Appendix P: Diagnosis

Dementia diagnosis

Review questions

- What are the most effective methods of primary assessment to decide whether a person with suspected dementia should be referred to a dementia service?
- What are the most effective methods of diagnosing dementia and dementia subtypes in specialist dementia diagnostic services?

P.1 Evidence tables

Evidence tables for this section are indexed by the initial of the first author's surname

P.1.1 A

Abdel-Aziz K, Larner AJ: Six-Item Cognitive Impairment Test (6CIT): pragmatic diagnostic accuracy study for dementia and MCI. Int Psychogeriatr 2015; 27: 991–997.	
Study type	Prospective cohort
Country	UK
Setting	Neurology -led memory clinic in a regional neuroscience centre
Inclusion criteria	Not stated
Exclusion criteria	Previous experience of 6 CIT test in primary care
Sex	50.6% male
Age	median 59 years (range 16-94)
Presentation	Suspected dementia
Reference standard	DSM-IV diagnostic criteria for dementia, Petersen criteria for MCI (Petersen et al., 1999)
Dementia versus non-dementia (including MCI)	
Index Test: MMSE (<23)	

Abdel-Aziz K, Larner AJ: Six-Item Cognitive Impairment Test (6CIT): pragmatic diagnostic accuracy study for dementia and MCI. Int Psychogeriatr 2015; 27: 991–997.								
MMSE ≤ 22/30 chosen for easy comparison to 6CIT test								
Results	**True positives:**	13	**False negatives:**	9	**False positives:**	19	**True negatives:**	109
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup of 6 CIT tested patients were tested with MMSE as well; MMSE cut off was not pre-specified as chosen for comparison to 6CIT test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: 6-item Cognitive Impairment Test (6CIT) (>9) 6-item Cognitive Impairment Test (6CIT) (>9)								
Results	**True positives:**	42	**False negatives:**	6	**False positives:**	43	**True negatives:**	154
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Alexander SK, Rittman T, Xureb JH, Bak TH, Hodges JR, Rowe JB. Validation of the new consensus criteria for the diagnosis of corticobasal degeneration. J Neurol Neurosurg Psychiatry 2014; 85: 923–927.	
Study type	Retrospective cohort
Country	UK

Alexander SK, Rittman T, Xureb JH, Bak TH, Hodges JR, Rowe JB. Validation of the new consensus criteria for the diagnosis of corticobasal degeneration. J Neurol Neurosurg Psychiatry 2014; 85: 923–927.								
Setting	Regional specialist clinics for Disorders of Movement and Cognition and Early-Onset Dementia at Addenbrooke's Hospital.							
Inclusion criteria	Patients attending the clinics between 1990 and 2013 for whom detailed clinical and pathological information was available.							
Exclusion criteria	Evidence of Lewy body disease, multiple system atrophy, Alzheimer's disease or amyotrophic lateral sclerosis; semantic or logopenic variant primary progressive aphasia; structural lesion suggestive of focal cause; granulin mutation or reduced plasma progranulin levels; TDP-43 or fused in sarcoma (FUS) mutations. Based on Armstrong et al. consensus paper exclusion criteria for both clinical research criteria for probable sporadic CBD and possible CBD.							
Sex	48.5% male							
Age	Mean age 67.8 years (SD 8.4)							
Presentation	Suspected CBD							
Reference standard	Neuropathology, details not specified.							
CBD (probable or possible) versus CBD mimic (corticobasal syndrome, but not CBD pathology)								
Index Test: CBD consensus criteria Armstrong et al (2013) corticobasal degeneration (CBD) consensus criteria								
Results	**True positives:**	18	**False negatives:**	1	**False positives:**	14	**True negatives:**	0
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Ampuero I, Alegre-Abarrategui J, Rodal I, Espana A, Ros R, Loez Sendon JL, Garcia Galloway E et al. On the diagnosis of CADASIL. Journal of Alzheimer's Disease 2009; 17: 787-794.	
Study type	Prospective cohort
Country	Spain
Setting	Banco de Tejidos para Invertigaciones Neurologicas, Universidad Commplutense de Madrid

Ampuero I, Alegre-Abarrategui J, Rodal I, Espana A, Ros R, Loez Sendon JL, Garcia Galloway E et al. On the diagnosis of CADASIL. Journal of Alzheimer's Disease 2009; 17: 787-794.								
Inclusion criteria	People with suspected CADASIL referred to the Banco de Tejidos para Invertigaciones Neurologicas							
Exclusion criteria	Not stated							
Sex	Not stated							
Age	Mean age 53.4 years (SD 13.1)							
Presentation	Suspected CADASIL							
Reference standard	Clinician diagnosis based on: 1) clinical history of unexplained recurrent strokes or transient ischemic attacks in people under 55 years old, vascular dementia or dominant inheritance and 2) MRI compatible with CADASIL. The presence of supporting clinical features was also considered.							
CADASIL versus CADASIL-like syndromes								
Index Test: Skin biopsy Skin biopsy, immunostaining pattern typical for CADASIL								
Results	**True positives:**	26	**False negatives:**	1	**False positives:**	20	**True negatives:**	43
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Andreasen N,Minthon L,Davidsson P,Vanmechelen E,Van-derstichele H,Winblad B,et al. Evaluation of CSF-tau and CSF-Abeta 42 as diagnostic markers for Alzheimer disease in clinical practice. ArchNeurol 2001; 58: 373–9.	
Study type	Prospective cohort
Country	Sweden
Setting	specialist hospital clinic
Inclusion criteria	People referred from primary care or community health service with cognitive impairment
Exclusion criteria	not stated

Andreasen N,Minthon L,Davidsson P,Vanmechelen E,Van-derstichele H,Winblad B,et al. Evaluation of CSF-tau and CSF-Abeta 42 as diagnostic markers for Alzheimer disease in clinical practice. ArchNeurol 2001; 58: 373–9.								
Sex	45.6% male							
Age	73.4 years (SD 7.1)							
Presentation	Suspected dementia							
Reference standard	DSM-IV for dementia diagnoses, probable and possible AD based on NINCDS-ADRDA criteria, VaD according to the National Institute of Neurological Disorders and Stroke-Association Internationale pour la Recherche et l'Enseignementen Neuroscience criteria, MCI according to the Petersen (1997) criteria, LBD according to consensus criteria (McKeith 1999). Other diagnoses using the DSM-IV and ICD-10.							
AD disease with varying certainty (probable and possible AD pooled) verus non- AD (VaD, LBD, MCI and non-dementia groups pooled).								
Index Test: Amyloid Beta 1-42 The Amyloid/P- Tau ratio was calculated using the formula Amyloid Beta 42/(240 + [1.18×T-tau])								
Results	**True positives:**	106	**False negatives:**	57	**False positives:**	32	**True negatives:**	43
Additional comments	Data on people diagnosed with other neurological conditions excluded from analysis as not in accessible format. N=3 people.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD disease with varying certainty (probable and possible AD pooled) versus VaD								
Index Test: Amyloid Beta 1-42 The Amyloid/P- Tau ratio was calculated using the formula Amyloid Beta 42/(240 + [1.18×T-tau])								
Results	**True positives:**	106	**False negatives:**	57	**False positives:**	12	**True negatives:**	11
Additional comments	Data on people diagnosed with other neurological conditions excluded from analysis as not in accessible format. N=3 people.							
Risk of bias	**Patient**	Low	**Index test:**	Low	**Reference**	Low	**Flow and**	Low

