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# Supplementary Table 1. Included studies.

| No. | Title | Author+year | References |
| --- | --- | --- | --- |
| 1 | Evaluation of the role of plasma level of p-tau(181p) protein for clinical diagnosis of Alzheimer's disease | Peng 2005 | 1 |
| 2 | Tau is reduced in AD plasma and validation of employed ELISA methods | Sparks 2012 | 2 |
| 3 | Plasma tau levels in Alzheimer's disease | Zetterberg 2013 | 3 |
| 4 | Evaluation of Selenium, Redox Status and Their Association with Plasma Amyloid/Tau in Alzheimer's Disease | Krishnan 2014 | 4 |
| 5 | The efficacy of plasma biomarkers in early diagnosis of Alzheimer's disease | Wang 2014 | 5 |
| 6 | Plasma tau as a window to the brain-negative associations with brain volume and memory function in mild cognitive impairment and early Alzheimer's disease | Chiu 2014 | 6 |
| 7 | Plasma Aβ but not tau is related to brain PiB retention in early Alzheimer's disease | Tzen 2014 | 7 |
| 8 | Identifying biomarkers of dementia prevalent among amnestic mild cognitively impaired ethnic female patients | Grewal 2016 | 8 |
| 9 | Plasma tau in Alzheimer disease | Mattsson 2016 | 9 |
| 10 | Study on analysis of peripheral biomarkers for Alzheimer's disease diagnosis | Rani  2017 | 10 |
| 11 | Plasma levels of Aβ42 and Tau identified probable Alzheimer's dementia: Findings in two cohorts | Lue 2017 | 11 |
| 12 | Analytical performance of reagent for assaying tau protein in human plasma and feasibility study screening neurodegenerative diseases | Yang 2017 | 12 |
| 13 | Association of plasma total tau level with cognitive decline and risk of mild cognitive impairment or dementia in the Mayo Clinic study on aging | Mielke 2017 | 13 |
| 14 | Quantification of plasma phosphorylated tau to use as a biomarker for brain Alzheimer pathology: Pilot case-control studies including patients with Alzheimer's | Tatebe 2017 | 14 |
| 15 | Assay of Plasma Phosphorylated Tau Protein (Threonine 181) and Total Tau Protein in Early-Stage Alzheimer's Disease | Yang 2018 | 15 |
| 16 | Plasma phospho-tau181 increases with Alzheimer's disease clinical severity and is associated with tau- and amyloid-positron emission tomography | Mielke 2018 | 16 |
| 17 | Brain Amyloid-beta Deposition and Blood Biomarkers in Patients with Clinically Diagnosed Alzheimer's Disease | Li 2019 | 17 |
| 18 | Potential Value of Plasma Amyloid-beta, Total Tau, and Neurofilament Light for Identification of Early Alzheimer's Disease | Shi 2019 | 18 |
| 19 | Associations between Plasma Biomarkers and Cognition in Patients with Alzheimer's Disease and Amnestic Mild Cognitive Impairment: A Cross-Sectional and Longitudinal Study | Tsai 2019 | 19 |
| 20 | Plasma tau complements CSF tau and P-tau in the diagnosis of Alzheimer's disease | Fossati 2019 | 20 |
| 21 | Discriminative Accuracy of Plasma Phospho-tau217 for Alzheimer Disease vs Other Neurodegenerative Disorders | Palmqvist 2020 | 21 |
| 22 | Blood phosphorylated tau 181 as a biomarker for Alzheimer's disease: a diagnostic performance and prediction modelling study using data from four prospective cohorts | Karikari 2020 | 22 |
| 23 | Blood plasma phosphorylated-tau isoforms track CNS change in Alzheimer's disease | Barthélemy 2020 | 23 |
| 24 | Diagnostic value of plasma phosphorylated tau181 in Alzheimer's disease and frontotemporal lobar degeneration | Thijssen 2020 | 24 |
| 25 | The Validation of Multifactor Model of Plasma A beta(42) and Total-Tau in Combination With MoCA for Diagnosing Probable Alzheimer Disease | Jiao 2020 | 25 |
| 26 | Plasma p-tau181 accurately predicts Alzheimer's disease pathology at least 8 years prior to post-mortem and improves the clinical characterisation of cognitive decline | Rodriguez 2020 | 26 |
| 27 | Classifications of Neurodegenerative Disorders Using a Multiplex Blood Biomarkers-Based Machine Learning Model | Lin 2020 | 27 |
| 28 | A longitudinal examination of plasma neurofilament light and total tau for the clinical detection and monitoring of Alzheimer's disease | Sugarman 2020 | 28 |
| 29 | Longitudinal plasma p-tau217 is increased in early stages of Alzheimer's disease | Carlgren 2020 | 29 |
| 30\* | Plasma P-tau181 in Alzheimer's disease: relationship to other biomarkers, differential diagnosis, neuropathology and longitudinal progression to Alzheimer's dementia\* | Janelidze 2020\* | 30 |
| 31 | Changes in Plasma Amyloid and Tau in a Longitudinal Study of Normal Aging, Mild Cognitive Imparment, and Alzheimer's Disease | Chen 2020 | 31 |
| 32 | The Correlations Between Plasma Fibrinogen With Amyloid-Beta and Tau Levels in Patients With Alzheimer's Disease | Fan 2020 | 32 |
| 33 | Indicators of rapid cognitive decline in amnestic mild cognitive impairment: The role of plasma biomarkers using magnetically labeled immunoassays | [Tsai 2020](https://pubmed.ncbi.nlm.nih.gov/?term=Tsai+CL&cauthor_id=32592947) | 33 |
| 34 | Plasma Tau and Neurofilament Light in Frontotemporal Lobar Degeneration and Alzheimer Disease | [Gala 2021](https://pubmed.ncbi.nlm.nih.gov/?term=Ill%C3%A1n-Gala+I&cauthor_id=33199433) | 34 |
| 35 | Diagnostic performance and prediction of clinical progression of plasma phospho-tau181 in the Alzheimer's Disease Neuroimaging Initiative | [Karikari 2021](https://pubmed-ncbi-nlm-nih-gov-443.webvpn.bjmu.edu.cn/?sort=date&term=Karikari+TK&cauthor_id=33106600) | 35 |
| 36 | Synergistic Association between Plasma Aβ(1-42) and p-tau in Alzheimer's Disease but Not in Parkinson's Disease or Frontotemporal Dementia | Chiu 2021 | 36 |
| 37 | Plasma neurofilament light and phosphorylated tau 181 as biomarkers of Alzheimer's disease pathology and clinical disease progression | [Clark 2021](https://www-ncbi-nlm-nih-gov-443.webvpn.bjmu.edu.cn/pubmed/?term=Clark%20C%5bAuthor%5d&cauthor=true&cauthor_uid=33766131) | 37 |
| 38 | Plasma Levels of Amyloid-β Peptides and Tau Protein in Mexican Patients with Alzheimer's Disease | [Mendieta 2021](https://pubmed-ncbi-nlm-nih-gov-443.webvpn.bjmu.edu.cn/?sort=date&term=Castillo-Mendieta+T&cauthor_id=34151786) | 38 |
| 39 | Plasma p-tau181, p-tau217, and other blood-based Alzheimer's disease biomarkers in a multi-ethnic, community study | [Brickman 2021](https://pubmed-ncbi-nlm-nih-gov-443.webvpn.bjmu.edu.cn/?sort=date&term=Brickman+AM&cauthor_id=33580742) | 39 |
| 40 | Prediction of future Alzheimer's disease dementia using plasma phospho-tau combined with other accessible measures | [Palmqvist 2021](https://pubmed-ncbi-nlm-nih-gov-443.webvpn.bjmu.edu.cn/?sort=date&term=Palmqvist+S&cauthor_id=34031605) | 40 |
| 41 | Longitudinal plasma phosphorylated tau 181 tracks disease progression in Alzheimer's disease | Chen 2021 | 41 |
| 42 | Detecting amyloid positivity in early Alzheimer's disease using combinations of plasma Aβ42/Aβ40 and p-tau | Janelidze 2021-1 | 42 |
| 43 | Associations of Plasma Phospho-Tau217 Levels With Tau Positron Emission Tomography in Early Alzheimer Disease | Janelidze 2021-2 | 43 |
| 44 | Plasma Biomarkers of Alzheimer's Disease in African Americans | Deniz 2021 | 44 |
| 45 | Plasma p-tau231: a new biomarker for incipient Alzheimer's disease pathology | Ashton 2021 | 45 |
| 46 | Blood biomarkers for dementia in Hispanic and non-Hispanic White adults | Gonzales 2021 | 46 |
| 47 | The diagnostic and prognostic capabilities of plasma biomarkers in Alzheimer's disease | Simrén2021 | 47 |
| 48 | Longitudinal Associations of Blood Phosphorylated Tau181 and Neurofilament Light Chain With Neurodegeneration in Alzheimer Disease | Moscoso 2021-1 | 48 |
| 49 | Plasma phosphorylated tau181 and neurodegeneration in Alzheimer's disease | Hansson 2021 | 49 |
| 50 | Plasma levels of phosphorylated tau 181 are associated with cerebral metabolic dysfunction in cognitively impaired and amyloid-positive individuals | Lussier 2021 | 50 |
| 51 | Plasma pTau181 predicts cortical brain atrophy in aging and Alzheimer’s disease | Tissot 2021 | 51 |
| 52 | The value of alzheimer's disease-associated neurofilament protein combined with AB1-42/P-TAU-181 ratio for the diagnosis of alzheimer's | Yan 2021 | 52 |
| 53 | Plasma P-tau181 to A beta 42 ratio is associated with brain amyloid burden and hippocampal atrophy in an Asian cohort of Alzheimer's disease patients with concomitant cerebrovascular disease | Chong 2021 | 53 |
| 54 | Association between polygenic risk score of Alzheimer's disease and plasma phosphorylated tau in individuals from the Alzheimer's Disease Neuroimaging Initiative | Zettergren 2021 | 54 |
| 55 | Time course of phosphorylated-tau181 in blood across the Alzheimer's disease spectrum | Moscoso 2021-2 | 55 |
| 56 | Detection of beta-amyloid positivity in Alzheimer's Disease Neuroimaging Initiative participants with demographics, cognition, MRI and plasma biomarkers | Tosun 2021 | 56 |

\*There are two separate studies in this paper, so we treat them as two different studies.

