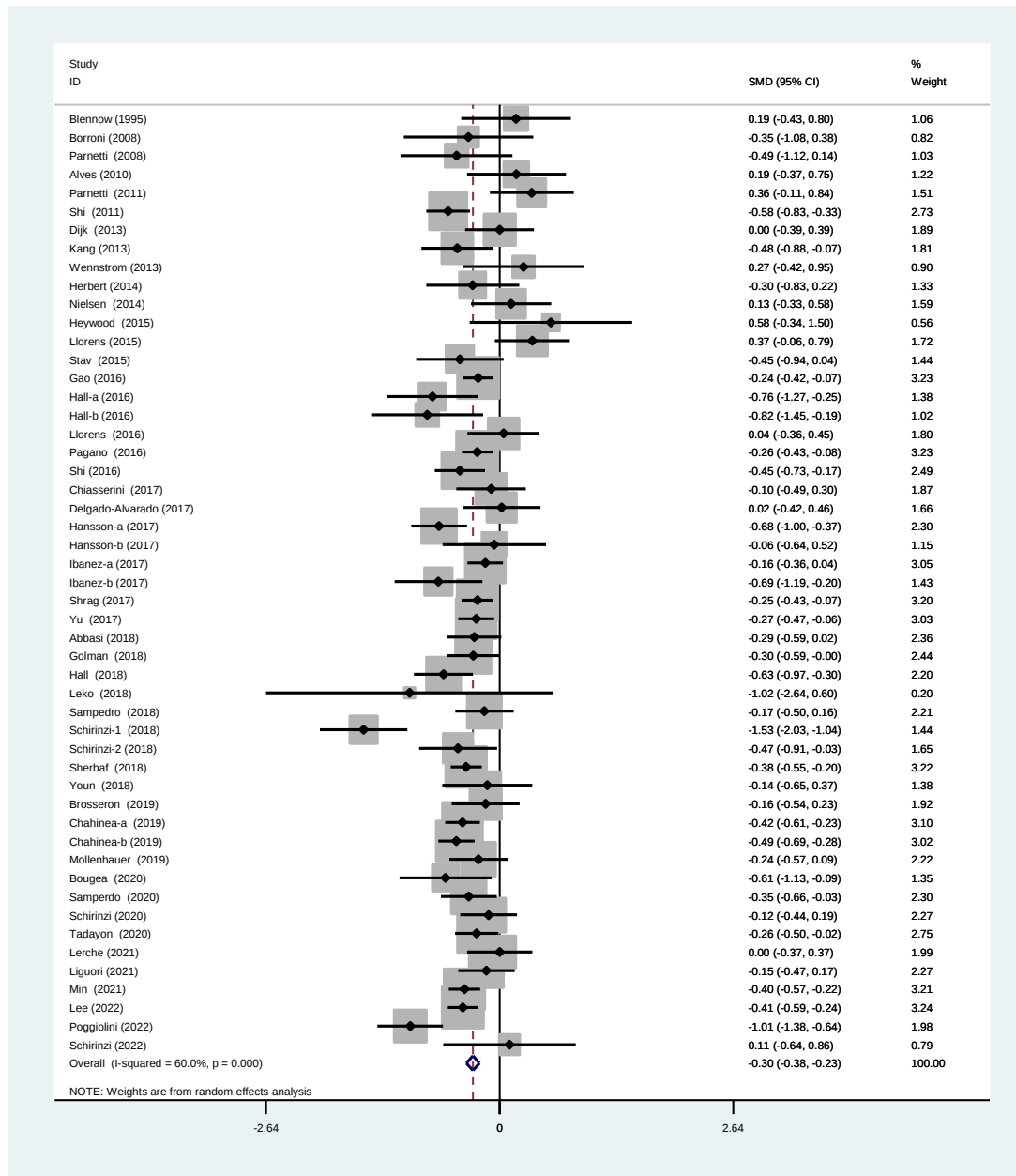


(F) PD&DLB

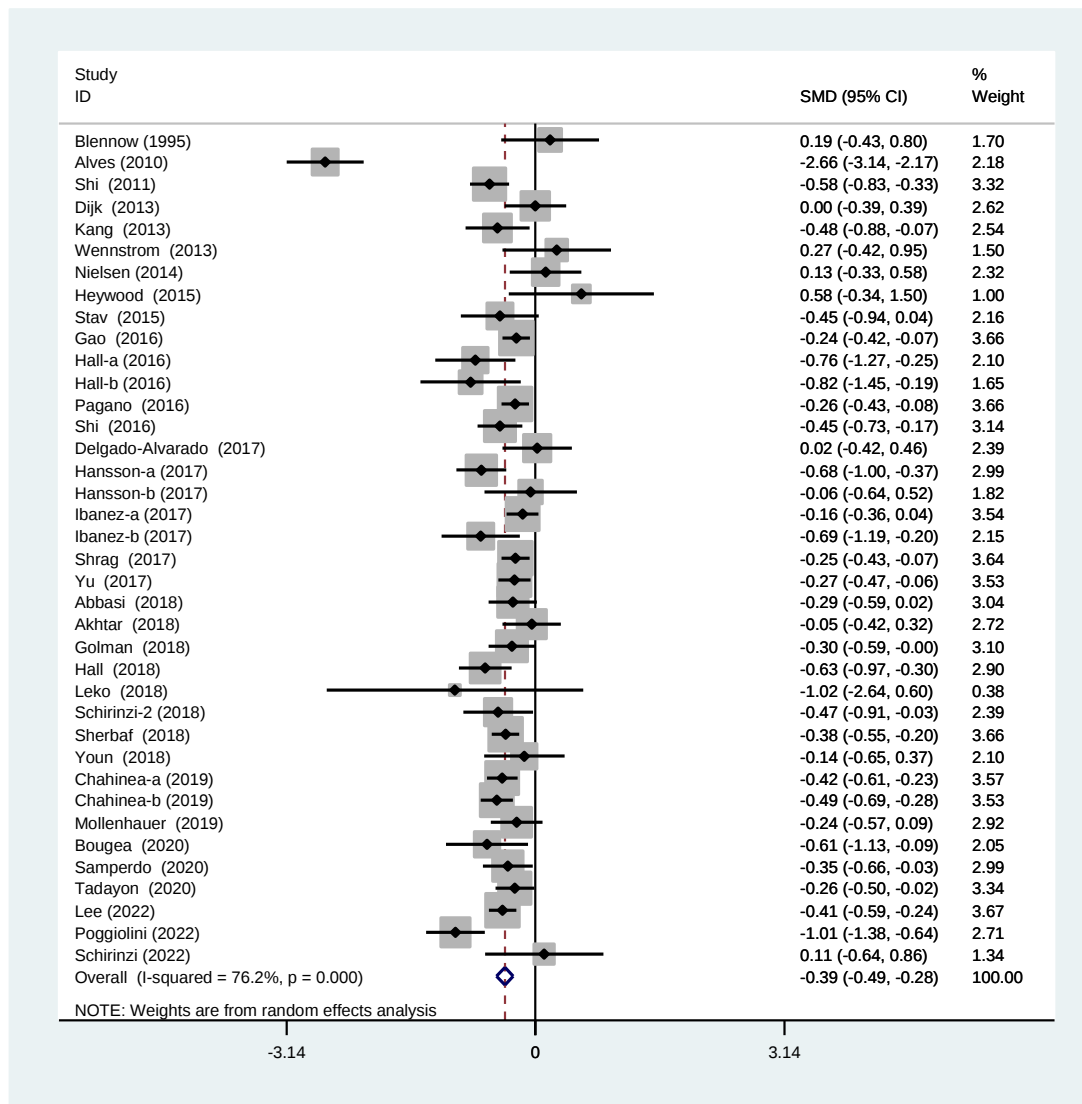


Supplementary material 8. Forest plot for p-tau in PD& Control group (A), PD&HC group (B), PD&OND group (C), PD&MSA group(D), PD&PSP(E), PD&DLB group(F) displaying effect size (risk ratio) calculated using a random effect model. ES, effective size; CI, confidence intervals; SMD, standardized mean difference.