Andreasen N,Minthon L,Davidsson P,Vanmechelen E,Van-derstichele H,Winblad B,et al. Evaluation of CSF-tau and CSF-Abeta 42 as diagnostic markers for Alzheimer disease in clinical practice. ArchNeurol 2001; 58: 373–9.								
	selection:				**standard:**		**timing:**	
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD disease with varying certainty (probable and possible AD pooled) versus LBD								
Index Test: Amyloid Beta 1-42 The Amyloid/P- Tau ratio was calculated using the formula Amyloid Beta 42/(240 + [1.18×T-tau])								
Results	**True positives:**	106	**False negatives:**	57	**False positives:**	3	**True negatives:**	6
Additional comments	Data on people diagnosed with other neurological conditions excluded from analysis as not in accessible format. N=3 people.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Probable AD verus non- AD (VaD, LBD, MCI and non-dementia groups pooled).								
Index Test: Amyloid Beta 1-42 The Amyloid/P- Tau ratio was calculated using the formula Amyloid Beta 42/(240 + [1.18×T-tau])								
Results	**True positives:**	99	**False negatives:**	6	**False positives:**	32	**True negatives:**	43
Additional comments	Data on people diagnosed with other neurological conditions excluded from analysis as not in accessible format. N=3 people.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low

Andreasen N,Minthon L,Davidsson P,Vanmechelen E,Van-derstichele H,Winblad B,et al. Evaluation of CSF-tau and CSF-Abeta 42 as diagnostic markers for Alzheimer disease in clinical practice. ArchNeurol 2001; 58: 373–9.								
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Probable AD versus VaD								
Index Test: Amyloid Beta 1-42 The Amyloid/P- Tau ratio was calculated using the formula Amyloid Beta 42/(240 + [1.18×T-tau])								
Results	**True positives:**	99	**False negatives:**	6	**False positives:**	12	**True negatives:**	11
Additional comments	Data on people diagnosed with other neurological conditions excluded from analysis as not in accessible format. N=3 people.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Probable AD versus LBD								
Index Test: Amyloid Beta 1-42 The Amyloid/P- Tau ratio was calculated using the formula Amyloid Beta 42/(240 + [1.18×T-tau])								
Results	**True positives:**	99	**False negatives:**	6	**False positives:**	3	**True negatives:**	6
Additional comments	Data on people diagnosed with other neurological conditions excluded from analysis as not in accessible format. N=3 people.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							

Andreasen N,Minthon L,Davidsson P,Vanmechelen E,Van-derstichele H,Winblad B,et al. Evaluation of CSF-tau and CSF-Abeta 42 as diagnostic markers for Alzheimer disease in clinical practice. ArchNeurol 2001; 58: 373–9.								
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Possible AD verus non- AD (VaD, LBD, MCI and non-dementia groups pooled).								
Index Test: Amyloid Beta 1-42 The Amyloid/P- Tau ratio was calculated using the formula Amyloid Beta 42/(240 + [1.18×T-tau])								
Results	**True positives:**	7	**False negatives:**	51	**False positives:**	32	**True negatives:**	43
Additional comments	Data on people diagnosed with other neurological conditions excluded from analysis as not in accessible format. N=3 people.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Possible versus VaD								
Index Test: Amyloid Beta 1-42 The Amyloid/P- Tau ratio was calculated using the formula Amyloid Beta 42/(240 + [1.18×T-tau])								
Results	**True positives:**	7	**False negatives:**	51	**False positives:**	12	**True negatives:**	11
Additional comments	Data on people diagnosed with other neurological conditions excluded from analysis as not in accessible format. N=3 people.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient**	Low	**Index test:**	Low	**Reference**	Low		

Andreasen N,Minthon L,Davidsson P,Vanmechelen E,Van-derstichele H,Winblad B,et al. Evaluation of CSF-tau and CSF-Abeta 42 as diagnostic markers for Alzheimer disease in clinical practice. ArchNeurol 2001; 58: 373–9.								
	selection:				**standard:**			
Overall indirectness	Not serious							
Possible AD versus LBD								
Index Test: Amyloid Beta 1-42 The Amyloid/P- Tau ratio was calculated using the formula Amyloid Beta 42/(240 + [1.18×T-tau])								
Results	**True positives:**	7	**False negatives:**	51	**False positives:**	3	**True negatives:**	6
Additional comments	Data on people diagnosed with other neurological conditions excluded from analysis as not in accessible format. N=3 people.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Apolinario D, Gomes Lichtenthaler D, Miksian Magaldi R, Thomaz Soares A, Busse AL, das Gracas Amaral JR, Jacob-Filho W, Dozzi Brucki SM. Using temporal orientation, catgory fluency, and word recall for detecting cognitive impairment: the 10- point cognitive screener (10-CS). Int J Geriatr Psychiatry 2016; 31: 4-12.	
Study type	Prospective cohort
Country	Brazil
Setting	Outpatient geriatric clinic, Sao Paulo
Inclusion criteria	≥ 60 years with suspected cognitive impairment and an available knowledgeable informant.
Exclusion criteria	Patients with moderate to severe dementia; people with delirium or who had sensory, motor or speech disturbances that precluded completion of the neuropsychological assessment.
Sex	35.7% male
Age	Mean age 74.7 years (SD 7.2)

Apolinario D, Gomes Lichtenthaler D, Miksian Magaldi R, Thomaz Soares A, Busse AL, das Gracas Amaral JR, Jacob-Filho W, Dozzi Brucki SM. Using temporal orientation, catgory fluency, and word recall for detecting cognitive impairment: the 10- point cognitive screener (10-CS). Int J Geriatr Psychiatry 2016; 31: 4-12.								
Presentation	Suspected dementia							
Reference standard	Dementia was diagnosed using the DSM-IV criteria							
Dementia versus not dementia								
Index Test: 10-point Cognitive Screener (10-CS) (≤5) 10-point cognitive screener (10-CS), a modified version of the six-item screener (Brazilian Portuguese language). Points added for education effects. Cut-off ≤ 5.								
Results	**True positives:**	73	**False negatives:**	33	**False positives:**	8	**True negatives:**	116
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Optimised thresholds were calculated and people with moderate to severe dementia were excluded from the study.)							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (Included patients were selected to be ≥ 60 years old and had on average only 4.7 years of schooling)							
Index Test: 10-point Cognitive Screener (10-CS) (≤6) 10-point cognitive screener (10-CS), a modified version of the six-item screener (Brazilian Portuguese language). Points added for education effects. Cut-off ≤ 6.								
Results	**True positives:**	86	**False negatives:**	20	**False positives:**	20	**True negatives:**	104
Additional comments								
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Optimised thresholds were calculated and people with moderate to severe dementia were excluded from the study.)							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall	Serious (Included patients were selected to be ≥ 60 years old and had on average only 4.7 years of schooling)							