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# Supplementary Table 2. Characteristics of included studies.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| No. | Year | First author | Study design | Region | Biomarker | | Methods | Center | Sample size,n | | Cohort | Age, mean(SD),year |
| 1 | 2005 | Peng | Cross-sectional | China | p-tau181 | | ELISA | NA | 88 | | NC/AD | 77.8(4.3)/77.2(3.9) |
| 2 | 2012 | Sparks | Prospective | USA | t-tau | | ELISA | NA | 206 | | NC/MCI/AD | 78.5(7.3)/78.7(12.3)/84.4(7.1) |
| 3 | 2013 | Zetterberg | Cross-sectional | Sweden | t-tau | | Simoa | NA | 154 | | NC/MCI/AD | 74 (6.7)/68 (9.3)/75 (6.2) |
| 4 | 2014 | Krishnan | Cross-sectional | India | t-tau | | ELISA | NA | 105 | | NC/AD/VD | 65.22(9.34)/71.00(8.72)/64.94(12.33) |
| 5 | 2014 | Wang | Cross-sectional | China | t-tau,  p-tau181 | | ELISA | NA | 273 | | NC/MCI/AD | 73.7(8.4)/76.6(9.1)/73.7(9.4) |
| 6 | 2014 | Chiu | Cross-sectional | Taiwan | t-tau | | IMR | NA | 60 | | NC/MCI/AD | 64.4(9.5)/71.2(9.7)/69.3(9.4) |
| 7 | 2014 | Tzen | Cross-sectional | Taiwan | t-tau | | IMR | NA | 45 | | NC/MCI/AD | 63.7(7.9)/69.2(10.4)/64.9(11.5) |
| 8 | 2016 | Grewal | Cross-sectional | USA | t-tau,  p-tau | | ELISA | NA | 75 | | NC/MCI | 72.97(1.60)/76.23(1.47); |
| 9 | 2016 | Mattsson | Prospective | USA,  Canada | t-tau | | Simoa | ADNI | 563 | | NC/MCI/AD | 75.9(4.9)/74.7(7.5)/75.2(7.4) |
| 10 | 2016 | Mattsson | Prospective | Sweden | t-tau | | Simoa | BioFINDER | 721 | | NC/SCD/MCI/AD | 72.9(4.9)/71.2(5.5)/76.4(4.7) |
| 11 | 2017 | Rani | Cross-sectional | India | t-tau | | ELISA | NA | 90 | | NC/AD | 67.46(8.29)/71.73 (8.84) |
| 12 | 2017 | Lue | Cross-sectional | Taiwan,  USA | t-tau | | IMR | BSHRI,NTUH | 124 | | NC/AD | 68.1(1.3)/75.9(1.4) |
| 13 | 2017 | Yang | Cross-sectional | Taiwan | t-tau | | IMR | NTUH | 215 | | NC/MCI/AD | 64.6 (8.6)/71.0 (10.3)/72.2 (9.9) |
| 14 | 2017 | Mielke | Prospective | USA | t-tau | | Simoa | MCSA | 458 | | NC/MCI | 80.8(4.8)/79.9(7.4) |
| 15 | 2017 | Tatebe | Cross-sectional | Japan | p-tau181 | | Simoa | NA | 35 | | NC/AD | 76.3(3.2)/77.4(7.7) |
| 16 | 2018 | Yang | Cross-sectional | Taiwan | p-tau181;  t-tau | | IMR | NA | 73 | | NC/MCI/AD | 67.5(7.1)/71.0(8.7)/78.8(7.9) |
| 17 | 2018 | Mielke | Prospective | USA | p-tau181;  t-tau | | Simoa,MSD | MCSA,ADRC | 269 | | NC/MCI/AD | 71.9(9.5)/71.4(10.7)/67.7(9.2) |
| 18 | 2019 | Li | Cross-sectional | China | t-tau | | Simoa | NA | 84 | | NC/MCI/AD | 61.78(10.52)/64.60(9.3)/ 68.39(9.65) |
| 19 | 2019 | Shi | Cross-sectional | China | t-tau | | Simoa | NA | 155 | | NC/MCI | 64.77(7.40)/64.53(7.68) |
| 20 | 2019 | Tsai | Cross-sectional | Taiwan | p-tau181;  t-tau | | IMR | NA | 90 | | NC/MCI/AD | 64.4(5.7)/72.4(7.6)/77.0(8.3) |
| 21 | 2019 | Fossati | Cross-sectional | USA | t-tau | Simoa | | NA | 97 | NC/AD | | 67.71 (8.54)/72.81 (9.69) |
| 22 | 2020 | Thomas K Karikari | NA | USA | p-tau181 | Simoa | | TRIAD,  BioFINDER | 989 | TRIAD:NC/MCI/AD BioFINDER-2：NC/MCI/AD | | TRIAD: 69.2 (9.7)/72.6 (6.8)/64.6 (9.2) BioFINDER-2:63.1 (5.0)/70.6 (8.1)/74.0 (6.9)/ |
| 23 | 2020 | Nicolas R Barthélemy | Cross-sectional | Washington | t-tau;  p-tau217;  p-tau181 | MS | | NA | 92 | NC/non aMCI/pre-AD/aMCI/AD | | 73(5)/75(8)/74(6)/76(6)/74(8) |
| 24 | 2020 | Elisabeth H Thijssen | Cross-sectional | NA | p-tau181 | MSD | | NA | 362 | NC/MCI/AD | | 60.6(22)/60.8(14)/65.0 (9) |
| 25 | 2020 | Jiao | Cross-sectional | China | t-tau | IMR | | NA | 97 | NC/AD | | 67.9(9.5)/68.1(9.0) |
| 26 | 2020 | Rodriguez | Prospective | Sweden | p-tau181 | Simoa | | Maudsley and King’s Healthcare Partners DCR | 111 | NC/MCI/AD | | 82.2(6.5)/87.1(6.1)/81.7(7.6) |
| 27 | 2020 | Palmqvist | Cross-sectional | Sweden | p-tau217;  p-tau181;  t-tau | MSD | | BioFINDER-2 | 699 | NC/MCI/AD | | 65.97(15.49)/70.08(8.99)/74.24(5.78) |
| 28 | 2020 | Lin | Cross-sectional | Taiwan | p-tau181;  t-tau | IMR | | NA | 291 | NC/MCI/AD | | 64.0(7.8)/72.9(7.9)/75.2(11.6) |
| 29 | 2020 | Sugarman | Prospective | USA | t-tau | Simoa | | BU ADC Clinical Core Registry | 579 | NC/MCI/AD | | 72.38(7.69)/74.99(7.24)/76.74(8.12) |
| 30 | 2020 | Carlgren | Prospective | Sweden | p-tau217 | MSD | | BioFINDER | 250 | NC/MCI | | 71.53(5.11)/70.24(5.54) |
| 31 | 2020 | Janelidze | Prospective | Sweden | p-tau181 | Simoa | | BioFINDER | 182 | NC/MCI/AD | | 74.74(5.86)/73.07(7.03)/72.64(8.47) |
| 32 | 2020 | Janelidze | Prospective | Sweden | p-tau181;  t-tau | Simoa | | BioFINDER | 344 | NC/MCI | | 71.63(4.95)/71.24(6.81) |
| 33 | 2020 | Chen | Prospective | Taiwan | p-tau181,  t-tau | ELISA | | NA | 82 | NC/MCI/AD | | 75.67(7.44)/78.84(5.77)/78.98(5.47) |
| 34 | 2020 | Fan | Cross-sectional | China | t-tau | Simoa | | NA | 135 | NC/MCI | | 68.42(8.52)/66.31(9.53) |
| 35 | 2020 | [Tsai](https://pubmed.ncbi.nlm.nih.gov/?term=Tsai+CL&cauthor_id=32592947) | Prospective | Taiwan | p-tau181;  t-tau | IMR | | NA | 53 | NC/MCI/AD | | 64.6(6.3)/72.8(7.7)/72.8(7.7) |
| 36 | 2021 | [Ignacio Illán-Gala](https://pubmed.ncbi.nlm.nih.gov/?term=Ill%C3%A1n-Gala+I&cauthor_id=33199433) | Cross-sectional | USA | t-tau | Simoa | | NA | 265 | AD/NC | | 65.2(10)/52.2(13) |
| 37 | 2021 | [Thomas K Karikari](https://pubmed-ncbi-nlm-nih-gov-443.webvpn.bjmu.edu.cn/?sort=date&term=Karikari+TK&cauthor_id=33106600) | Prospective | USA,  Canada | p-tau181 | Simoa | | ANDI | 1177 | NC/MCI/AD | | 74.19(6.58)/72.48（7.56）/74.3(8.09) |
| 38 | 2021 | Ming-Jang Chiu | Cross-sectional | Taiwan,  Sweden | p-tau181 | IMR | | NA | 158 | NC/MCI/AD | | 65.1(6.8)/72.7(7.8)/76.7(7.5) |
| 39 | 2021 | Christopher Clark | Cross-sectional | Switzerland | p-tau181 | Simoa | | NA | 218 | NC/MCI | | 68.53 ( 7.31)/74 (6.6) |
| 40 | 2021 | Tzayaka Castillo-Mendieta | Cross-sectional | Mexico | t-tau;  p-tau | ELISA | | NA | 101 | NC/MCI/AD | | 80.5(8.18)/82.08(8.62)/78.0(9.07) |
| 41 | 2021 | Adam M Brickman | Cross-sectional | USA,  Spain | p-tau181;  p-tau217 | MSD | | NA | 453 | NC/AD | | Pathological status:84.93 (7.45)/87.38 (6.04) Clinical status:81.01 (6.31)/82.99 (6.49) PET amyloid status:82.16 (5.19)/84.25 (4.55) |
| 42 | 2021 | Sebastian Palmqvist | Prospective | Sweden | p-tau181;  p-tau217 | Simoa | | BioFINDER,  ANDI | 883 | AD/MCI | | biofinder:72.1 (4.91)/70.2 (5.73) ANDI:73.2 (6.98)/71.2 (7.14) |
| 43 | 2021 | Shi-Dong Chen | Prospective | USA | p-tau;  t-tau | Simoa | | ADNI | 1184 | NC/MCI/AD | | 74.9(0.33)/72.9(0.34)/75.3(0.53) |
| 44 | 2021 | Shorena Janelidze-1 | Cross-sectional | Sweden | p-tau217 | MSD | | BioFINDER | 895 | NC/MCI | | BioFINDER1:72 (5.22)/71 (6.74) BioFINDER2:64 (16.38)/71 (7.48) |
| 45 | 2021 | Shorena Janelidze-2 | Prospective | Sweden | p-tau217 | MSD | | BioFINDER | 490 | NC/MCI | | 64.3(16.38) /72.1(7.77) |
| 46 | 2021 | Kaancan Deniz | Cross-sectional | USA | t-tau | Simoa | | NA | 321 | NC/AD | | 82.7(8.15)/78.2(8.97) |
| 47 | 2021 | Nicholas J Ashton | Prospective | Canada | p-tau181 | Simoa | | NA | 313 | NC/MCI/AD/non AD | | 69.2 (10.2)/69.8 (7.1)/65.7 (9.2)/66.7 (7.1) |
| 48 | 2021 | Mitzi M Gonzales | Cross-sectional | USA,  Spain | t-tau | Simoa | | NA | 1843 | NC/MCI/AD | | 63(8)/72(8)/70(9) 73(9)/75(8)/75(9) |
| 49 | 2021 | Joel Simrén | Prospective | Finland,  Italy,  England | p-tau181 | Simoa | | NA | 309 | NC/MCI/AD | | 73 (6.14)/74.47 (5.89)/76.35 |
| 50 | 2021 | Alexis Moscoso-1 | Prospective | Sweden | p-tau181 | Simoa | | ADNI | 1113 | NC/CI | | 74.8 (6.6)/73.6 (8) |
| 51 | 2021 | Oskar Hansson | Prospective | Sweden | p-tau181 | Simoa | | ADNI | 1067 | NC/MCI/AD | | 73.6(5.8)/71.9(7.4)/74.4(8.2) |
| 52 | 2021 | Firoza Z Lussier | Cross-sectional | Sweden | p-tau181 | Simoa | | ADNI | 1212 | Cross-sectional：NC/MCI Longitudinal:  NC/MCI | | Cross-sectional:73.00(7.48)/72.48(7.81) Longitudinal：75.12(7.83)/71.59(8.44) |
| 53 | 2021 | Cécile Tissot | Cross-sectional | NA | p-tau181 | Simoa | | ADNI | 1122 | NC/MCI | | 74.40 (6.50)/73.61 (7.94) |
| 54 | 2021 | Congy ang yan | Cross-sectional | China | p-tau181 | ELISA | | NA | 105 | NC/AD | | 66.46(4.23)/68.12(4.25) |
| 55 | 2021 | Joyce R. Chong | Cross-sectional | Singapore | p-tau181;  t-tau | Simoa | | NA | 200 | NC/MCI/AD/VAD | | 74(6)/76(6)/77(8)/75(9) |
| 56 | 2021 | Anna Zettergren | Cross-sectional | Sweden | p-tau181 | Simoa | | ADNI | 818 | NC/MCI/AD | | 73.8 (6.1)/72.6 (7.8)/75.5 (7.9) |
| 57 | 2021 | Alexis Moscoso-2 | Cross-sectional | USA,  Canada | p-tau181 | Simoa | | ADNI | 1063 | NC/MCI/AD | | 74.7 (6.7)/72.8 (7.9)/75.1 (7.8) |
| 58 | 2021 | Duygu Tosun | Cross-sectional | USA | p-tau181 | Simoa | | ADNI | 852 | NC/MCI | | 73.39(5.97)/72(7.45) |