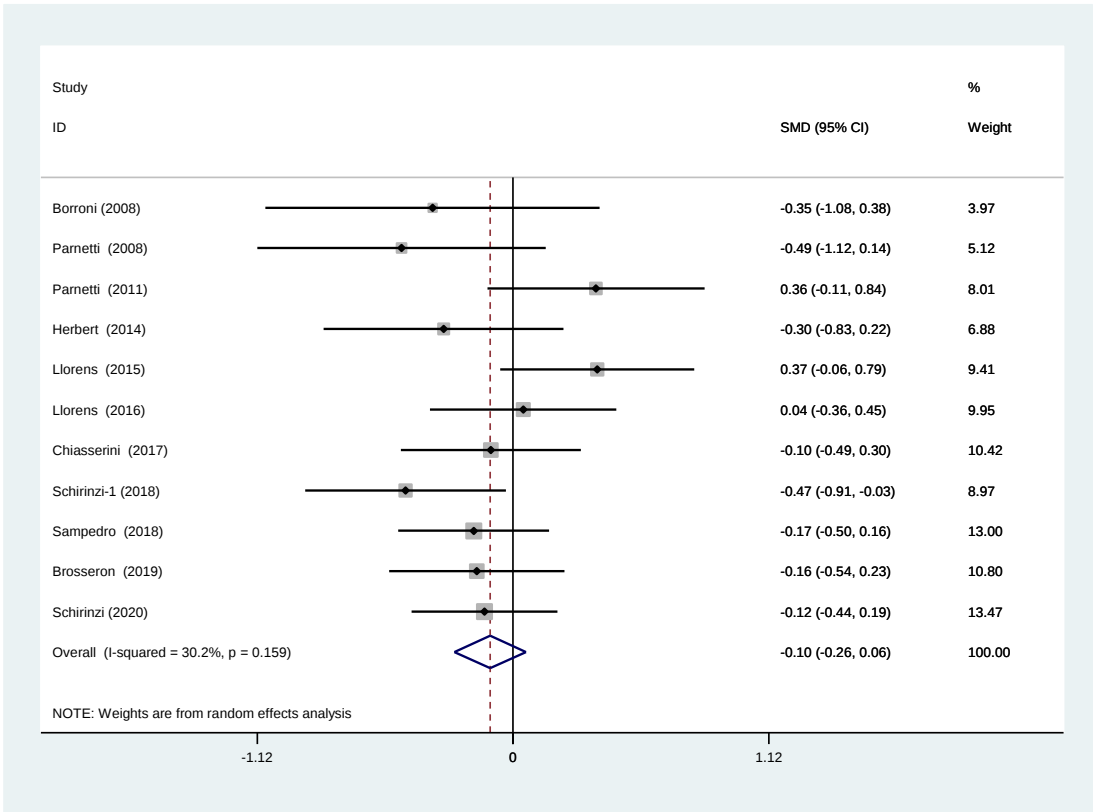
(A) PD& Control group



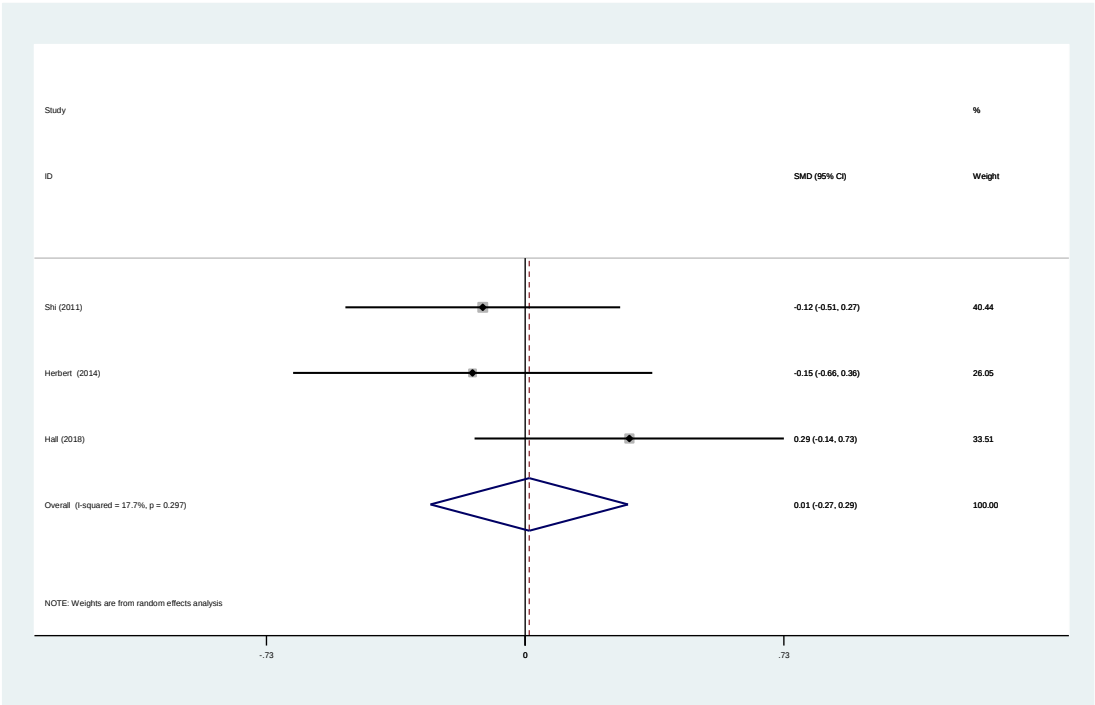
(B) PD&HC group



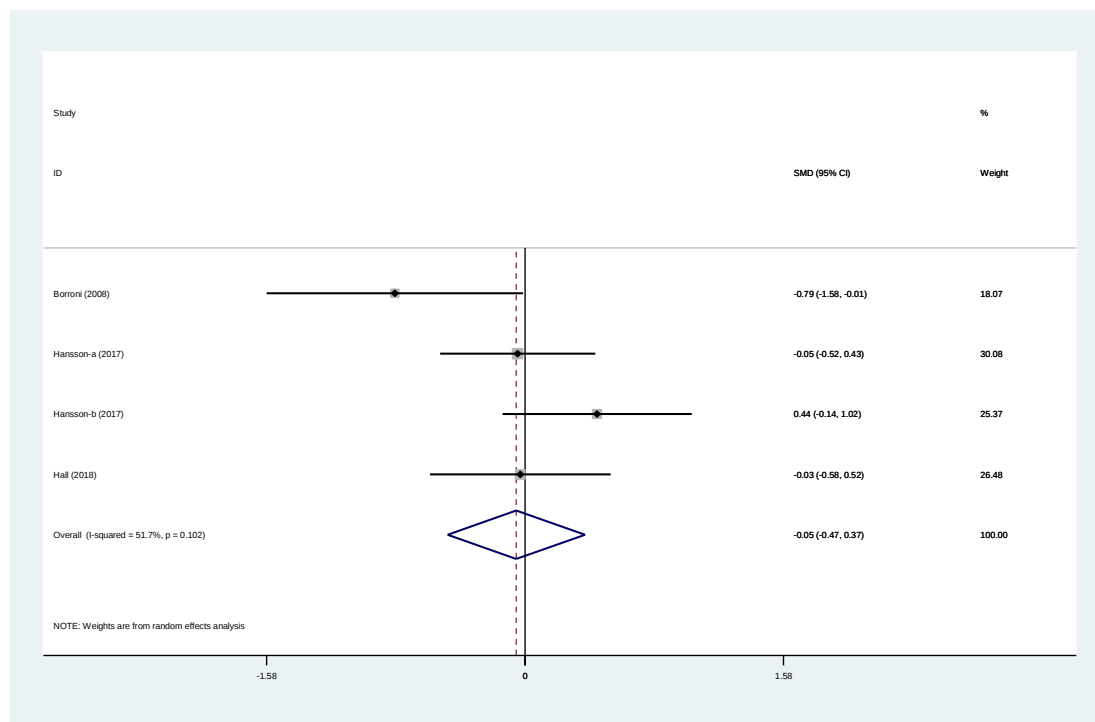
(C) PD&OND group



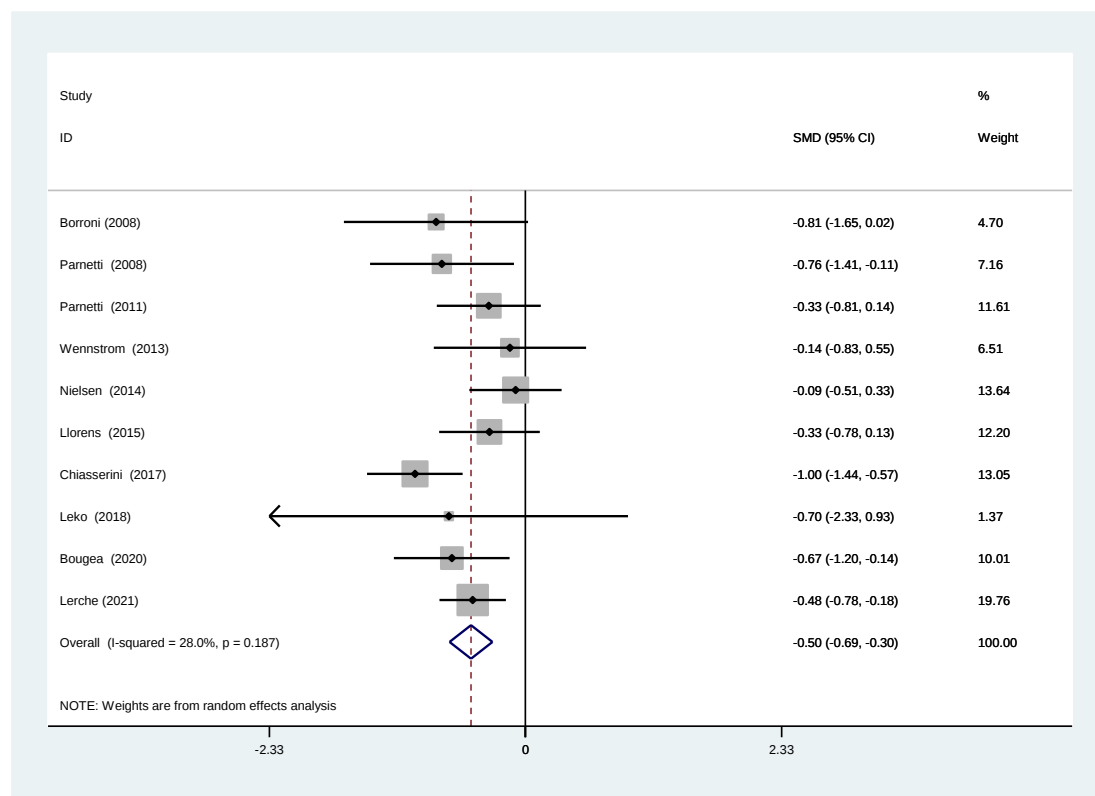
(D) PD&MSA group



(E) PD&PSP

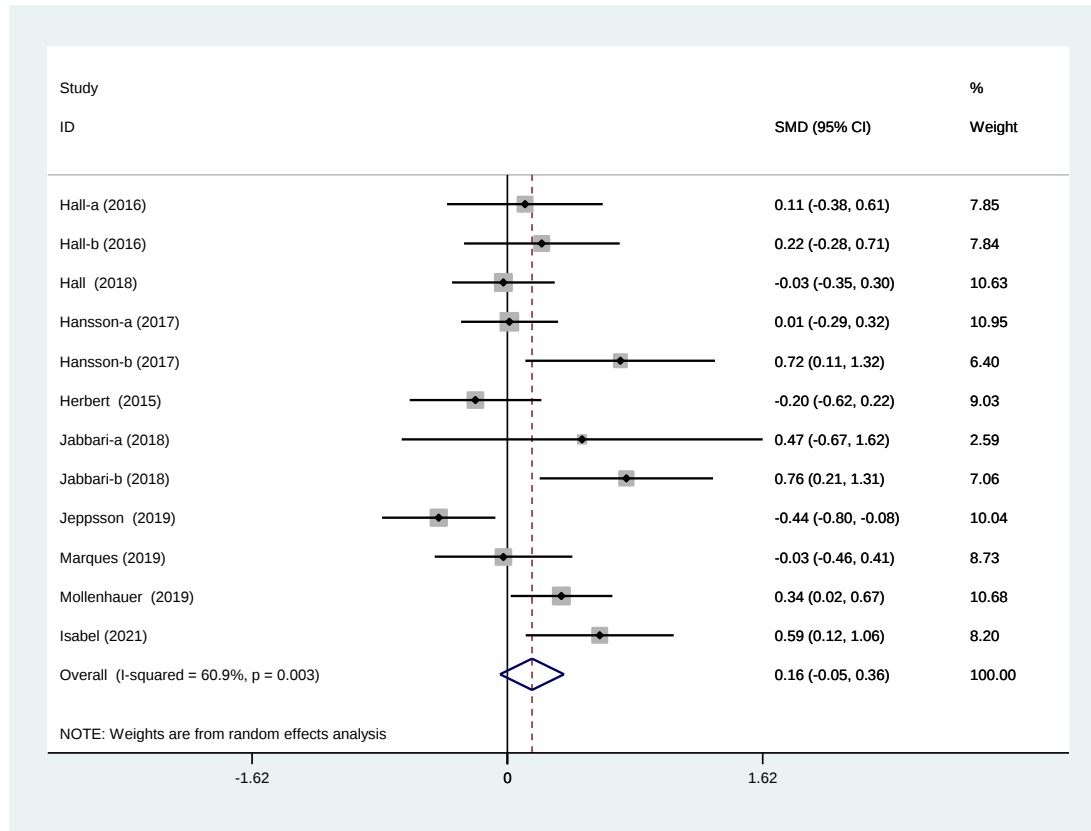


(F) PD&DLB