Apolinario D, Gomes Lichtenthaler D, Miksian Magaldi R, Thomaz Soares A, Busse AL, das Gracas Amaral JR, Jacob-Filho W, Dozzi Brucki SM. Using temporal orientation, catgory fluency, and word recall for detecting cognitive impairment: the 10- point cognitive screener (10-CS). Int J Geriatr Psychiatry 2016; 31: 4-12.							
indirectness							
Index Test: 10-point Cognitive Screener (10-CS) (≤7) 10-point cognitive screener (10-CS), a modified version of the six-item screener (Brazilian Portuguese language). Points added for education effects. Cut-off ≤ 7.							
Results	**True positives:**	100	**False negatives:**	6	**False positives:**	50	**True negatives:** 74
Additional comments							
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Serious (Optimised thresholds were calculated and people with moderate to severe dementia were excluded from the study.)						
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Serious (Included patients were selected to be ≥ 60 years old and had on average only 4.7 years of schooling)						
Index Test: 10-point Cognitive Screener (10-CS) (≤8) 10-point cognitive screener (10-CS), a modified version of the six-item screener (Brazilian Portuguese language). Points added for education effects. Cut-off ≤ 8.							
Results	**True positives:**	103	**False negatives:**	3	**False positives:**	74	**True negatives:** 50
Additional comments							
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Serious (Optimised thresholds were calculated and people with moderate to severe dementia were excluded from the study.)						
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Serious (Included patients were selected to be ≥ 60 years old and had on average only 4.7 years of schooling)						

Arslan E, Ekmekcioglu O, Gortan FA, Engin Akcan ZF, Erkan ME, Emlu HM, Hala M, Cermik TF, Sonmezoglu K. The value of FDG-PET/CT by using 3-dimensional stereotactic surface projection software analysis in the differential diagnosis of dementia. Turkish Journal of Medical Sciences, 2016; 45: 1149-1158.							
Study type	Retrospective cohort						
Country	Turkey						
Setting	Not stated						
Inclusion criteria	People with dementia who had been subjected to PET imaging as part of their dementia diagnosis.						
Exclusion criteria	Not stated						
Sex	29.0% male						
Age	Mean age 61.4 years (8.6)						
Presentation	Dementia subtype diagnosis						
Reference standard	Probable diagnosis of dementia based on criteria developed by NINCDS-ADRDA and/or frontotemporal lobar degeneration. Data from neuropsychological tests were also taken into consideration.						
AD versus non-AD dementias							
Index Test: FDG-PET 18F-FDG PET attenuation-corrected PET/CT (Siemens Biograph LSO HI-RES PET-CT, USA) images were acquired. After iterative reconstruction, 0.3-cm-thick section images from both CT and PET were obtained in the transaxial, coronal, and sagittal planes. Visual assessment of PET images was performed by evaluating the changes in FDG uptake in both the cortical and subcortical areas. The axial sectional images of PET were also evaluated with 3D-SSP software (NEUROSTAT). The images were imported into a template with the Talairach coordinates in a standard format and were compared with a normal database of matched ages.							
Results	**True positives:**	12	**False negatives:**	5	**False positives:**	14	**True negatives:** 17
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Unclear	**Reference standard:**	Unclear	**Flow and timing:** Low
Overall risk of bias	Serious (Unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard and if the imaging patterns were pre-specified; the reference standard results were interpreted independently of the index test results.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						

Arslan E, Ekmekcioglu O, Gortan FA, Engin Akcan ZF, Erkan ME, Emlu HM, Hala M, Cermik TF, Sonmezoglu K. The value of FDG-PET/CT by using 3-dimensional stereotactic surface projection software analysis in the differential diagnosis of dementia. Turkish Journal of Medical Sciences, 2016; 45: 1149-1158.							
FTD versus non-FTD dementias							
Index Test: FDG-PET 18F-FDG PET attenuation-corrected PET/CT (Siemens Biograph LSO HI-RES PET-CT, USA) images were acquired. After iterative reconstruction, 0.3-cm-thick section images from both CT and PET were obtained in the transaxial, coronal, and sagittal planes. Visual assessment of PET images was performed by evaluating the changes in FDG uptake in both the cortical and subcortical areas. The axial sectional images of PET were also evaluated with 3D-SSP software (NEUROSTAT). The images were imported into a template with the Talairach coordinates in a standard format and were compared with a normal database of matched ages.							
Results	**True positives:**	8	**False negatives:**	9	**False positives:**	11	**True negatives:** 20
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Unclear	**Reference standard:**	Unclear	**Flow and timing:** Low
Overall risk of bias	Serious (Unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard and if the imaging patterns were pre-specified; the reference standard results were interpreted independently of the index test results.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						

P.1.2 B

Bachetta J-P, Kovari E, Merlo M, Canuto A, Herrman FR, Bouras C, Gold G, Hof PR and Giannakopoulos P. Validation of the clinical criteria for possible vascular dementia in the oldest-old.	
Study type	Retrospective cohort
Country	Switzerland
Setting	Department of Geriatrics and Psychiatry at the University of Geneva School of Medicine
Inclusion criteria	Diagnosis of dementia and subsequent autopsy examination; > 90 years old; evaluated within 6 months of death (including complete neuropsychological, neurology and mental status assessments).
Exclusion criteria	Patients with major neuropsychiatric illness, alcoholism or Parkinson's disease.
Sex	19.1% male

Bachetta J-P, Kovari E, Merlo M, Canuto A, Herrman FR, Bouras C, Gold G, Hof PR and Giannakopoulos P. Validation of the clinical criteria for possible vascular dementia in the oldest-old.								
Age	Mean age 94.6 years (SD 2.8)							
Presentation	Dementia							
Reference standard	AD was assesed according to Braak, CERAD and NIA-Reagan criteria. VaD was assessed based on the presence of both macroscopic and microscopic vascular pathology. Cases that satisfied both neuropathological criteria for AD and the study autopsy criteria for VaD were classified as having mixed dementias.							
VaD versus AD and mixed dementia (AD plus VaD)								
Index Test: NINDS-AIREN criteria NINDS-AIREN criteria								
Results	**True positives:**	20	**False negatives:**	16	**False positives:**	20	**True negatives:**	54
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (Participants were selected to be >90 years old)							
Index Test: ADDTC criteria ADDTC criteria (State of California Alzheimer's Disease Diagnostic and Treatment Centres criteria)								
Results	**True positives:**	21	**False negatives:**	15	**False positives:**	19	**True negatives:**	55
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall	Serious (Participants were selected to be >90 years old)							

Bachetta J-P, Kovari E, Merlo M, Canuto A, Herrman FR, Bouras C, Gold G, Hof PR and Giannakopoulos P. Validation of the clinical criteria for possible vascular dementia in the oldest-old.								
indirectness								
Index Test: Hachinski ischemic score, HIS (≥7) HIS, Hachinski ischemic score, total score ≥ 7.								
Results	**True positives:**	20	**False negatives:**	16	**False positives:**	25	**True negatives:**	49
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (Participants were selected to be >90 years old)							