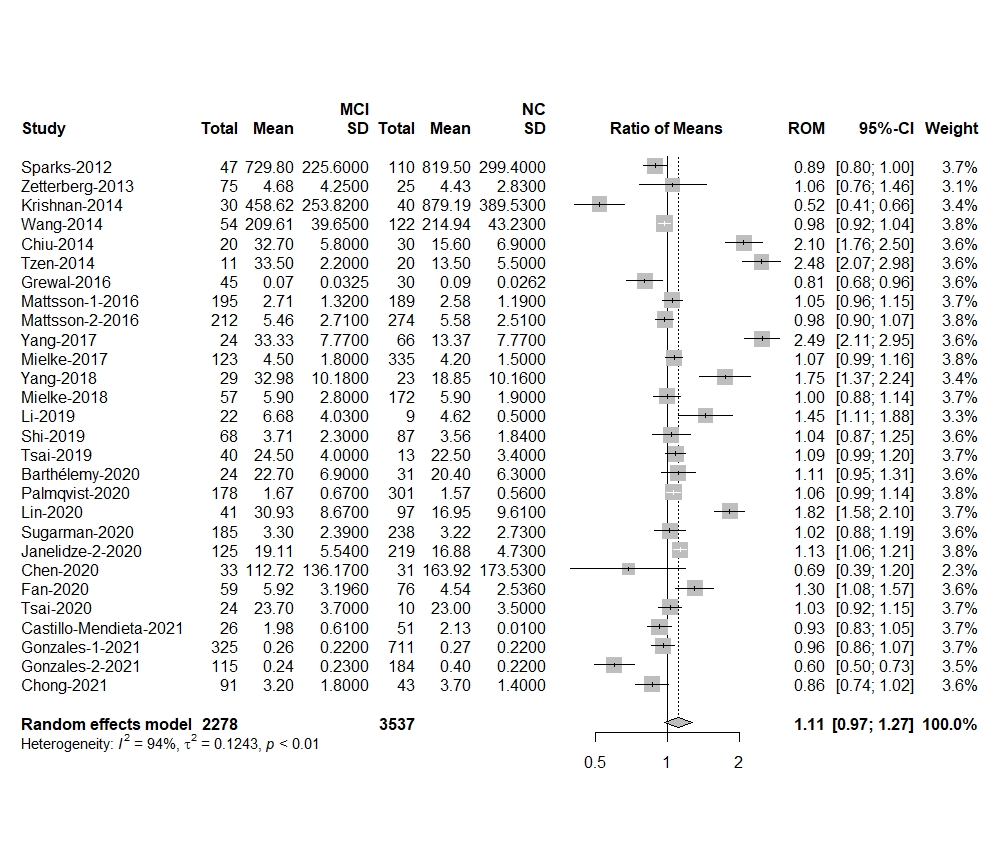
# Supplementary Table 3. The modified QUADAS

|  |  |
| --- | --- |
| Patient Selection | 1-Was a consecutive or random sample of patients enrolled? Yes/No/Unclear 2-Was a case-control design avoided? Yes/No/Unclear 3-Did the study avoid inappropriate exclusions? Yes/No/Unclear 4-Could the selection of patients have introduced bias? RISK: LOW/HIGH/UNCLEAR 5-Are there Concerns That the Included Patients and Setting Do Not Match the Review Question? CONCERN: LOW/HIGH/UNCLEAR |
| Index Test | 6-Were the index test results interpreted without knowledge of the results of the reference standard? Yes/No/Unclear 7-If a threshold was used, was it prespecified? Yes/No/Unclear 8-Could the Conduct or Interpretation of the Index Test Have Introduced Bias? RISK: LOW/HIGH/UNCLEAR have introduced bias?  9-Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW /HIGH/UNCLEAR |
| Reference Standard | 10-Is the reference standard likely to correctly classify the target condition? Yes/No/Unclear  11-Were the reference standard results interpreted without knowledge of the results of the index test? Yes/No/Unclear 12-Could the Reference Standard, Its Conduct, or Its Interpretation Have Introduced Bias? RISK: LOW /HIGH/UNCLEAR 13-Are there Concerns That the Target Condition as Defined by the Reference Standard Does Not Match the Question? CONCERN: LOW/HIGH/UNCLEAR |
| Flow and Timing | 14-Was there an appropriate interval between the index test and reference standard? Yes/No/Unclear 15-Did all patients receive the same reference standard? Yes/No/Unclear 16-Were all patients included in the analysis? Yes/No/Unclear 17-Could the Patient Flow Have Introduced Bias? RISK: LOW/HIGH/UNCLEAR |

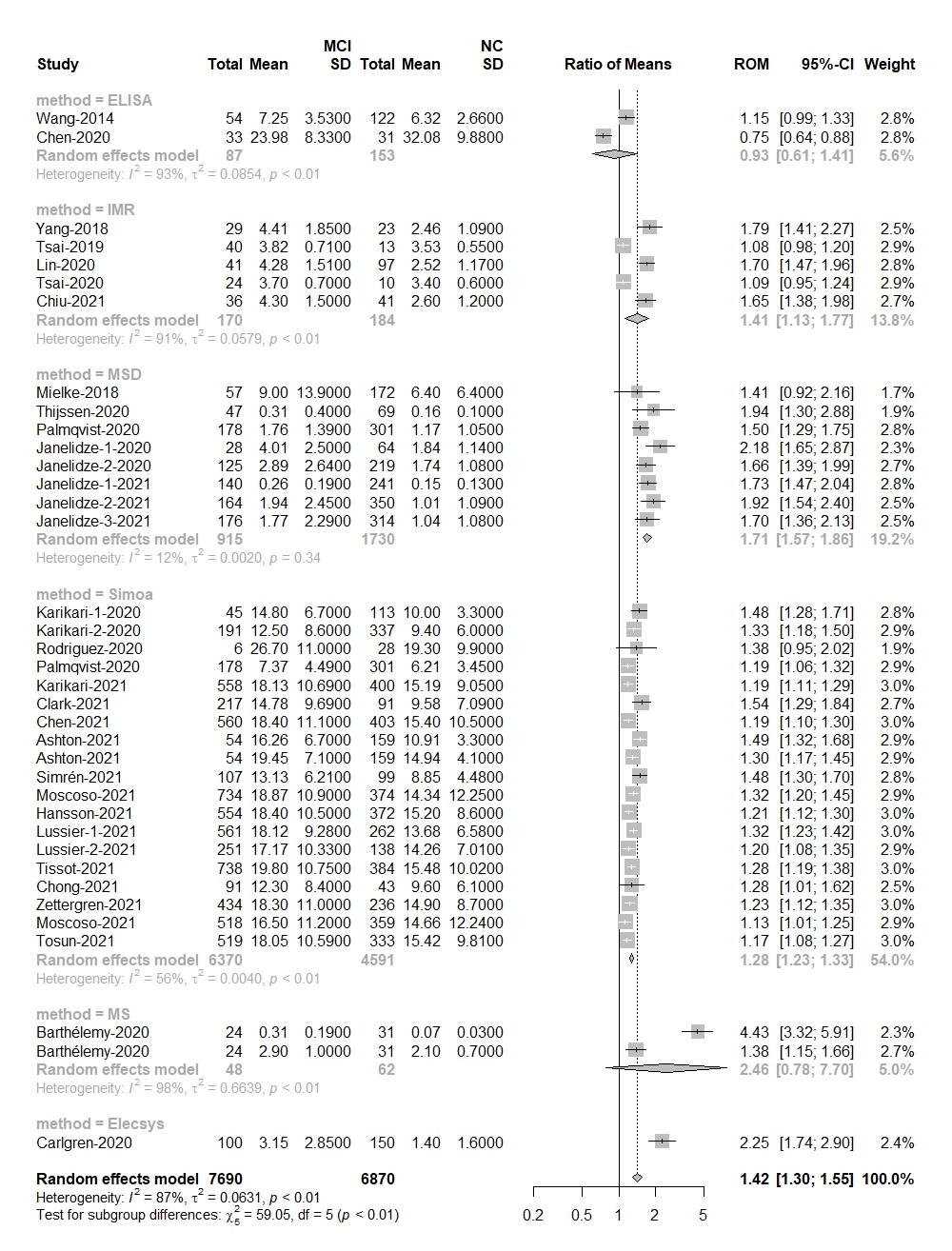
# Supplementary Table 4. Quality assessment of cohort studies