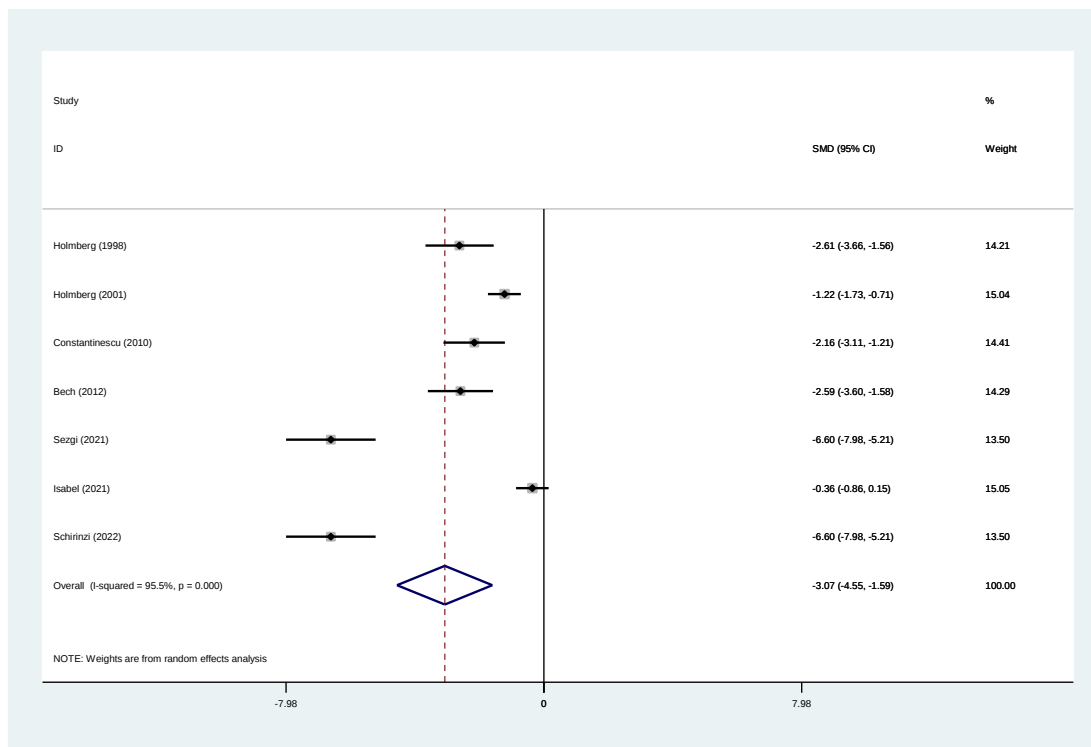


Supplementary material 9. Forest plot for NFL in PD&HC group (A), PD&MSA group(B), PD&PSP(C), PD&CBD group(D) displaying effect size (risk ratio) calculated using a random effect model. ES, effective size; CI, confidence intervals; SMD, standardized mean difference.