Bahl JM, Heegaard NH, Falkenhorst G, Laursen H, Hogenhaven H, Molbak K, Jespersgaard C, Hougs L, Waldemar G, Johannsen P, Christiansen M. The diagnostic efficiency of biomarkers in sporadic Creutzfeldt-Jakob disease compared to Alzheimer's disease. Neurobiol Aging 2009; 30:1834–1841	
Study type	Prospective cohort
Country	Denmark
Setting	Not stated
Inclusion criteria	Patients with suspected CJD who were then diagnosed as having probable or definite sporadic CJD or not having CJD.
Exclusion criteria	Patients with suspected CJD who were then diagnosed as having possible CJD were excluded from study
Sex	50% male (for whole population, data for subgroups not presented)
Age	Not stated
Presentation	Rapidly progressive dementia leading to suspected CJD
Reference standard	Diagnosis by a national expert committee using WHO classification criteria of sporadic Creutzfeldt-Jakob disease (Brown et al., 2003).
CJD versus not CJD	

Bahl JM, Heegaard NH, Falkenhorst G, Laursen H, Hogenhaven H, Molbak K, Jespersgaard C, Hougs L, Waldemar G, Johannsen P, Christiansen M. The diagnostic efficiency of biomarkers in sporadic Creutzfeldt-Jakob disease compared to Alzheimer's disease. Neurobiol Aging 2009; 30:1834–1841							
Index Test: Total Tau total tau (500pg/ml)							
Results	**True positives:**	19	**False negatives:**	2	**False positives:**	17	**True negatives:** 99
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:** High
Overall risk of bias	Very serious (Exclusion of possible CJD group from index tests may inflate test sensitivity; test cut off not pre-specified)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: p-tau/total tau CSF P-tau/total tau of above 0.04 is CJD positive							
Results	**True positives:**	18	**False negatives:**	3	**False positives:**	12	**True negatives:** 104
Additional comments							
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:** High
Overall risk of bias	Very serious (Exclusion of possible CJD group from index tests may inflate test sensitivity; test cut off not pre-specified)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: Neuron-specific enolase CSF neuron-specific enolase (NSE) using 35ng/ml cut off							
Results	**True positives:**	16	**False negatives:**	4	**False positives:**	15	**True negatives:** 132

Bahl JM, Heegaard NH, Falkenhorst G, Laursen H, Hogenhaven H, Molbak K, Jespersgaard C, Hougs L, Waldemar G, Johannsen P, Christiansen M. The diagnostic efficiency of biomarkers in sporadic Creutzfeldt-Jakob disease compared to Alzheimer's disease. Neurobiol Aging 2009; 30:1834–1841								
Additional comments								
Risk of bias	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Exclusion of possible CJD group from index tests may inflate test sensitivity)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: CSF 14-3-3 immunoblotting CSF 14-3-3 protein								
Results	**True positives:**	18	**False negatives:**	1	**False positives:**	33	**True negatives:**	117
Additional comments								
Risk of bias	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Exclusion of possible CJD group from index tests may inflate test sensitivity)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Bastide L, De Breucker S, Van den Berge M, Fery P, Pepersack T, Bier JC. The Addenbrooke's Cognitive Examination Revised Is as Effective as the Original to Detect Dementia in a French-Speaking Population. Dement Geriatr Cogn Disord 2012; 34: 337–343.	
Study type	Prospective cohort
Country	Belgium
Setting	Erasme Hospital Memory Clinic

Bastide L, De Breucker S, Van den Berge M, Fery P, Pepersack T, Bier JC. The Addenbrooke's Cognitive Examination Revised Is as Effective as the Original to Detect Dementia in a French-Speaking Population. Dement Geriatr Cogn Disord 2012; 34: 337–343.								
Inclusion criteria	People examined at the memory clinic between November 2007 and October 2011 that had been followed at least 6 months and had an MMSE score of ≥20/30.							
Exclusion criteria	People with cognitive impairment due to alcohol intake or head traumas; people with post-traumatic stress disorders, siderosis, encephalitis sequelae, meningioma, CREST syndrome or frontal cavernoma; people being treated for hepatitis C.							
Sex	0.4% male							
Age	Mean age 79.0 years (SD 13.0)							
Presentation	Suspected dementia							
Reference standard	Diagnosis was based on all clinical and investigational results. The diagnosis of dementia was based on the DSM-III criteria; AD was based on the National Institute of Neurological and Communicative Disorders, Stroke-Alzheimer's Disease and Related Disorders Association criteria. The patients who were diagnosed as having FTLD fulfilled the clinical criteria of the Work Group on Frontotemporal Dementia and Pick's Disease while the diagnosis of DLB was based on the criteria published by McKeith et al.(1996)							
Dementia versus not dementia (including MCI)								
Index Test: Addenbrooke's Cognitive Examination-Revised, ACE-R (<83) Addenbrooke's Cognitive Examination Revised (ACE-R), French version, 83/100								
Results	**True positives:**	118	**False negatives:**	10	**False positives:**	60	**True negatives:**	132
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Optimised test cut-offs used.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<24) MMSE, 24/30								
Results	**True positives:**	50	**False negatives:**	78	**False positives:**	4	**True negatives:**	188
Additional comments								

Bastide L, De Breucker S, Van den Berge M, Fery P, Pepersack T, Bier JC. The Addenbrooke's Cognitive Examination Revised Is as Effective as the Original to Detect Dementia in a French-Speaking Population. Dement Geriatr Cogn Disord 2012; 34: 337–343.								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Optimised test cut-offs used.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<27) MMSE 27/30								
Results	**True positives:**	103	**False negatives:**	25	**False positives:**	49	**True negatives:**	143
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Optimised test cut-offs used.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Beinhoff U, Hilbert V, Bittner D, Gron G and Riepe MW. Screening for cognitive impairment: a triage for out patient care. Dementia and Geriatric Cognitive Disorders 2005; 20: 278–285.	
Study type	Prospective cohort
Country	Germany
Setting	University of Ulm memory clinic.
Inclusion criteria	People seeking first time advice on subjective memory complaints at the outpatient clinic
Exclusion criteria	not stated
Sex	51.7% male

Beinhoff U, Hilbert V, Bittner D, Gron G and Riepe MW. Screening for cognitive impairment: a triage for out patient care. Dementia and Geriatric Cognitive Disorders 2005; 20: 278–285.								
Age	mean age 64.7 years (SD 7.5)							
Presentation	subjective memory complaints							
Reference standard	AD was diagnosed according to the NINCDS-ADRDA criteria, MCI according to the criteria of Petersen et al., and major depressive disorder according to DSM-IV criteria. Subjects were considered as healthy controls (HC) only when findings on extensive neuropsychological, clinical, radiological, and laboratory investigations were normal and medical history was free from any neurological or psychiatric disease.							
Dementia versus no dementia								
Index Test: Clock Drawing Test, CDT, Shulman scoring method (>0) Clock Drawing Test, CDT, Shulman scoring method with maximum score of 6. Cut off score 1/6 (>0).								
Results	**True positives:**	57	**False negatives:**	9	**False positives:**	79	**True negatives:**	87
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Clock Drawing Test, CDT, Shulman scoring method (>1) Clock Drawing Test, CDT, Shulman scoring method with maximum score of 6. Cut off score 2/6 (>1).								
Results	**True positives:**	47	**False negatives:**	19	**False positives:**	20	**True negatives:**	146
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.)							
Indirectness	**Patient**	Low	**Index test:**	Low	**Reference**	Low		