| First author | Year | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Ignacio Illán-Gala | 2021 | Yes | No | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | No | Yes | Yes | Low |
| Thomas K Karikari | 2021 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | No | Yes | Yes | Low |
| Ming-Jang Chiu | 2021 | No | No | Yes | Low | Low | Yes | No | Unclear | Low | Unclear | Unclear | Unclear | Low | No | No | Yes | High |
| Christopher Clark | 2021 | Yes | No | Yes | Low | Low | Yes | No | Low | Low | Yes | Yes | Low | Low | Unclear | Yes | Yes | Low |
| Tzayaka Castillo-Mendieta | 2021 | Yes | No | Yes | Low | Low | No | No | High | Low | Unclear | Unclear | Unclear | Low | Unclear | Unclear | Yes | Unclear |
| Adam M Brickman | 2021 | No | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | No | Yes | Low |
| Sebastian Palmqvist | 2021 | Yes | Yes | Yes | Low | Low | No | Yes | Unclear | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Shi-Dong Chen | 2021 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | No | Yes | Low |
| Shorena Janelidze-1 | 2021 | Yes | No | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | No | Yes | Low |
| Shorena Janelidze-2 | 2021 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Kaancan Deniz | 2021 | Unclear | No | Yes | Unclear | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Nicholas J Ashton | 2021 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Mitzi M Gonzales | 2021 | No | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Unclear | Unclear | Unclear | Low | Yes | No | No | High |
| Joel Simrén | 2021 | No | No | No | High | Low | Yes | Yes | Low | Low | Unclear | Yes | Unclear | Low | Unclear | Yes | Yes | Low |
| Alexis Moscoso -1 | 2021 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | No | Yes | No | High |
| Oskar Hansson | 2021 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | No | Low |
| Firoza Z Lussier | 2021 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Cécile Tissot | 2021 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Unclear | Yes | Unclear | Low | Yes | No | No | High |
| Congy ang yan | 2021 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Joyce R. Chong | 2021 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | No | Low |
| Anna Zettergren | 2021 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Alexis Moscoso-2 | 2021 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Duygu Tosun | 2021 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | No | Low |
| Thomas K Karikari | 2020 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Shorena Janelidze | 2020 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Nicolas R Barthélemy | 2020 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Elisabeth H Thijssen | 2020 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Fubin Jiao | 2020 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Juan Lantero Rodriguez | 2020 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Sebastian Palmqvist | 2020 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | No | No | High |
| Chin-Hsien Lin | 2020 | Unclear | Yes | Yes | Unclear | Low | Yes | Yes | Low | Low | Unclear | Unclear | Unclear | Unclear | Unclear | Unclear | Yes | Unclear |
| Michael A Sugarman | 2020 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Niklas MattssonCarlgren | 2020 | Unclear | Yes | Unclear | High | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Ting-Bin Chen | 2020 | Unclear | Yes | Unclear | Unclear | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Dong-Yu Fan | 2020 | Yes | Yes | No | High | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Unclear | Yes | Yes | Low |
| Chia-Lin Tsai | 2020 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Wei-Wei Li | 2019 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Yachen Shi | 2019 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Chia-Lin Tsai | 2019 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Silvia Fossati | 2019 | Unclear | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Che-Chuan Yang | 2018 | Yes | Yes | Yes | Low | Low | No | No | High | Low | No | No | High | High | Unclear | Yes | Yes | Unclear |
| Michelle M Mielke | 2018 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Palaniswamy Rani | 2017 | Unclear | Yes | No | High | Low | Yes | Yes | Low | Low | Unclear | Yes | Unclear | Low | Yes | Yes | Yes | Low |
| Lih-Fen Lue | 2017 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Unclear | Unclear | Unclear | Unclear | Yes | No | Yes | Low |
| Shieh-Yueh Yang | 2017 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | No | No | High | High | Unclear | Unclear | Yes | Unclear |
| Michelle M Mielke | 2017 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Harutsugu Tatebe | 2017 | Unclear | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Rinko Grewal | 2016 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Unclear | Unclear | Unclear | Unclear | Unclear | Unclear | Yes | Unclear |
| Niklas Mattsson | 2016 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Sreeram Krishnan | 2014 | Yes | Yes | No | Low | Low | Yes | Yes | Low | Low | Unclear | Unclear | Unclear | Unclear | Unclear | Unclear | Yes | Unclear |
| Tao Wang | 2014 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Unclear | Unclear | Unclear | Unclear | Unclear | Unclear | Yes | Unclear |
| Ming-Jang Chiu | 2014 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Kai-Yuan Tzen | 2014 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| Henrik Zetterberg | 2013 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Yes | Yes | Yes | Low |
| D Larry Sparks | 2012 | Yes | Yes | Yes | Low | Low | Yes | Yes | Low | Low | No | Yes | Low | High | Yes | Yes | Yes | Low |
| Dantao Peng | 2005 | No | Yes | Yes | Low | Low | Yes | Yes | Low | Low | Unclear | Unclear | Unclear | Unclear | Unclear | Unclear | Yes | Unclear |

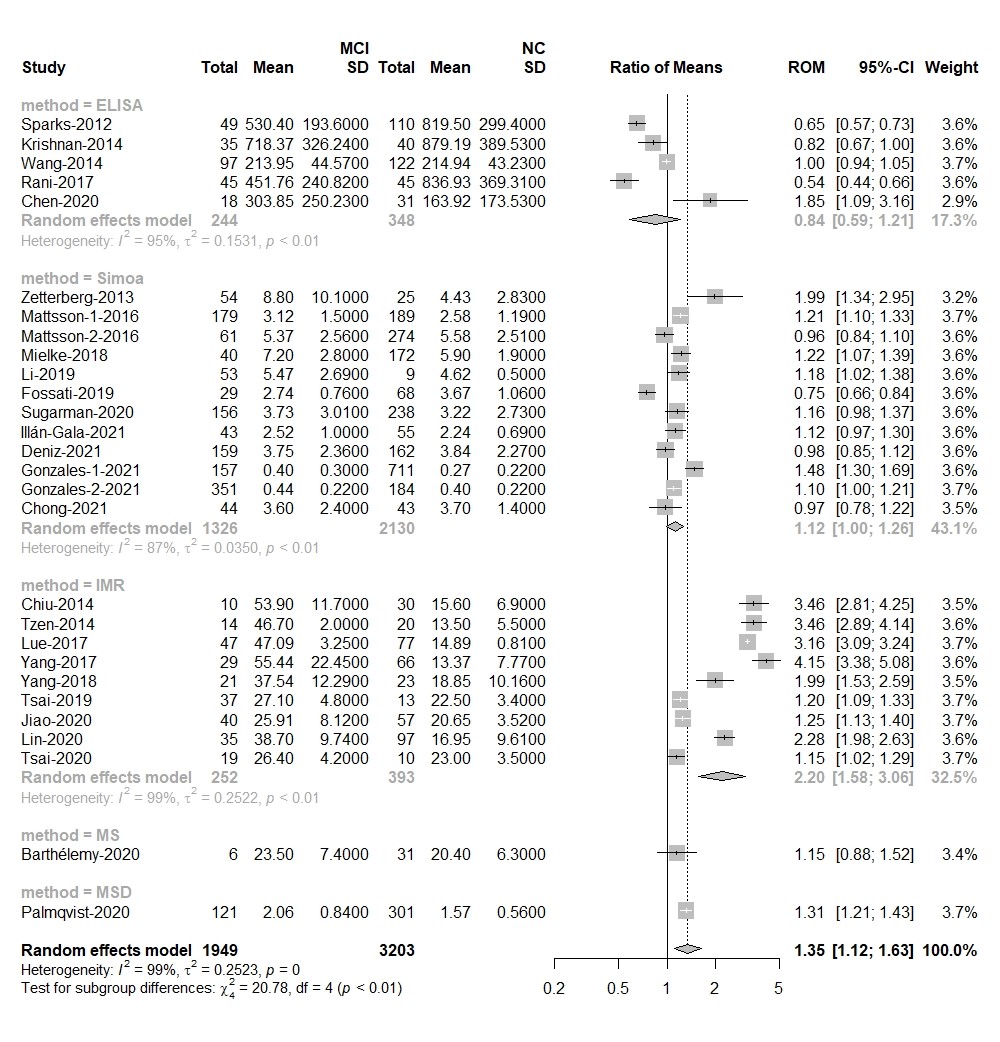
# Supplementary Fig.1. MCI to control ratio for blood t-tau