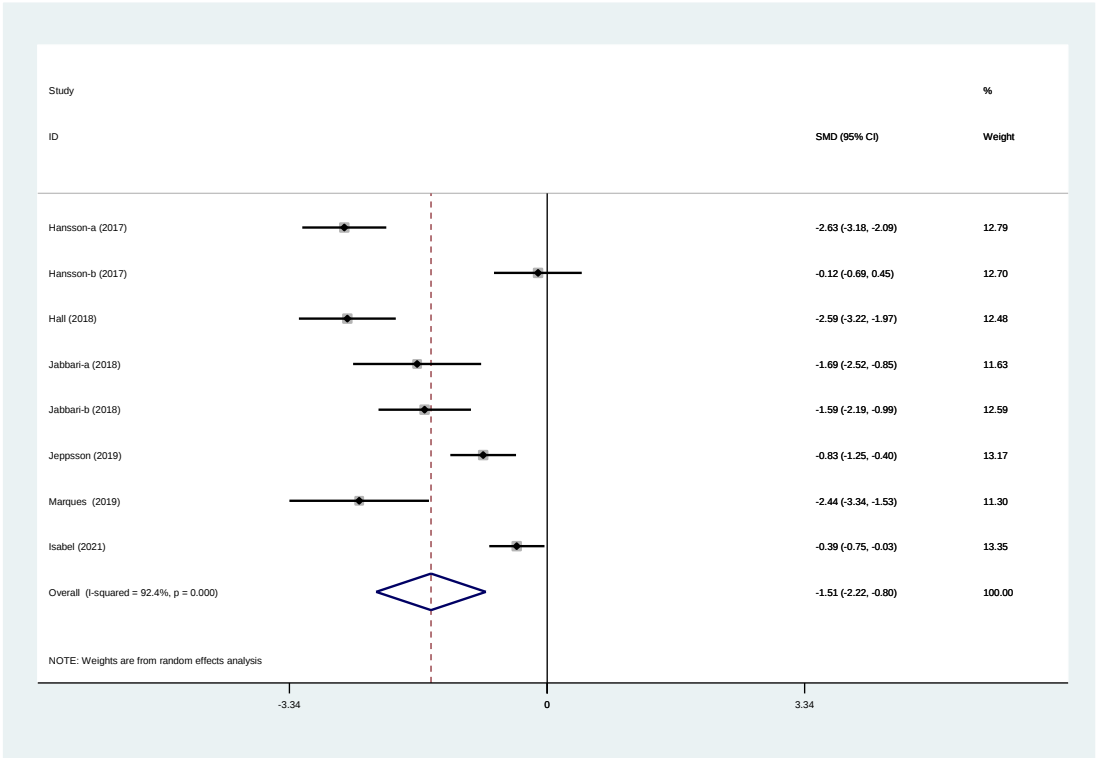
(A) PD& HC group



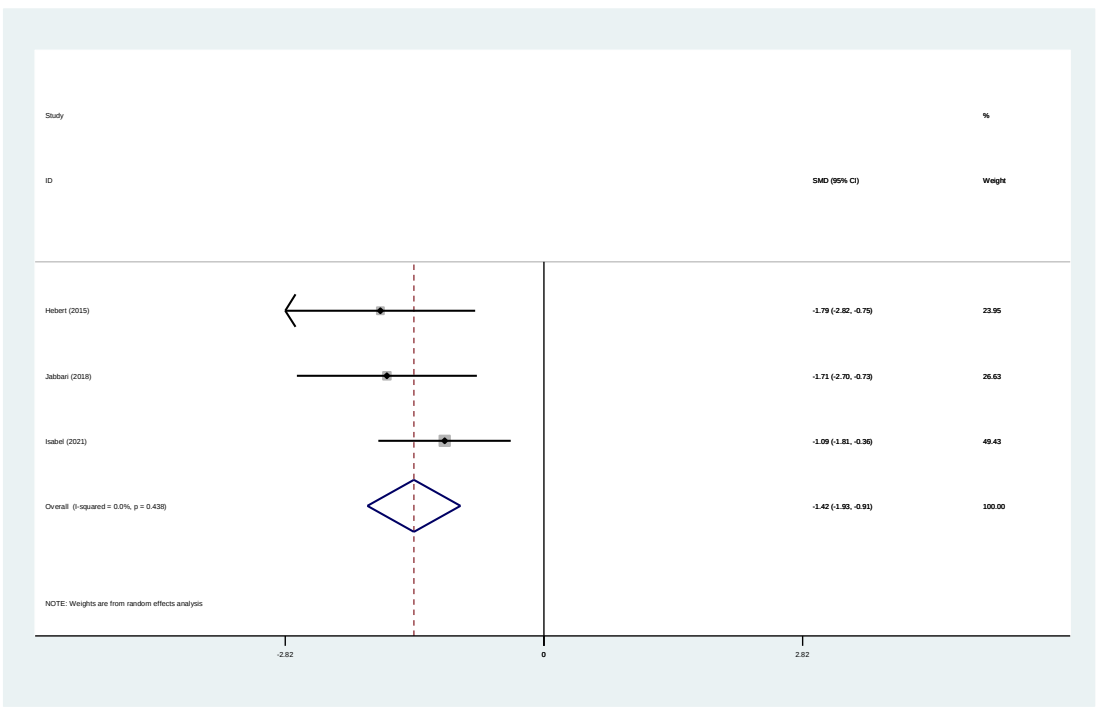
(B) PD&MSA group



(C) PD&PSP group

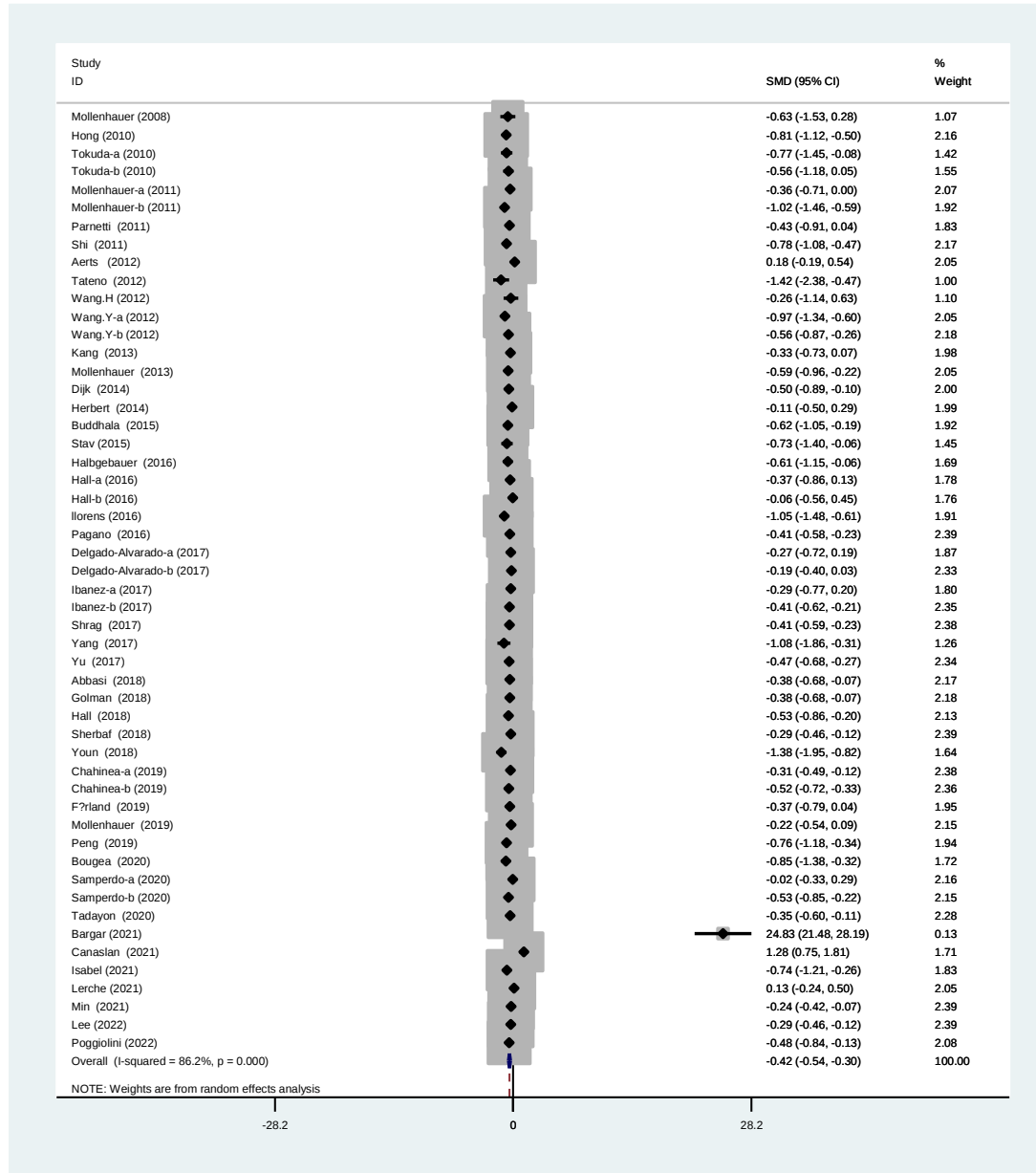


(D) PD&CBD group

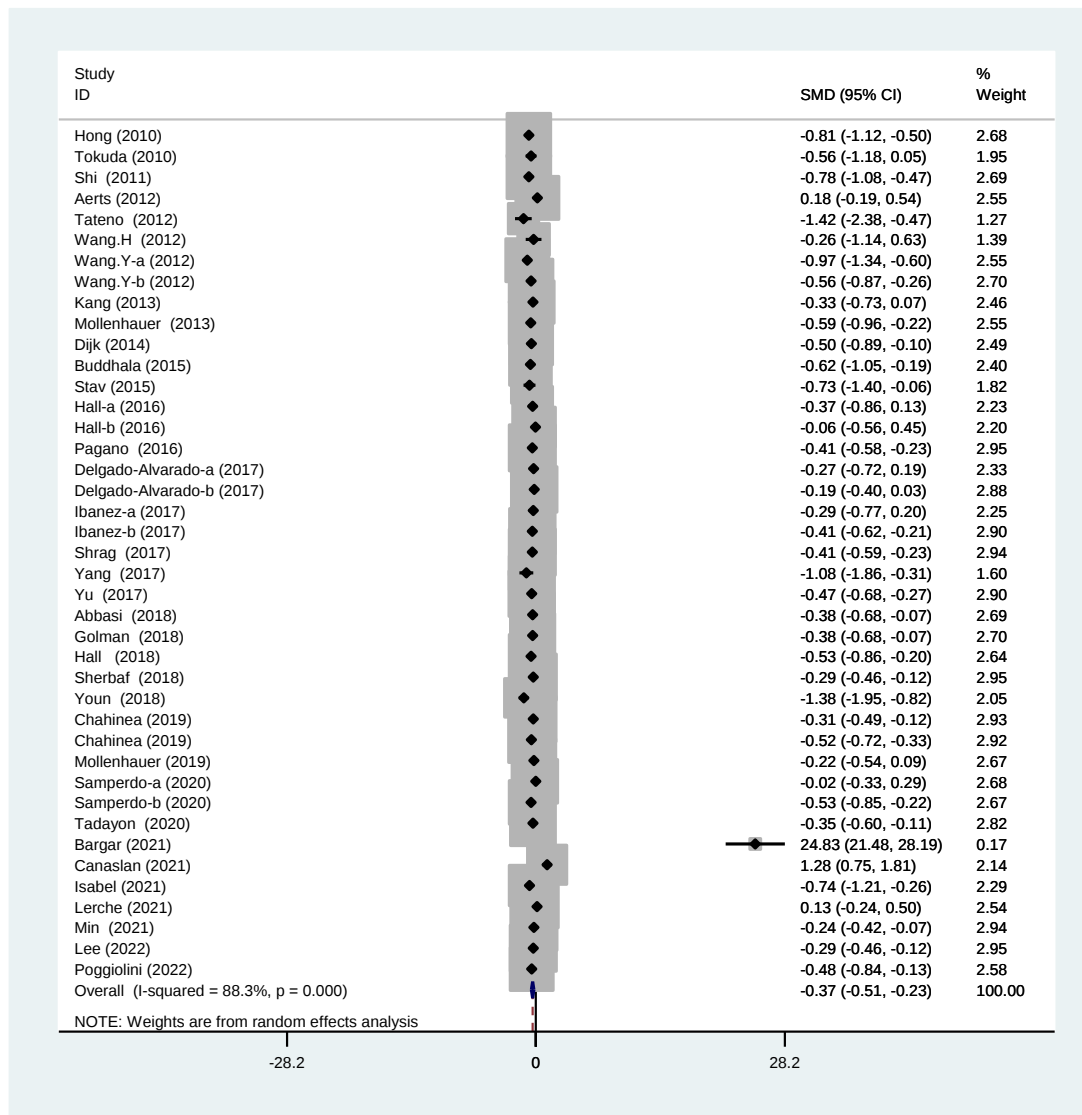


Supplementary material 10. Forest plot for t- α -syn in PD& Control group (A), PD&HC group (B), PD&OND group (C), PD&MSA group(D), PD&PSP(E), PD&DLB group(F) displaying effect size (risk ratio) calculated using a random effect model. ES, effective size; CI, confidence intervals; SMD, standardized mean difference.