Beinhoff U, Hilbert V, Bittner D, Gron G and Riepe MW. Screening for cognitive impairment: a triage for out patient care. Dementia and Geriatric Cognitive Disorders 2005; 20: 278–285.								
	selection:				**standard:**			
Overall indirectness	Not serious							
Index Test: Clock Drawing Test, CDT, Shulman scoring method (>2) Clock Drawing Test, CDT, Shulman scoring method with maximum score of 6. Cut off score 3/6 (>2).								
Results	**True positives:**	19	**False negatives:**	47	**False positives:**	4	**True negatives:**	162
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Letter Sorting Test, LST (<3) LST (letter sorting test), < 3. The task is to spell a 5-letter word forwards, backwards and in alphabetical order. One point per correct answer.								
Results	**True positives:**	53	**False negatives:**	13	**False positives:**	52	**True negatives:**	114
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall	Not serious							

Beinhoff U, Hilbert V, Bittner D, Gron G and Riepe MW. Screening for cognitive impairment: a triage for out patient care. Dementia and Geriatric Cognitive Disorders 2005; 20: 278–285.								
indirectness								
Index Test: Letter Sorting Test, LST (<2) LST (letter sorting test), < 2. The task is to spell a 5-letter word forwards, backwards and in alphabetical order. One point per correct answer.								
Results	**True positives:**	29	**False negatives:**	37	**False positives:**	12	**True negatives:**	154
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Letter Sorting Test, LST (<1) LST (letter sorting test), < 1. The task is to spell a 5-letter word forwards, backwards and in alphabetical order. One point per correct answer.								
Results	**True positives:**	8	**False negatives:**	58	**False positives:**	2	**True negatives:**	164
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Orientation, OR (<8)								

Beinhoff U, Hilbert V, Bittner D, Gron G and Riepe MW. Screening for cognitive impairment: a triage for out patient care. Dementia and Geriatric Cognitive Disorders 2005; 20: 278–285.								
OR (Orientation), <8. Eight questions about time, place and situation within about a minute. Score out of 8. Uses a subsection of the ADAS-Cog test.								
Results	**True positives:**	43	**False negatives:**	23	**False positives:**	16	**True negatives:**	150
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Orientation, OR (<7)								
OR (Orientation), <7. Eight questions about time, place and situation within about a minute. Score out of 8. Uses a subsection of the ADAS-Cog test.								
Results	**True positives:**	26	**False negatives:**	40	**False positives:**	2	**True negatives:**	164
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Memory Impairment Screen, MIS (<8)								
MIS (Memory Impairment Screen), 8. Tests delayed free and cued recall of 4 items. Score out of 12.								
Results	**True positives:**	65	**False**	1	**False positives:**	113	**True negatives:**	53

Beinhoff U, Hilbert V, Bittner D, Gron G and Riepe MW. Screening for cognitive impairment: a triage for out patient care. Dementia and Geriatric Cognitive Disorders 2005; 20: 278–285.								
			negatives:					
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Memory Impairment Screen, MIS (<7) MIS (Memory Impairment Screen), 7. Tests delayed free and cued recall of 4 items. Score out of 12.								
Results	**True positives:**	61	**False negatives:**	5	**False positives:**	78	**True negatives:**	88
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Memory Impairment Screen, MIS (<6) MIS (Memory Impairment Screen), 6. Tests delayed free and cued recall of 4 items. Score out of 12.								
Results	**True positives:**	58	**False negatives:**	8	**False positives:**	50	**True negatives:**	116
Additional comme								

Beinhoff U, Hilbert V, Bittner D, Gron G and Riepe MW. Screening for cognitive impairment: a triage for out patient care. Dementia and Geriatric Cognitive Disorders 2005; 20: 278–285.								
nts								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Memory Impairment Screen, MIS (<5) MIS (Memory Impairment Screen), 5. Tests delayed free and cued recall of 4 items. Score out of 12.								
Results	**True positives:**	54	**False negatives:**	12	**False positives:**	31	**True negatives:**	135
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Boston Naming Test, BNT (<15) Boston Naming Test, 15. Tests ability to name 15 line drawings. Score out of 15.								
Results	**True positives:**	47	**False negatives:**	19	**False positives:**	62	**True negatives:**	104
Additional comments								
Risk of bias	**Patient**	Low	**Index test:**	High	**Reference**	Low	**Flow and**	Low

Beinhoff U, Hilbert V, Bittner D, Gron G and Riepe MW. Screening for cognitive impairment: a triage for out patient care. Dementia and Geriatric Cognitive Disorders 2005; 20: 278–285.								
	selection:				**standard:**		**timing:**	
Overall risk of bias	Serious (Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Boston Naming Test, BNT (<14) Boston Naming Test, 14. Tests ability to name 15 line drawings. Score out of 15.								
Results	**True positives:**	36	**False negatives:**	30	**False positives:**	27	**True negatives:**	139
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Boston Naming Test, BNT (<13) Boston Naming Test, 13. Tests ability to name 15 line drawings. Score out of 15.								
Results	**True positives:**	26	**False negatives:**	40	**False positives:**	11	**True negatives:**	155
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and							

Beinhoff U, Hilbert V, Bittner D, Gron G and Riepe MW. Screening for cognitive impairment: a triage for out patient care. Dementia and Geriatric Cognitive Disorders 2005; 20: 278–285.								
	reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Verbal category fluency (animal naming), VF (<24) Verbal category fluency, <24. Tests ability to generate as many category names in given time. In this case the category was animals and time duration was 60 secs.								
Results	**True positives:**	65	**False negatives:**	1	**False positives:**	115	**True negatives:**	51
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Verbal category fluency (animal naming), VF (<23) Verbal category fluency, <23. Tests ability to generate as many category names in given time. In this case the category was animals and time duration was 60 secs.								
Results	**True positives:**	64	**False negatives:**	2	**False positives:**	102	**True negatives:**	64
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and							

Beinhoff U, Hilbert V, Bittner D, Gron G and Riepe MW. Screening for cognitive impairment: a triage for out patient care. Dementia and Geriatric Cognitive Disorders 2005; 20: 278–285.								
	reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Verbal category fluency (animal naming), VF (<22) Verbal category fluency, <22. Tests ability to generate as many category names in given time. In this case the category was animals and time duration was 60 secs.								
Results	**True positives:**	63	**False negatives:**	3	**False positives:**	90	**True negatives:**	76
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Verbal category fluency (animal naming), VF (<21) Verbal category fluency, <21. Tests ability to generate as many category names in given time. In this case the category was animals and time duration was 60 secs.								
Results	**True positives:**	62	**False negatives:**	4	**False positives:**	79	**True negatives:**	87
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and							

Beinhoff U, Hilbert V, Bittner D, Gron G and Riepe MW. Screening for cognitive impairment: a triage for out patient care. Dementia and Geriatric Cognitive Disorders 2005; 20: 278–285.								
	reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Verbal category fluency (animal naming), VF (<20) Verbal category fluency, <20. Tests ability to generate as many category names in given time. In this case the category was animals and time duration was 60 secs.								
Results	**True positives:**	62	**False negatives:**	4	**False positives:**	70	**True negatives:**	96
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: **Verbal category fluency (animal naming), VF (<19)** Verbal category fluency, <19. Tests ability to generate as many category names in given time. In this case the category was animals and time duration was 60 secs.								
Results	**True positives:**	56	**False negatives:**	10	**False positives:**	61	**True negatives:**	105
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and							