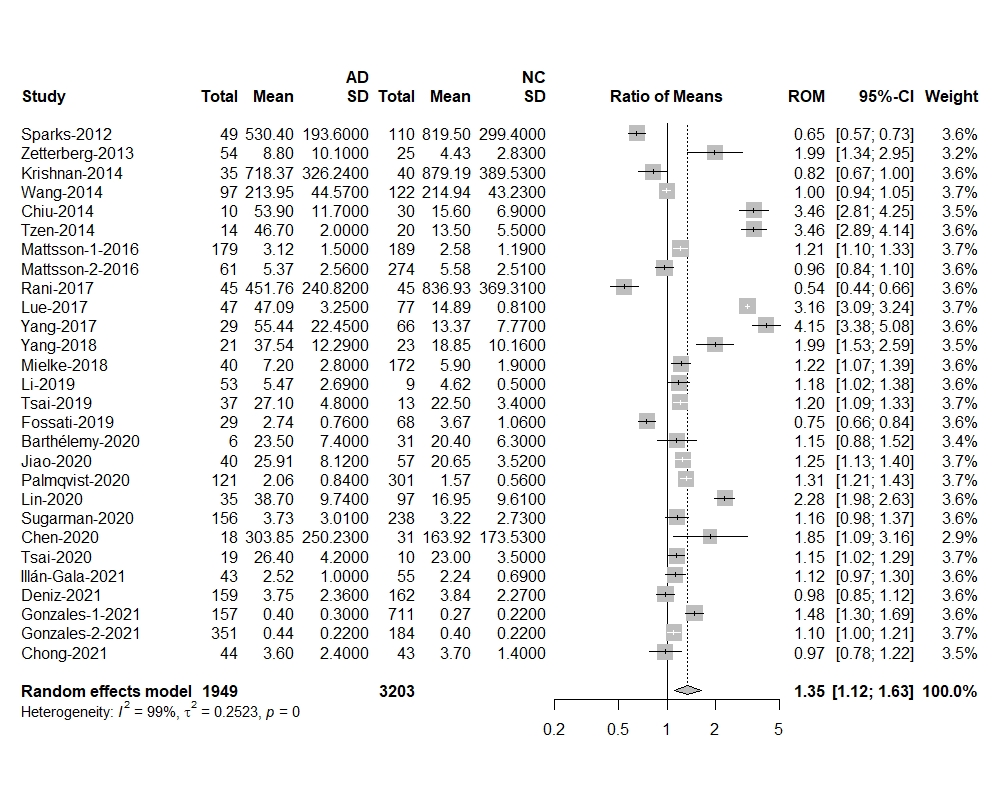
# Supplementary Fig.2. Subgroup Analysis:MCI to control ratio for blood p-tau



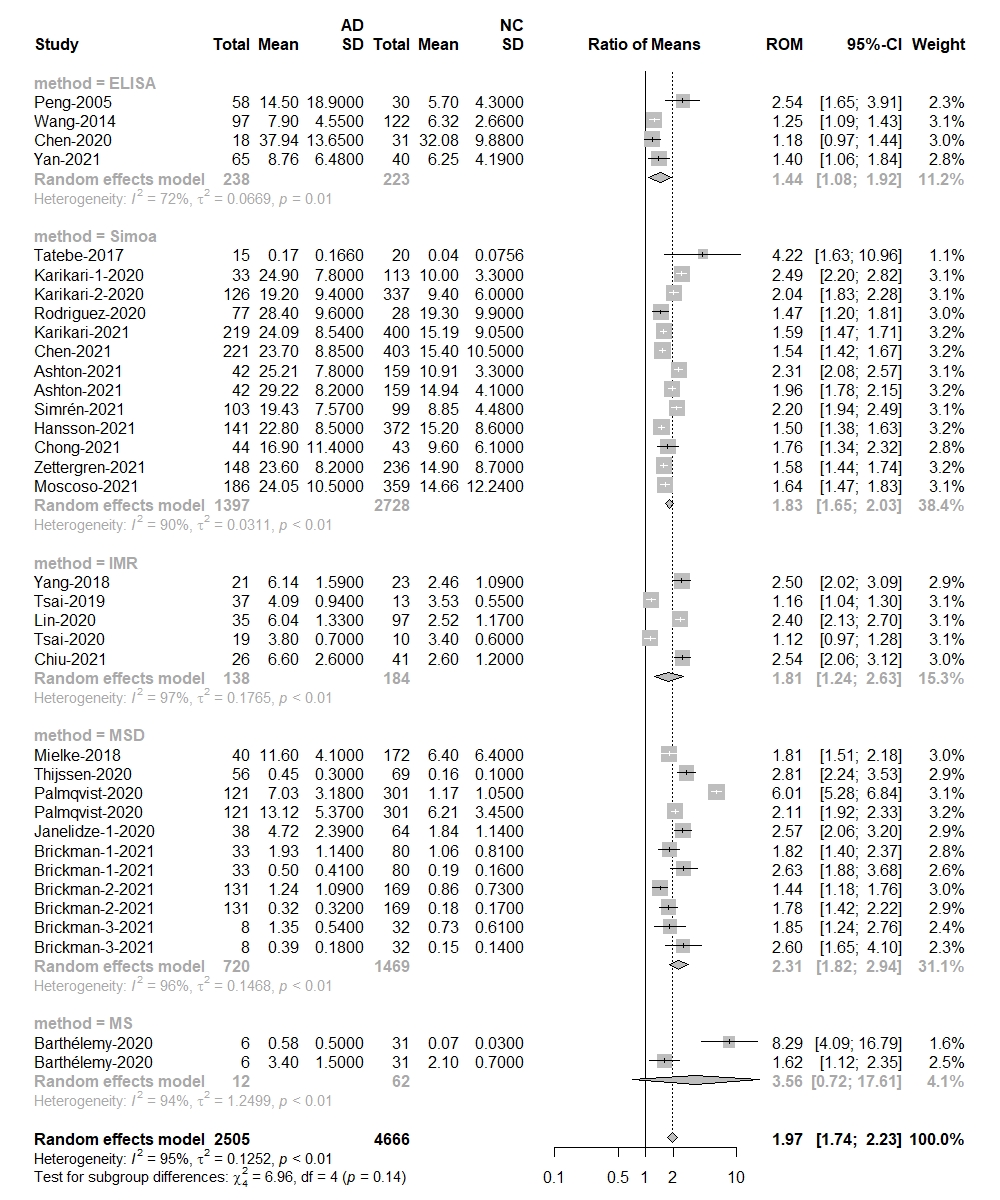
# Supplementary Fig.3. Subgroup Analysis:MCI to control ratio for blood t-tau



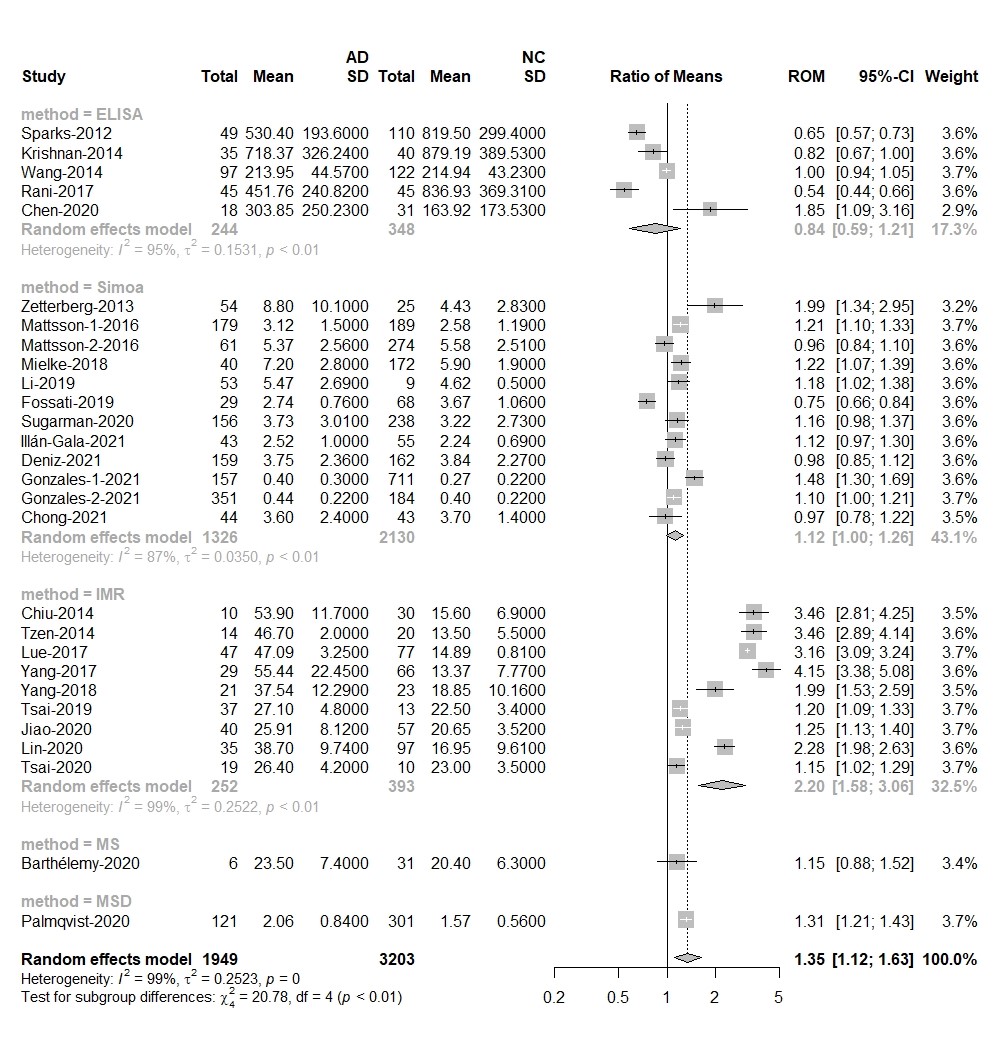
# Supplementary Fig.4. AD to control ratio for blood t-tau