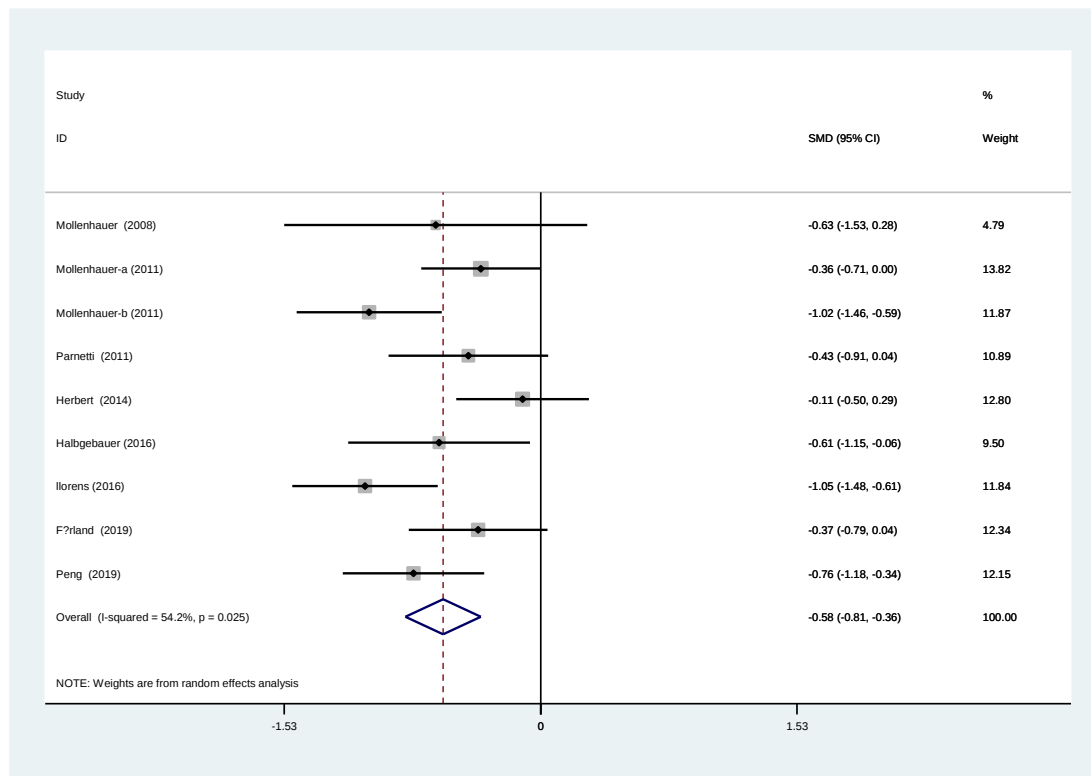
(A) PD& Control group



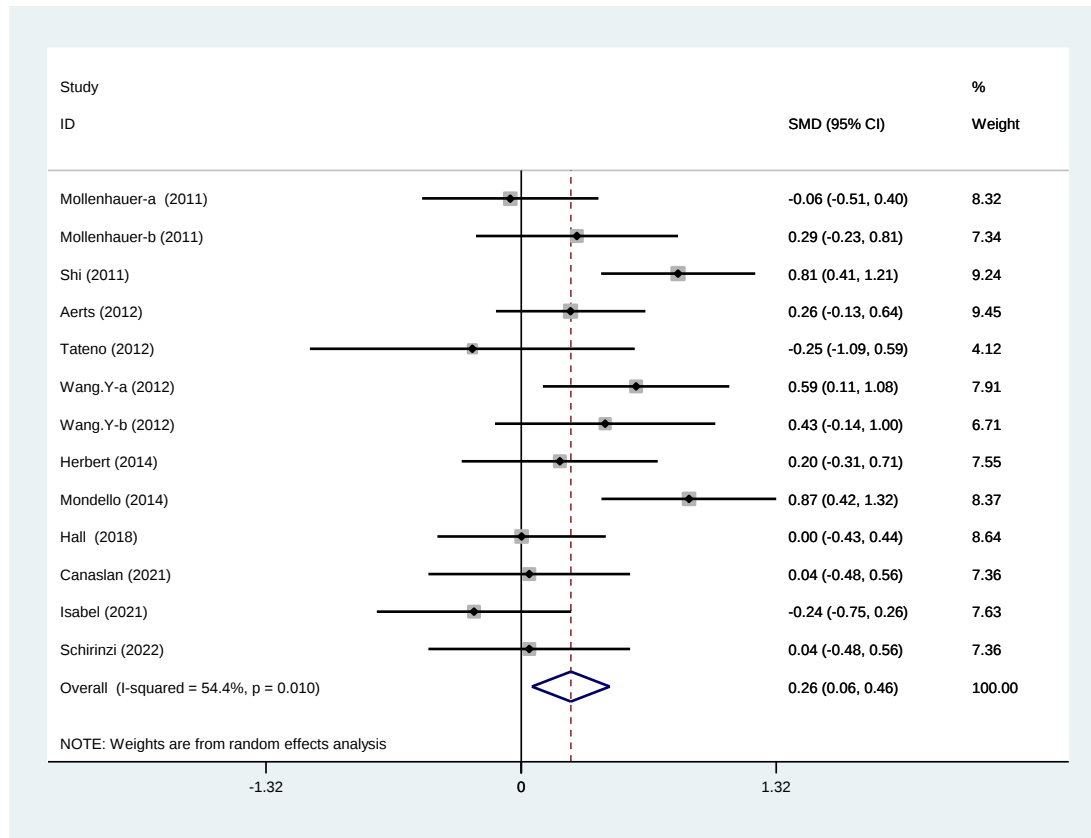
(B) PD&HC group



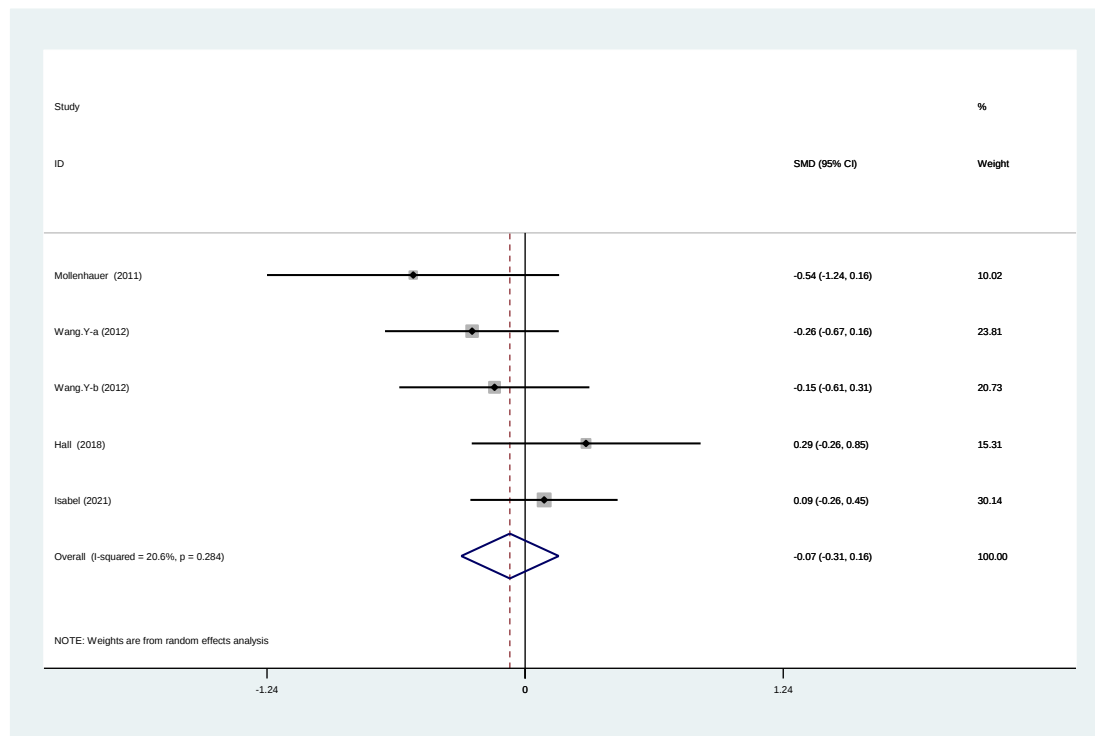
(C) PD&OND group



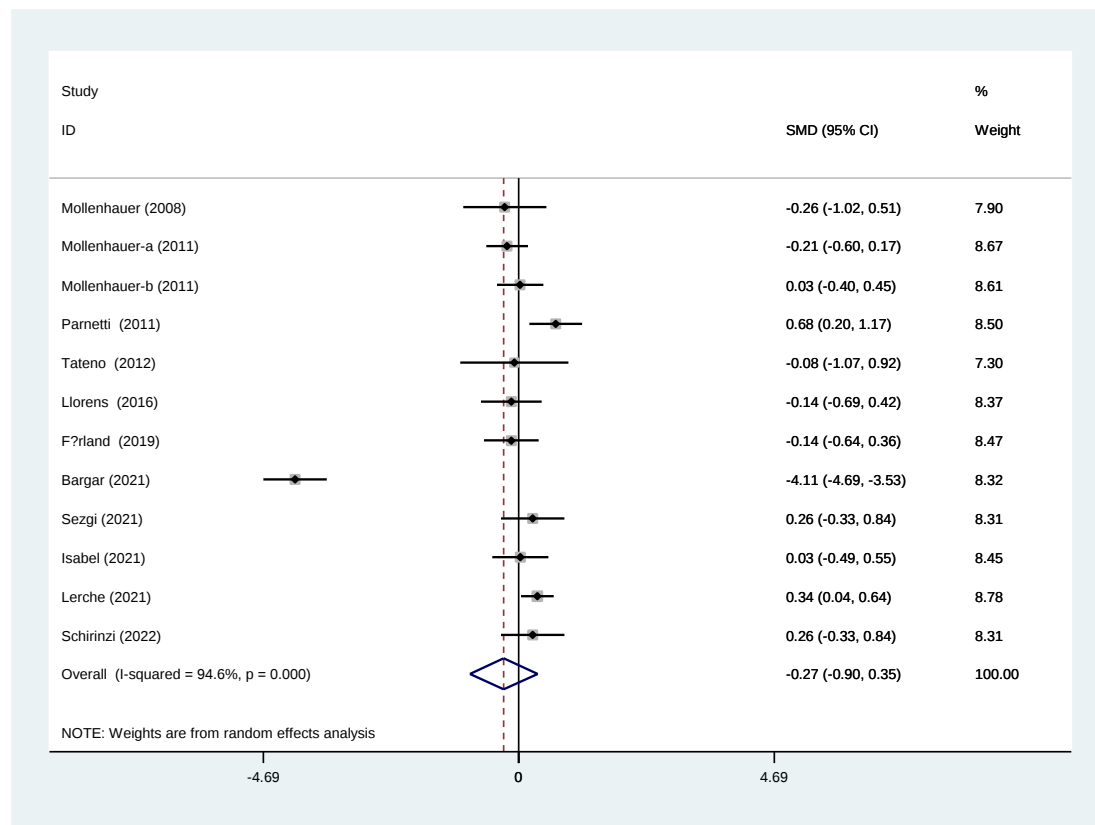
(D) PD&MSA group



(E) PD&PSP

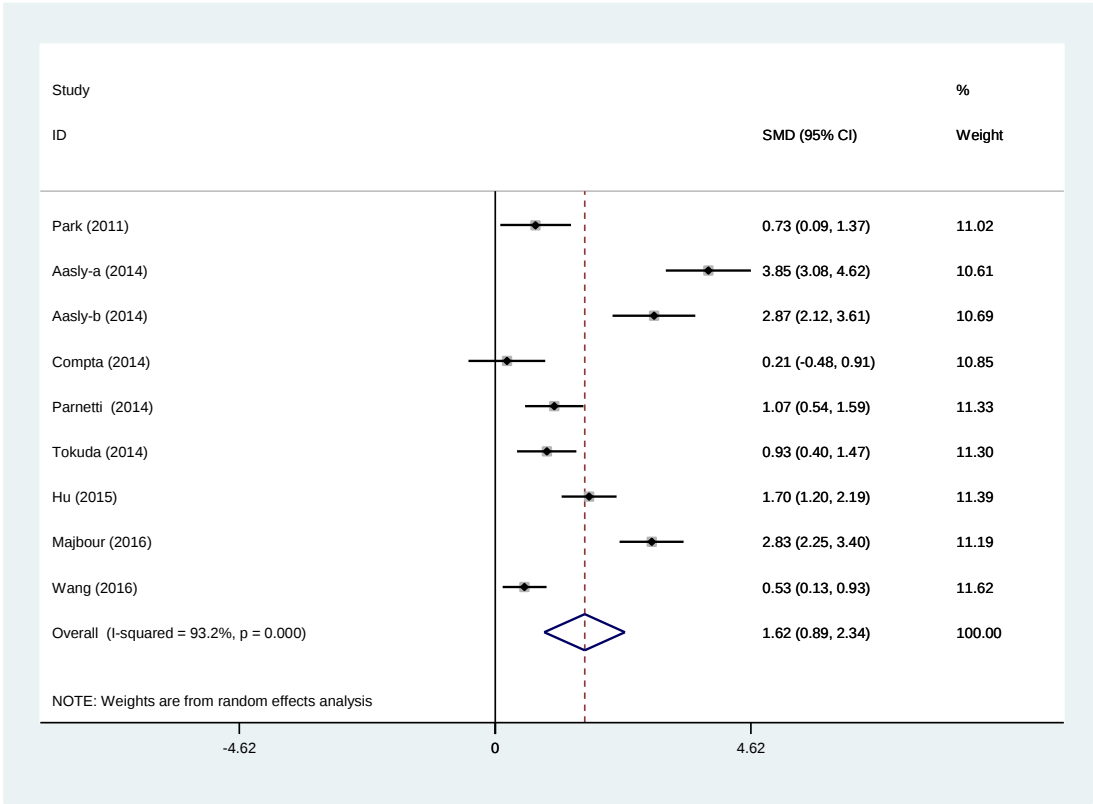


(F) PD&DLB

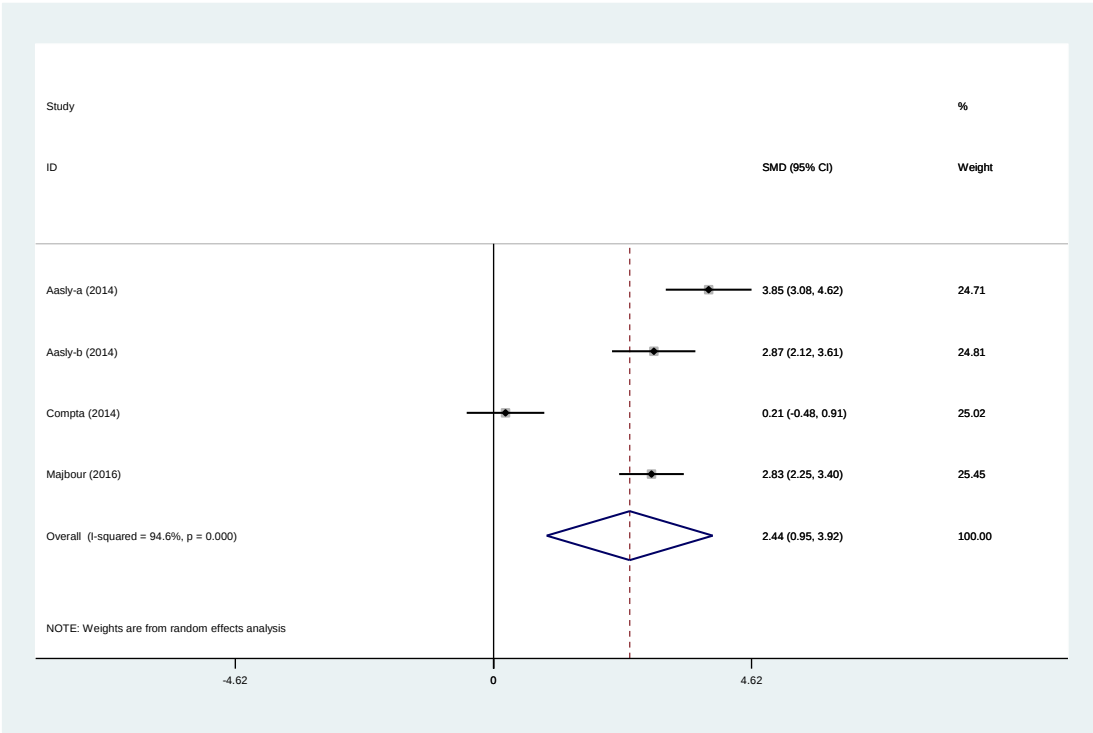


Supplementary material 11. Forest plot for o- α -syn and p- α -syn in PD& Control group. (A) o- α -syn in PD &Control group; (B) o- α -syn in PD&HC group; (C) o- α -syn in PD&OND group; (D) p- α -syn in PD &Control group; effect size (risk ratio) calculated using a random effect model. ES, effective size; CI, confidence intervals; SMD, standardized mean difference.