Beinhoff U, Hilbert V, Bittner D, Gron G and Riepe MW. Screening for cognitive impairment: a triage for out patient care. Dementia and Geriatric Cognitive Disorders 2005; 20: 278–285.								
	reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Berger G, Frolich L, Weber B, Pantel J. Diagnostic test accuracy of the clock drawing test: the relevance of "Time setting" in screening dementia. J of Geriatr Pscych and Neurology 2008; 21: 250-260.								
Study type	Prospective cohort							
Country	Germany							
Setting	Memory clinic of the University of Frankfurt am Main							
Inclusion criteria	People vising the memory clinic with suspected dementia.							
Exclusion criteria	People who received a final diagnosis of FTD, DLB or MCI.							
Sex	38.0% male							
Age	Mean age 71.5 years (SD 8.9)							
Presentation	Suspected dementia							
Reference standard	Dementia was diagnosed using the DSM-IV criteria and AD using NINCDS-ADRDA; VaD using NINDS-AIREN.							
Dementia versus not dementia								
Index Test: Clock Drawing Test, CDT, Shulman scoring method (>3) Clock Drawing Test, CDT (Shulman method), cut-off 2/3 (>3), time setting included (1 perfect, 6 no reasonable representation of a clock)								
Results	**True positives:**	301	**False negatives:**	33	**False positives:**	56	**True negatives:**	72
Risk of bias	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (People who received a final diagnosis of FTD, DLB or MCI were excluded from the study.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		

Berger G, Frolich L, Weber B, Pantel J. Diagnostic test accuracy of the clock drawing test: the relevance of "Time setting" in screening dementia. J of Geriatr Pscych and Neurology 2008; 21: 250-260.								
Overall indirectness	Not serious							
Index Test: Clock Drawing Test, CDT, Lin scoring method (<3) Clock Drawing Test, CDT (Lin method), cut-off 3/2 (<3), time setting included (scores 0-3, higher better)								
Results	**True positives:**	294	**False negatives:**	40	**False positives:**	65	**True negatives:**	63
Additional comments								
Risk of bias	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (People who received a final diagnosis of FTD, DLB or MCI were excluded from the study.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Clock Drawing Test, CDT, Manos and Wu scoring method (<8) Clock Drawing Test, CDT (Manos and Wu method),cut-off 8/7 (<8), time setting included, (0 to 10, higher better)								
Results	**True positives:**	271	**False negatives:**	63	**False positives:**	51	**True negatives:**	77
Additional comments								
Risk of bias	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (People who received a final diagnosis of FTD, DLB or MCI were excluded from the study.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Clock Drawing Test, CDT, Manos and Wu scoring method (<9)								

Berger G, Frolich L, Weber B, Pantel J. Diagnostic test accuracy of the clock drawing test: the relevance of "Time setting" in screening dementia. J of Geriatr Pscych and Neurology 2008; 21: 250-260.								
Clock Drawing Test, CDT (Manos and Wu method), cut-off 9/8 (<9), time setting included (0 to 10, higher better)								
Results	**True positives:**	311	**False negatives:**	23	**False positives:**	81	**True negatives:**	47
Additional comments								
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Very serious (People who received a final diagnosis of FTD, DLB or MCI were excluded from the study and an optimised threshold was used.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Clock Drawing Test, CDT, Wolf-Klein scoring method (<7) Clock Drawing Test, CDT (Wolf-Klein method), cut-off 7/6 (<7), time setting not included (scores 0-10, higher better)								
Results	**True positives:**	194	**False negatives:**	140	**False positives:**	24	**True negatives:**	104
Additional comments								
Risk of bias	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (People who received a final diagnosis of FTD, DLB or MCI were excluded from the study.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Clock Drawing Test, CDT, Watson scoring method (>4) Clock Drawing Test, CDT (Watson method), cut-off 3/4 (>4), time setting not included (score 0-7, lower better)								
Results	**True positives:**	240	**False negatives:**	94	**False positives:**	46	**True negatives:**	82

Berger G, Frolich L, Weber B, Pantel J. Diagnostic test accuracy of the clock drawing test: the relevance of "Time setting" in screening dementia. J of Geriatr Pscych and Neurology 2008; 21: 250-260.								
Additional comments								
Risk of bias	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (People who received a final diagnosis of FTD, DLB or MCI were excluded from the study.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Bergman H, Chertkow H, Wolfson C, Stern J, Rush C, Whitehead V, Dixon R. HM-PAO (CERETEC) SPECT brain scanning in the diagnosis of Alzheimer's disease. J Am Geriatr Soc 1997; 45: 15–20								
Study type	Prospective cohort							
Country	Canada							
Setting	Jewish General Hospital (McGill University) Memory clinic whose primary function is AD diagnosis.							
Inclusion criteria	Referral to the memory clinic.							
Exclusion criteria	Not stated							
Sex	50.0% male							
Age	mean age 75.4 years(SD 8.1)							
Presentation	Suspected dementia							
Reference standard	Diagnosis involved a battery of neuropsychological tests, clinical and neurological evaluation, laboratory investigation, and CT scans. Diagnosis was repeated after 12 months and then 6 monthly. Diagnostic criteria used: NINCDS-ADRDA for AD; patients not meeting the AD criteria after 1 year were classified as cognitive impairment no dementia; patients with a clinical diagnosis of VaD, a Hachinski score of >4 supported by a CT scan were classified as having VaD.							
AD versus non-AD (VaD and cognitive impairment no dementia groups)								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT imaged using a single-headed camera. Data obtained over a 360 degree rotation and 64x 64 matrix. Results were classified according to the Holman (1992) system. Pattern A was considered normal. Images classified by 2 nuclear medicine specialists.								
Results	**True positives:**	39	**False**	19	**False positives:**	29	**True negatives:**	13

Bergman H, Chertkow H, Wolfson C, Stern J, Rush C, Whitehead V, Dixon R. HM-PAO (CERETEC) SPECT brain scanning in the diagnosis of Alzheimer's disease. J Am Geriatr Soc 1997; 45: 15–20								
			negatives:					
Additional comments	The control group was excluded as recruited separately and did not have suspected dementia at baseline. Analysis was carried out on a subset of SPECT patterns by the authors therefore we excluded them all due to risk of reporting bias, except the analysis using pattern A (normal). Here not having Pattern A is positive for AD.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Beaudry P, Cohen P, Brandel JP, et al. 14-3-3 protein, neuron-specific enolase, and S-100 protein in cerebrospinal fluid of patients with Creutzfeldt-Jakob disease. Dement Geriatr Cogn Disord 1999; 10: 40–46.								
Study type	Prospective cohort							
Country	France							
Setting	Not stated, but samples provided by the French national CJD surveillance network							
Inclusion criteria	People with suspected CJD							
Exclusion criteria	Not stated							
Sex	47.3% male							
Age	Not stated							
Presentation	Rapidly progressive dementia leading to suspected CJD							
Reference standard	Criteria for CJD based on Masters et al. (1979)							
CJD (definite, probable and possible) versus not CJD								
Index Test: CSF 14-3-3 immunoblotting CSF 14-3-3 protein detected by immunoblotting								
Results	**True positives:**	66	**False negatives:**	15	**False positives:**	0	**True negatives:**	48