# Supplementary Fig.5. Subgroup Analysis: AD to control ratio for blood p-tau

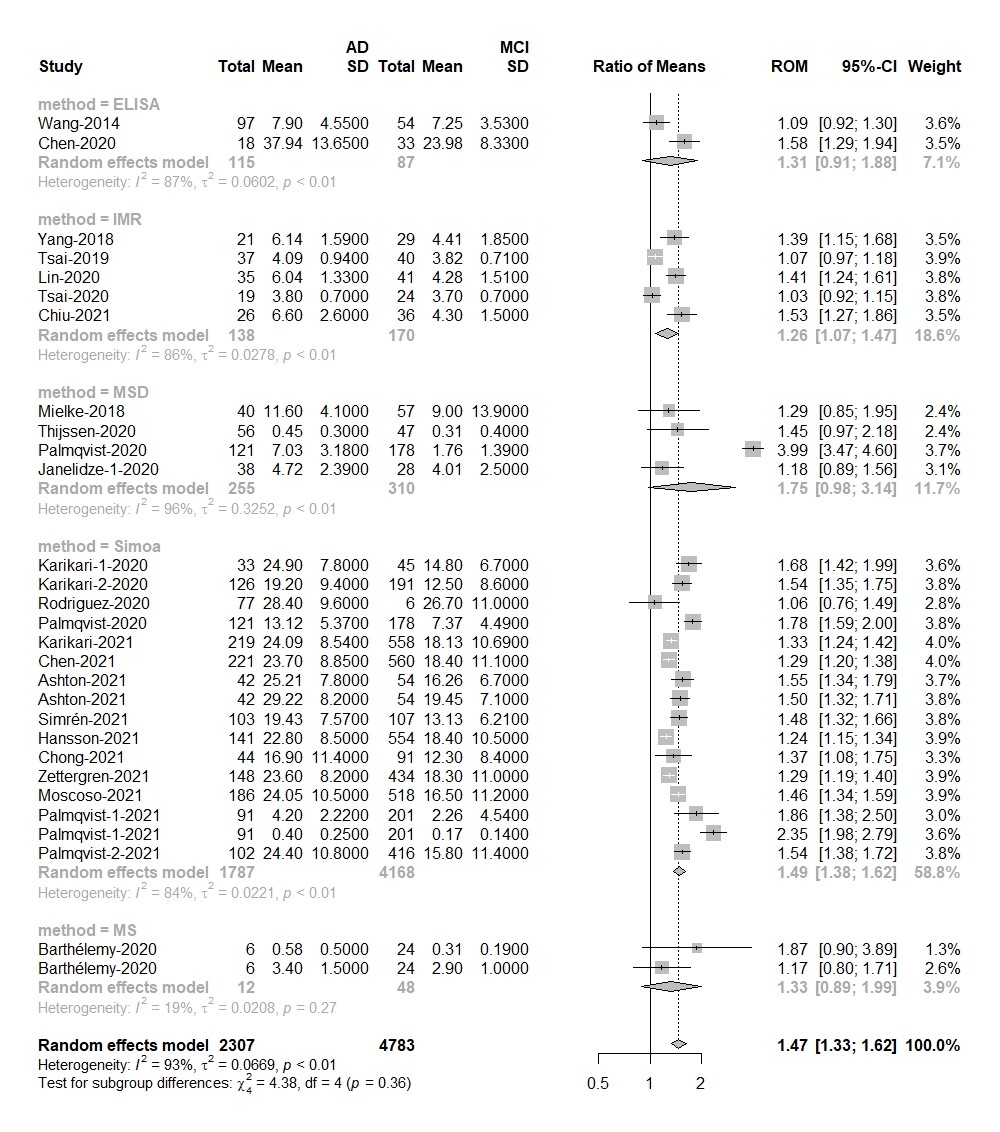


# Supplementary Fig.6. Subgroup Analysis:AD to control ratio for blood t-tau

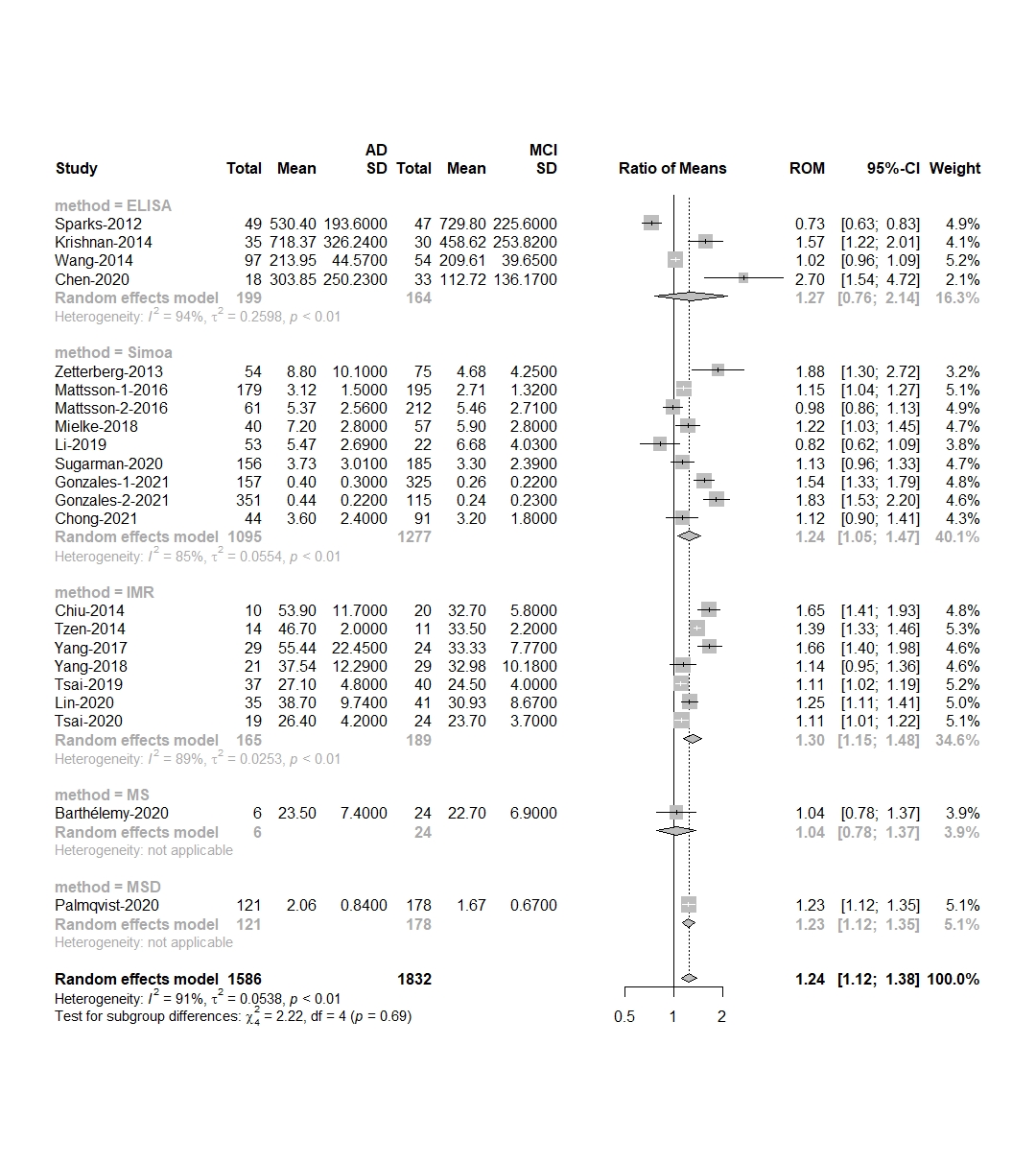


# Supplementary Fig.7. AD to MCI ratio for blood t-taumci-ad-t-tau

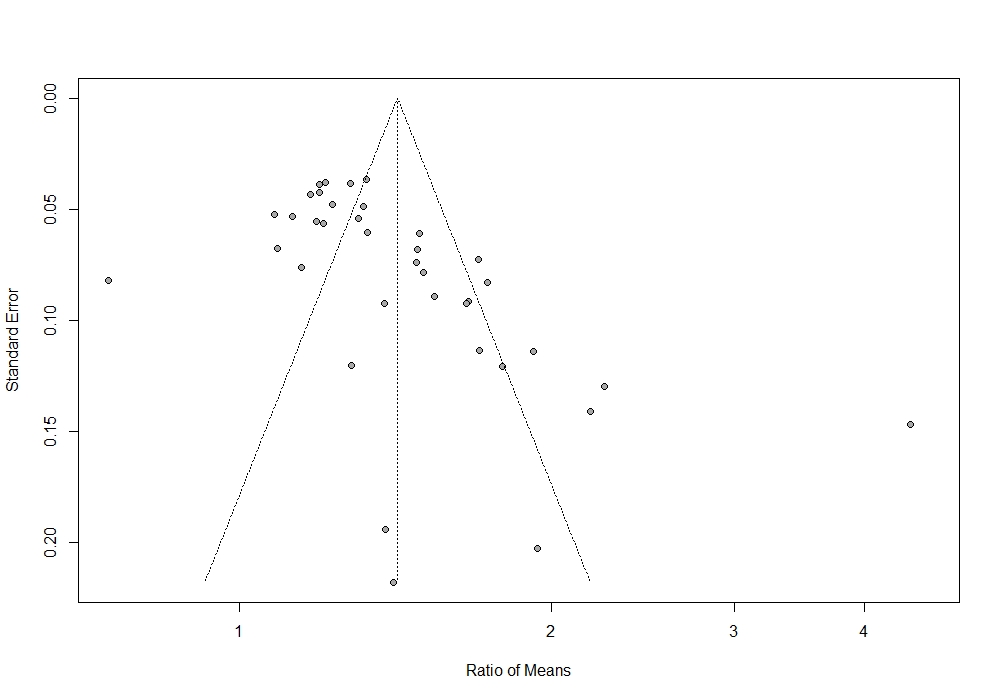
# Supplementary Fig.8. Subgroup Analysis:AD to MCI ratio for blood p-tau



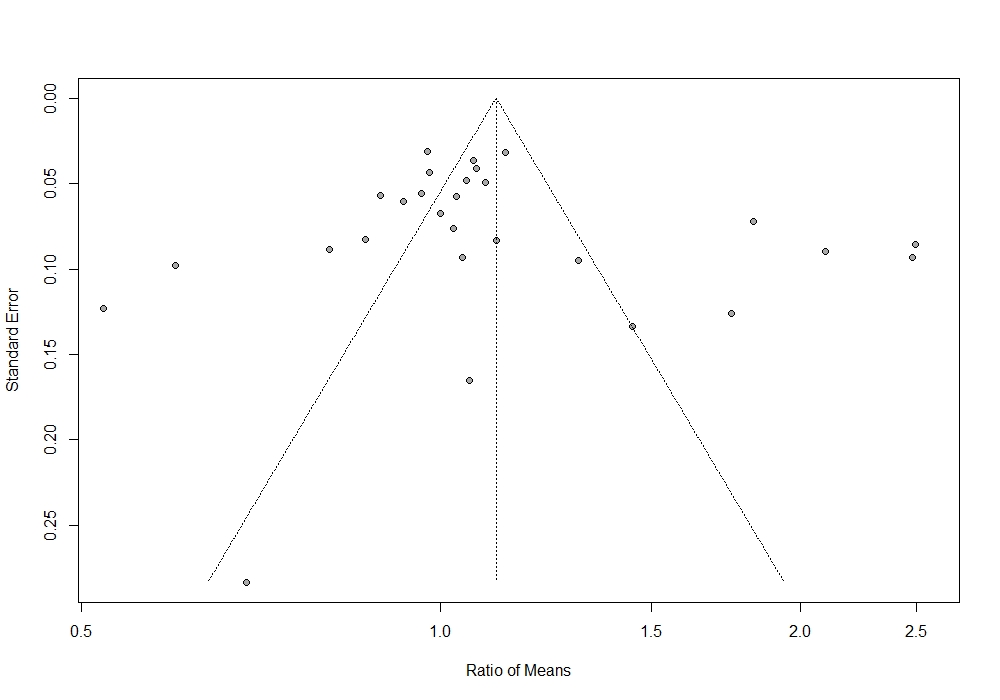
# Supplementary Fig.9. Subgroup Analysis:AD to MCI ratio for blood t-tau