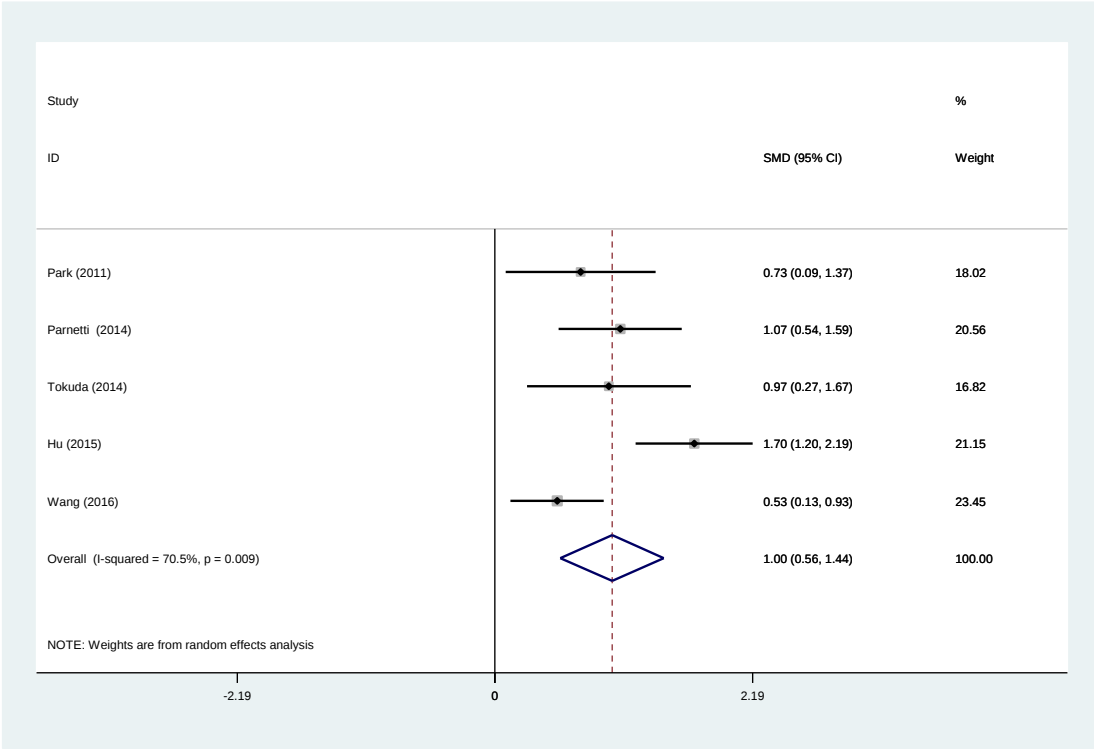
(A) o- α -syn in PD& Control group



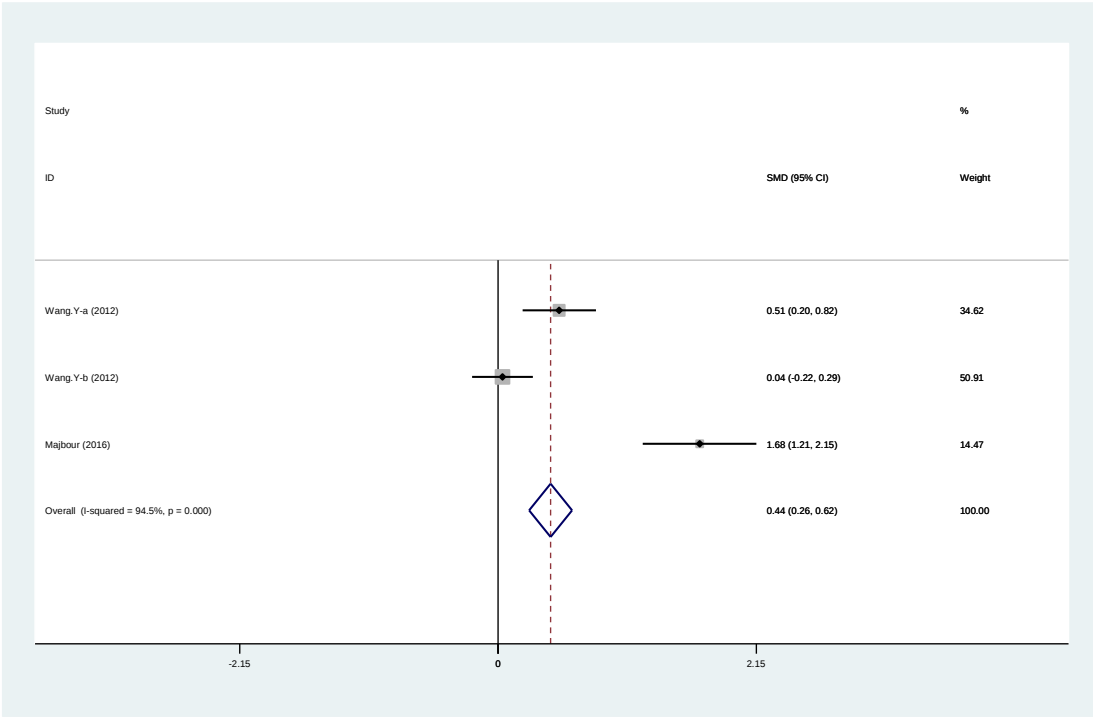
(B) o- α -syn in PD&HC group



(C) o- α -syn in PD&OND group



(D) p- α -syn in PD &Control group



Supplementary Table 12. Summary of subgroup analysis results of assay type, age and disease process. (A) Subgroup analysis results of α -syn; (B) Subgroup analysis results of NFL; (C) Subgroup analysis results of p-tau; (D) Subgroup analysis results of t-tau; (E) Subgroup analysis results of A β 42;

(A) Subgroup analysis results of α -syn;

t-α-syn					
Moderator	Subgroup	N	S	SMD (95%CI)	I²
1.Assay type	ELISA	6501	46	-0.413(-0.498 to -0.327)	66.8%
	RT-QulC	3762	2	12.118(-12.691 to 36.927)	99.5%
	Luminex	396	4	-0.668(-0.915 to -0.421)	52.1%
2.Age	High	1679	19	-0.317(-0.690 to 0.057)	93.0%
	Low	3935	21	-0.428(-0.522 to -0.334)	59.2%
3.Disease process	De novo	1453	10	-0.429(-0.569 to -0.289)	56.4%
	Non-de novo	5551	35	-0.411(-0.569 to -0.254)	88.7%

(B) Subgroup analysis results of NFL;

NFL					
Moderator	Subgroup	N	S	SMD (95%CI)	I²
1.Age	High	587	6	0.269(0.025 to 0.513)	47.8%
	Low	185	4	-0.010(-0.463 to 0.443)	77.0%
2.Disease process	De novo	1191	8	0.162(-0.030 to 0.354)	0.0%
	Non-de novo	568	7	0.327(-0.051 to 0.705)	82.4%

(C) Subgroup analysis results of p-tau;

p-tau					
Moderator	Subgroup	N	S	SMD (95%CI)	I²
1. Assay type	ELISA	6274	46	-0.301 (-0.380 to -0.222)	61.4%
	Luminex	396	3	-0.461(-0.745 to -0.178)	32.8%
	Others*	149	2	-0.139(-0.384 to 0.107)	0.0%
2.Age	High	1469	19	-0.249(-0.462 to -0.037)	79.1%
	Low	4392	28	-0.316(-0.372 to -0.259)	10.3%
3.Disease process	De novo	1191	8	-0.520(-0.271 to -0.368)	51.1%
	Non-de novo	5445	39	-0.249(-0.329 to -0.170)	56.4%

(D) Subgroup analysis results of t-tau;

t-tau					
Moderator	Subgroup	N	S	SMD (95%CI)	I ²
1. Assay type	ELISA	5919	57	-0.256(-0.345 to -0.166)	68.3%
	Luminex	396	2	-0.406(-0.615 to -0.197)	0.0%
	Others*	177	3	-0.44(-0.506 to -0.291)	0.0%
2.Age	High	1951	22	-0.265(-0.389 to 0.018)	28.7%
	Low	6925	56	-0.258(-0.325 to -0.190)	53.8%
3.Disease process	De novo	1265	7	-0.391(-0.504 to -0.278)	21.4%
	Non-de novo	6103	49	-0.287(-0.387 to -0.187)	70.4%

(E) Subgroup analysis results of A β 42;

A β 42					
Moderator	Subgroup	N	S	SMD (95%CI)	I ²
1. Assay type	ELISA	6560	57	-0.228(-0.303 to -0.153)	58.7%
	Luminex	396	2	-0.405(-0.614 to -0.196)	0.0%
	Others*	177	3	-0.328(-0.546 to -0.109)	0.0%
2.Age	High	2005	20	-0.184(-0.304 to -0.065)	53.6%
	Low	6431	51	-0.247(-0.321 to -0.173)	59.3%
3.Disease process	De novo	1206	8	-0.279(-0.396 to -0.162)	24.7%
	Non-de novo	5720	44	-0.237(-0.318 to -0.156)	59.5%

Subgroups of assay type, age and disease process based on tertiles of study averages. ES, effect size; CI, confidence intervals; S, number of included studies; N, number of patients; α -synuclein, α -syn; NFL, neurofilament light-chain protein; A β 42, the 42-amino-acid form of A β ; t-tau, total tau; p-tau, phosphorylated tau; *, Innotech Phospho-Tau (181) -assay, Fujirebio GmbH INNOTEST assay, (CSF) lactate concentration and Quantitative analysis of cerebrospinal fluid.