Beaudry P, Cohen P, Brandel JP, et al. 14-3-3 protein, neuron-specific enolase, and S-100 protein in cerebrospinal fluid of patients with Creutzfeldt-Jakob disease. Dement Geriatr Cogn Disord 1999; 10: 40–46.								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Serious (Optimised test cut-offs were used and it was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
CJD (excluding possible CJD) versus not CJD								
Index Test: CSF 14-3-3 immunoblotting CSF 14-3-3 protein detected by immunoblotting								
Results	**True positives:**	62	**False negatives:**	7	**False positives:**	0	**True negatives:**	48
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Serious (Optimised test cut-offs were used and it was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test. Subgroup analysis excluding <10% population so not downgraded for risk of bias.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
CJD versus not CJD								
Index Test: Neuron-specific enolase neuron-specific enolase (NSE), > 25ng/ml detected by ELISA								
Results	**True positives:**	59	**False negatives:**	22	**False positives:**	4	**True negatives:**	43
Additional comme	NSE was not measure in 1 sample							

Beaudry P, Cohen P, Brandel JP, et al. 14-3-3 protein, neuron-specific enolase, and S-100 protein in cerebrospinal fluid of patients with Creutzfeldt-Jakob disease. Dement Geriatr Cogn Disord 1999; 10: 40–46.								
nts								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Serious (Optimised test cut-offs were used and it was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
CJD (excluding possible CJD) versus not CJD								
Index Test: Neuron-specific enolase neuron-specific enolase (NSE), > 25ng/ml detected by ELISA								
Results	**True positives:**	55	**False negatives:**	14	**False positives:**	4	**True negatives:**	43
Additional comments	NSE was not measure in 1 sample							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Serious (Optimised test cut-offs were used and it was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test. Subgroup analysis excluding <10% population so not downgraded for risk of bias.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
CJD versus not CJD								
Index Test: S100B, 2.5ng/ml S-100 glial protein, >2.5ng/ml, measured using an immuno-luminometric assay								

Beaudry P, Cohen P, Brandel JP, et al. 14-3-3 protein, neuron-specific enolase, and S-100 protein in cerebrospinal fluid of patients with Creutzfeldt-Jakob disease. Dement Geriatr Cogn Disord 1999; 10: 40–46.								
Results	**True positives:**	71	**False negatives:**	10	**False positives:**	7	**True negatives:**	41
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Serious (Optimised test cut-offs were used and it was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
CJD (excluding possible CJD) versus not CJD								
Index Test: S100B, 2.5ng/ml S-100 glial protein, >2.5ng/ml, measured using an immuno-luminometric assay								
Results	**True positives:**	65	**False negatives:**	4	**False positives:**	7	**True negatives:**	41
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Serious (Optimised test cut-offs were used and it was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test. Subgroup analysis excluding <10% population so not downgraded for risk of bias.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Bonello M and Larner AJ. Applause sign: screening utility for dementia and cognitive impairment. Postgraduate Medicine 2016; 128: 250–253.	
Study type	Prospective cohort
Country	UK

Bonello M and Larner AJ. Applause sign: screening utility for dementia and cognitive impairment. Postgraduate Medicine 2016; 128: 250–253.								
Setting	Cognitive disorders clinic							
Inclusion criteria	New referrals to the cognitive disorders clinic seen over a 12-month period (January 2014–January 2015).							
Exclusion criteria	None							
Sex	49.2% male							
Age	Median age 61 years (range 18-91)							
Presentation	Cognitive impairment							
Reference standard	Clinician diagnosis using DSM-IV for dementia and Petersen (1999) for mild cognitive impairment.							
Dementia versus not dementia								
Index Test: Applause sign (<3) Applause sign, <3								
Results	**True positives:**	28	**False negatives:**	24	**False positives:**	33	**True negatives:**	190
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Boutoleau-Bretonniere C, Lebouviera T, Delaroche O, Lamy E, Evrard C, Charriau T, et al. Value of neuropsychological testing, imaging, and CSF biomarkers for the differential diagnosis and prognosis of clinically ambiguous dementia. Journal of Alzheimer's Disease 2012; 28(2):323-36.	
Study type	Prospective cohort
Country	France
Setting	Neurological memory Centre
Inclusion criteria	Based on CAD criteria: 1) dementia according to DSM-IV criteria; 2) cognitive changes of moderate severity (MMSE ≥ 18); 3) clinical symptoms at inclusion not fulfilling existing criteria for FTD, VaD, PD, LBD, progressive supranuclear palsy/corticobasal degeneration spectrum ; 4) presence of ≥1 "atypical feature" for AD listed in criteria III to V of

Boutoleau-Bretonniere C, Lebouviera T, Delaroche O, Lamy E, Evrard C, Charriau T, et al. Value of neuropsychological testing, imaging, and CSF biomarkers for the differential diagnosis and prognosis of clinically ambiguous dementia. Journal of Alzheimer's Disease 2012; 28(2):323-36.							
	NINCDS-ADRDA criteria						
Exclusion criteria	1) Clinical symptoms at inclusion fulfilling existing criteria for FTD, VaD, PD, LBD, progressive supranuclear palsy/corticobasal degeneration spectrum; 2) a major depressive disorder based on DSM-IV-TR criteria that is not being treated; 3) rapidly progressing dementia (<1 year since symptoms onset); 4) neoplastic, inflammatory, infectious, toxic or metabolic causes as evidenced by imaging and routine blood tests; 5) abnormal CSF (>5.109 leukocytes/mL and/or total protein level >1g/L); 6) advanced or unstable disease; 7) contraindications to MRI or SPECT imaging; 8) investigators unable to obtain CSF.						
Sex	61.7% male						
Age	Mean age 63.9 years (SD 9.4)						
Presentation	Clinically ambiguous dementia (CAD) as defined by CAD criteria at baseline						
Reference standard	Clinician diagnosis at 24 month follow up based on: Neary 1998 (FTD); NINCDS-ADRDA (AD); NINDS-AIREN (VaD); McKeith consensus criteria (DLB); psychiatric disorders using DSM-IV-TR; AD based on 4 criteria. AD criteria: 1) patients did not fit into either of the aforementioned criteria for non-AD dementia; 2) patients fulfilled NINCDS-ADRDA criteria I and II for probable AD; 3) 2-years follow-up evidenced a deterioration in memory impairment (drop in FCSRT total recall score ≥4) and in global cognitive functioning (drop in MMSE score ≥3); 4) initial atypical features did not appear meaningful in retrospect (i.e., gait disturbances that did not evolve into overt parkinsonism, or initial psychiatric, cognitive and/or behavioural symptoms that were relegated to the background in hindsight).						
FTD versus non-FTD							
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT. Images taken with a multiple headed camera. Threshold is pre-specified; visual interpretation of the SPECT images. Details: Sixty-four 20 s views over a 360◦ elliptical orbit taken using a three-headed gamma camera and reformatted into a matrix of 128×128. 99 mTc-HMPAO fixation was analysed regionally for frontal, parietal, temporal and occipital regions on the left and right. According to the pattern of 99mTc-HMPAO fixation, results were classified in four categories: Hypoperfusion of the AD type (temporoparietal hypoperfusion, whatever the perfusion of the frontal lobes); hypoperfusion of the FTD type (frontal±temporal hypoperfusion, no posterior defect); hypoperfusion of another type; normal SPECT. FTD type pattern used for analysis here.							
Results	**True positives:**	8	**False negatives:**	3	**False positives:**	10	**True negatives:** 39
Additional comments	Patients tested at baseline and formal reference diagnosis made at 24 months follow up. Calculations for FTD versus non -FTD used information in Archer 2015 Cochrane review that was obtained from the authors. Data for neuropsychological test results was not included in our analyses as the study only presents the results of selected tests						