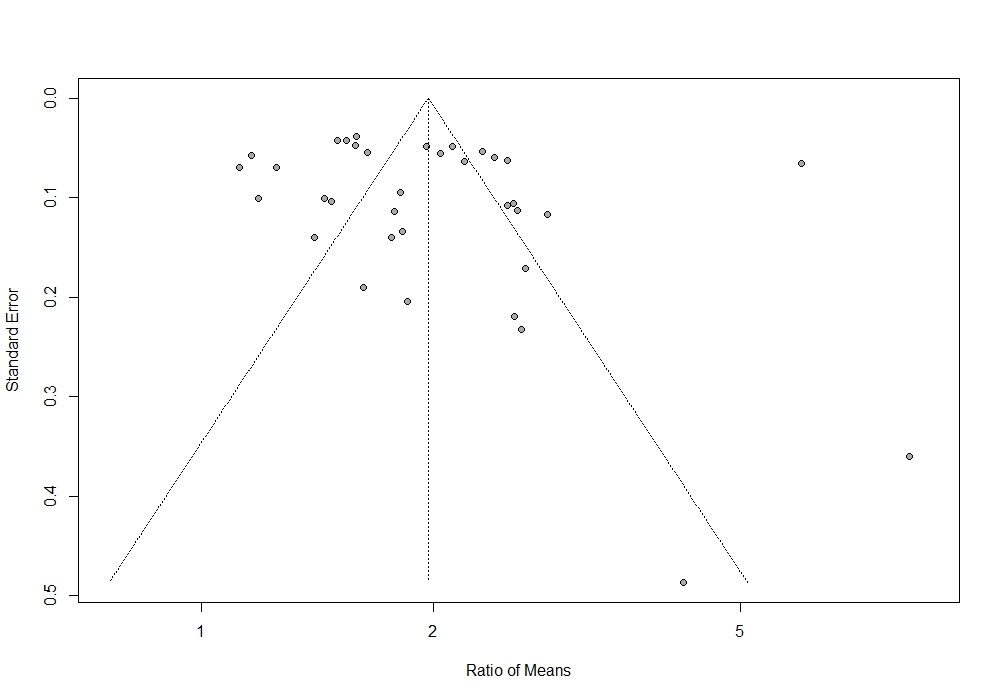
# Supplementary Fig.10. Funnel plot of blood p-tau in MCI samples vs controls



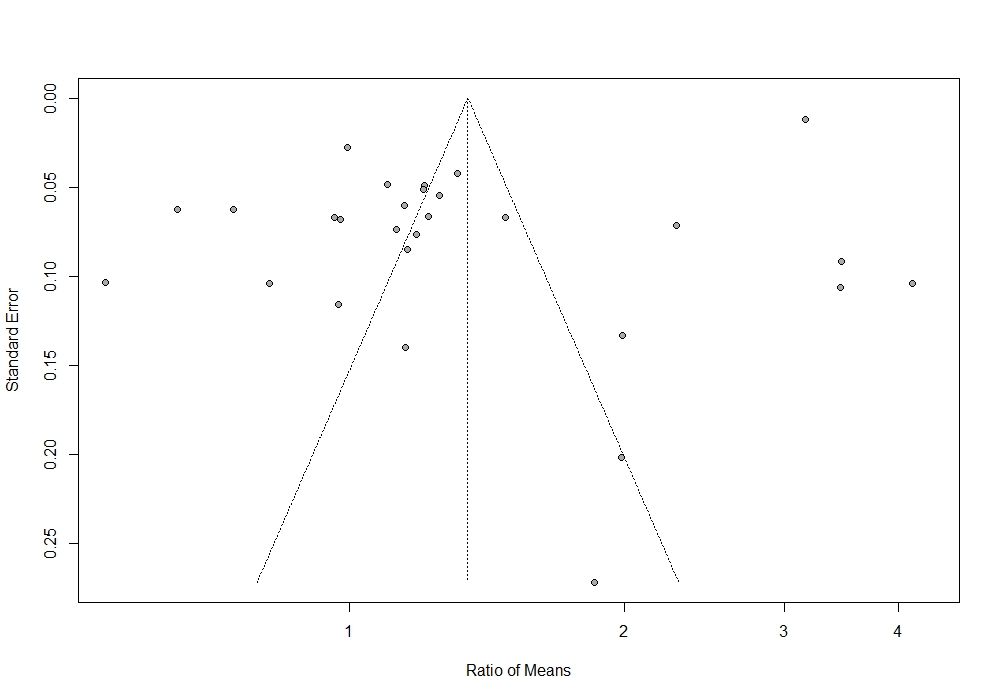
# Supplementary Fig.11. Funnel plot of blood t-tau in MCI samples vs controls



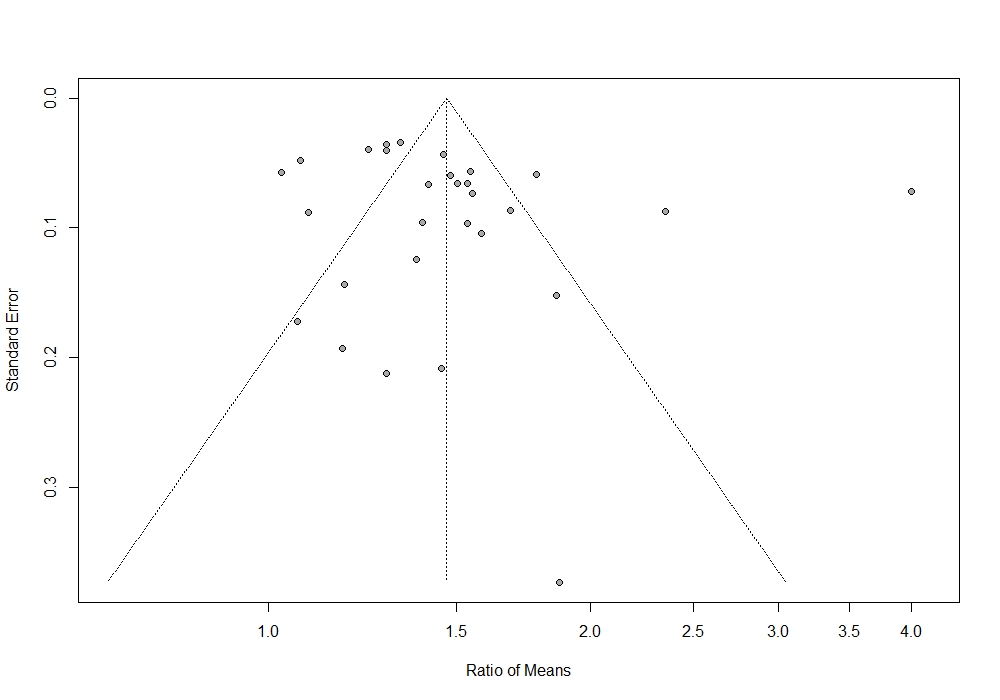
# Supplementary Fig.12. Funnel plot of blood p-tau in AD samples vs controls



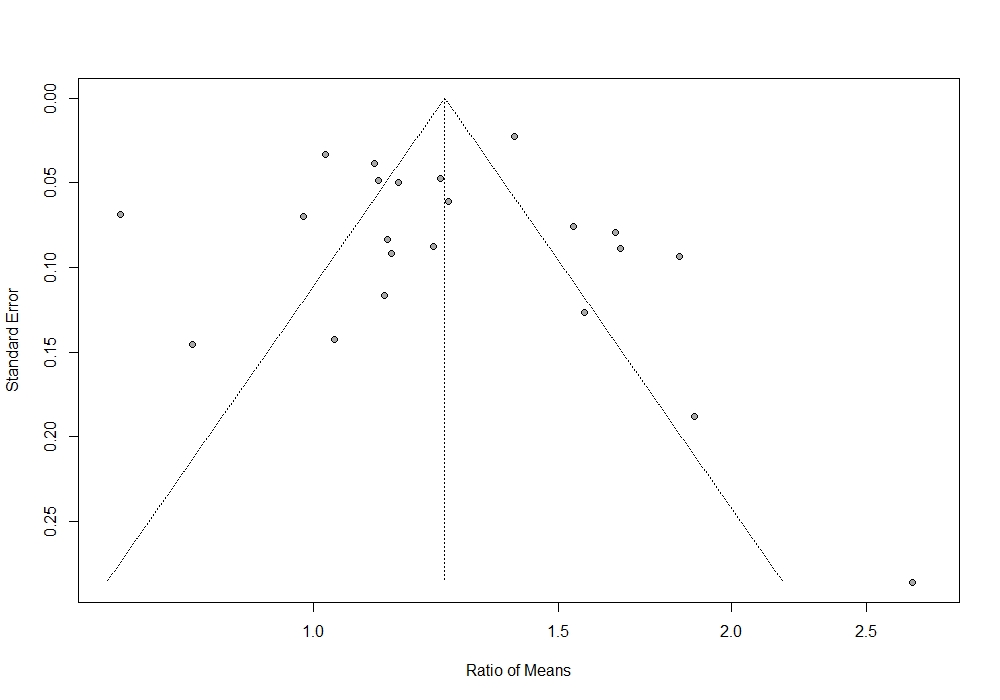
# Supplementary Fig.13. Funnel plot of blood t-tau in AD samples vs controls



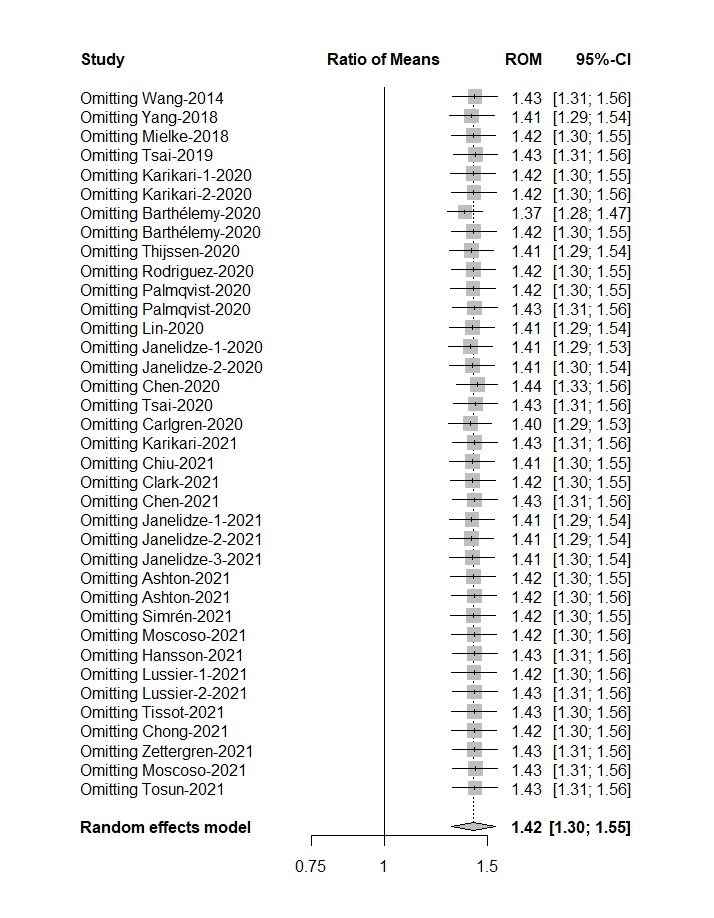
# Supplementary Fig.14. Funnel plot of blood p-tau in AD samples vs MCI



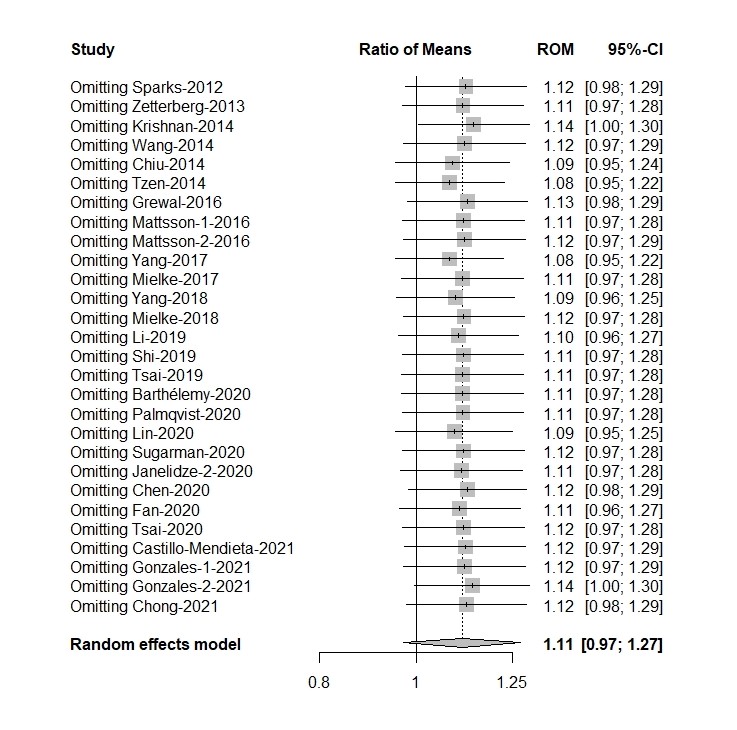
# Supplementary Fig.15. Funnel plot of blood t-tau in AD samples vs MCI



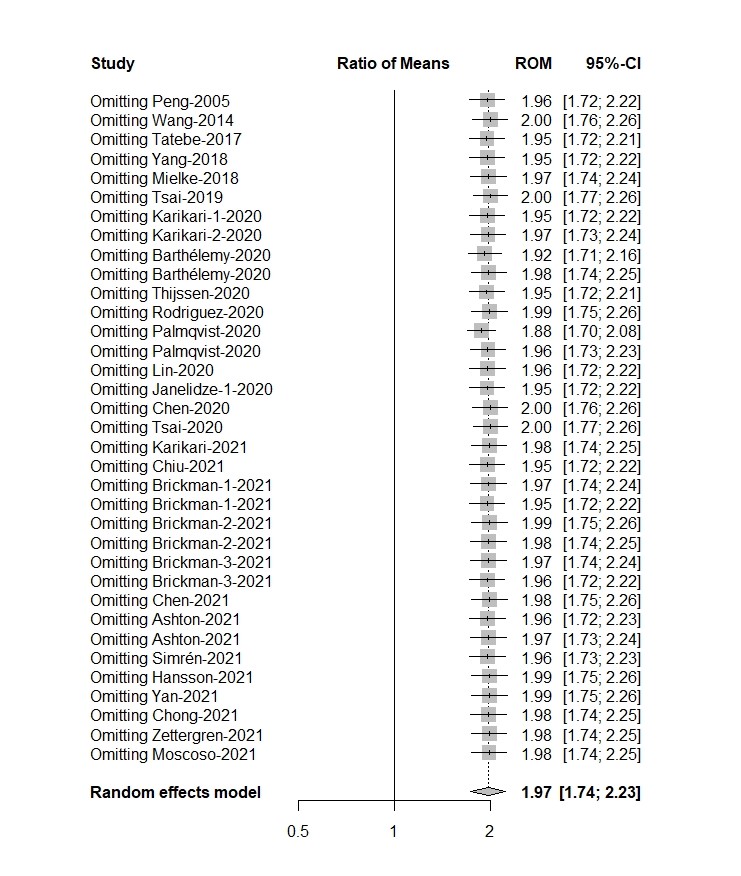
# Supplementary Fig.16. Sensitivity analysis of blood p-tau in MCI samples vs controls



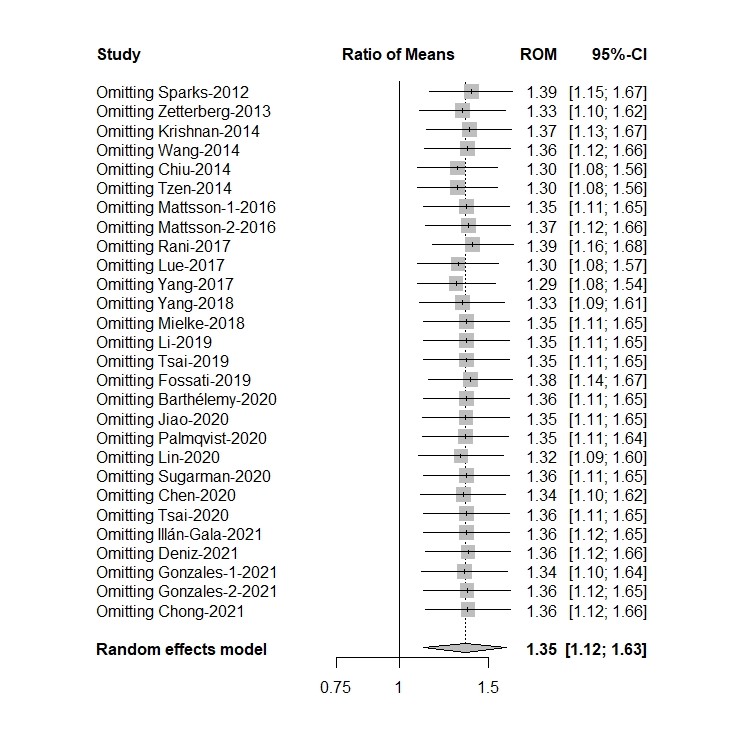
# Supplementary Fig.17. Sensitivity analysis of blood t-tau in MCI samples vs controls



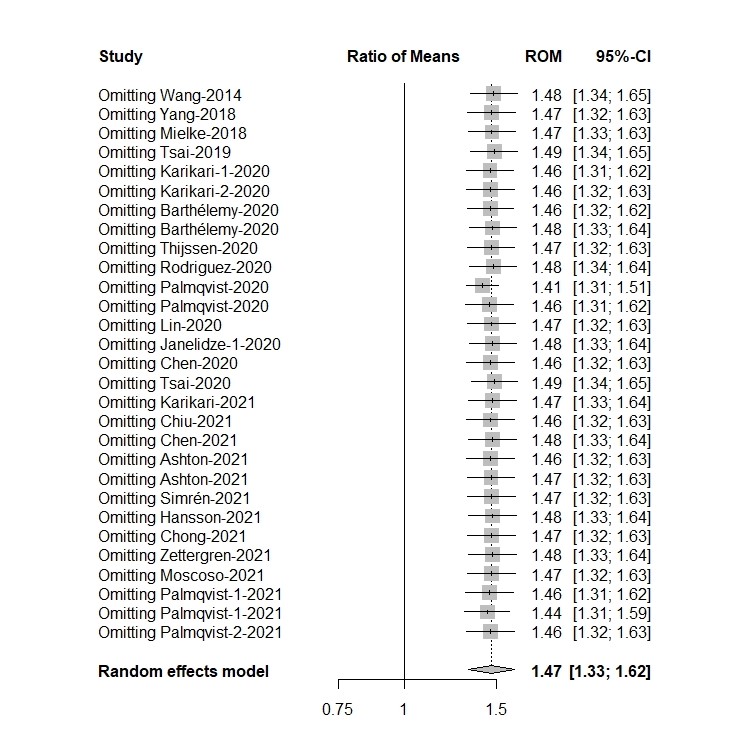
# Supplementary Fig.18. Sensitivity analysis of blood p-tau in AD samples vs controls



# Supplementary Fig.19. Sensitivity analysis of blood t-tau in AD samples vs controls



# Supplementary Fig.20. Sensitivity analysis of blood p-tau in AD samples vs MCI



# Supplementary Fig.21. Sensitivity analysis of blood t-tau in AD samples vs MCI