Boutoleau-Bretonniere C, Lebouviera T, Delaroche O, Lamy E, Evrard C, Charriau T, et al. Value of neuropsychological testing, imaging, and CSF biomarkers for the differential diagnosis and prognosis of clinically ambiguous dementia. Journal of Alzheimer's Disease 2012; 28(2):323-36.								
	resulting in a high risk of reporting bias.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
FTD versus AD								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT. Images taken with a multiple headed camera. Threshold is pre-specified; visual interpretation of the SPECT images. Details: Sixty-four 20 s views over a 360◦ elliptical orbit taken using a three-headed gamma camera and reformatted into a matrix of 128×128. 99 mTc-HMPAO fixation was analysed regionally for frontal, parietal, temporal and occipital regions on the left and right. According to the pattern of 99mTc-HMPAO fixation, results were classified in four categories: Hypoperfusion of the AD type (temporoparietal hypoperfusion, whatever the perfusion of the frontal lobes); hypoperfusion of the FTD type (frontal±temporal hypoperfusion, no posterior defect); hypoperfusion of another type; normal SPECT. FTD type pattern used for analysis here.								
Results	**True positives:**	8	**False negatives:**	3	**False positives:**	1	**True negatives:**	17
Additional comments	Patients tested at baseline and formal reference diagnosis made at 24 months follow up.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Boutoleau-Bretonniere C, Lebouviera T, Delaroche O, Lamy E, Evrard C, Charriau T, et al. Value of neuropsychological testing, imaging, and CSF biomarkers for the differential diagnosis and prognosis of clinically ambiguous dementia. Journal of Alzheimer's Disease 2012; 28(2):323-36.								
FTD versus VaD								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT. Images taken with a multiple headed camera. Threshold is pre-specified; visual interpretation of the SPECT images. Details: Sixty-four 20 s views over a 360◦ elliptical orbit taken using a three-headed gamma camera and reformatted into a matrix of 128×128. 99 mTc-HMPAO fixation was analysed regionally for frontal, parietal, temporal and occipital regions on the left and right. According to the pattern of 99mTc-HMPAO fixation, results were classified in four categories: Hypoperfusion of the AD type (temporoparietal hypoperfusion, whatever the perfusion of the frontal lobes); hypoperfusion of the FTD type (frontal±temporal hypoperfusion, no posterior defect); hypoperfusion of another type; normal SPECT. FTD type pattern used for analysis here.								
Results	**True positives:**	8	**False negatives:**	3	**False positives:**	2	**True negatives:**	6
Additional comments	Patients tested at baseline and formal reference diagnosis made at 24 months follow up.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
FTD versus non-FTD dementia plus unclassifiable								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT. Images taken with a multiple headed camera. Threshold is pre-specified; visual interpretation of the SPECT images. Details: Sixty-four 20 s views over a 360◦ elliptical orbit taken using a three-headed gamma camera and reformatted into a matrix of 128×128. 99 mTc-HMPAO fixation was analysed regionally for frontal, parietal, temporal and occipital regions on the left and right. According to the pattern of 99mTc-HMPAO fixation, results were classified in four categories: Hypoperfusion of the AD type (temporoparietal hypoperfusion, whatever the perfusion of the frontal lobes); hypoperfusion of the FTD type (frontal±temporal hypoperfusion, no posterior defect); hypoperfusion of another type; normal SPECT. FTD type pattern used for analysis here.								
Results	**True positives:**	8	**False**	3	**False positives:**	10	**True negatives:**	35

Boutoleau-Bretonniere C, Lebouviera T, Delaroche O, Lamy E, Evrard C, Charriau T, et al. Value of neuropsychological testing, imaging, and CSF biomarkers for the differential diagnosis and prognosis of clinically ambiguous dementia. Journal of Alzheimer's Disease 2012; 28(2):323-36.								
			negatives:					
Additional comments	Patients tested at baseline and formal reference diagnosis made at 24 months follow up.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used but <10% study population discarded)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus non-AD dementia plus unclassifiable								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT. Images taken with a multiple headed camera. Threshold is pre-specified; visual interpretation of the SPECT images. Details: Sixty-four 20 s views over a 360◦ elliptical orbit taken using a three-headed gamma camera and reformatted into a matrix of 128×128. 99 mTc-HMPAO fixation was analysed regionally for frontal, parietal, temporal and occipital regions on the left and right. According to the pattern of 99mTc-HMPAO fixation, results were classified in four categories: Hypoperfusion of the AD type (temporoparietal hypoperfusion, whatever the perfusion of the frontal lobes); hypoperfusion of the FTD type (frontal±temporal hypoperfusion, no posterior defect); hypoperfusion of another type; normal SPECT. FTD type pattern used for analysis here.								
Results	**True positives:**	14	**False negatives:**	4	**False positives:**	13	**True negatives:**	25
Additional comments	Patients tested at baseline and formal reference diagnosis made at 24 months follow up.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used but <10% study population discarded)							
Indirectness	**Patient**	Low	**Index test:**	Low	**Reference**	Low		

Boutoleau-Bretonniere C, Lebouviera T, Delaroche O, Lamy E, Evrard C, Charriau T, et al. Value of neuropsychological testing, imaging, and CSF biomarkers for the differential diagnosis and prognosis of clinically ambiguous dementia. Journal of Alzheimer's Disease 2012; 28(2):323-36.								
	selection:				**standard:**			
Overall indirectness	Not serious							
AD versus VaD								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT. Images taken with a multiple headed camera. Threshold is pre-specified; visual interpretation of the SPECT images. Details: Sixty-four 20 s views over a 360◦ elliptical orbit taken using a three-headed gamma camera and reformatted into a matrix of 128×128. 99 mTc-HMPAO fixation was analysed regionally for frontal, parietal, temporal and occipital regions on the left and right. According to the pattern of 99mTc-HMPAO fixation, results were classified in four categories: Hypoperfusion of the AD type (temporoparietal hypoperfusion, whatever the perfusion of the frontal lobes); hypoperfusion of the FTD type (frontal±temporal hypoperfusion, no posterior defect); hypoperfusion of another type; normal SPECT. FTD type pattern used for analysis here.								
Results	**True positives:**	14	**False negatives:**	4	**False positives:**	4	**True negatives:**	4
Additional comments	Patients tested at baseline and formal reference diagnosis made at 24 months follow up.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus FTD								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT. Images taken with a multiple headed camera. Threshold is pre-specified; visual interpretation of the SPECT images. Details: Sixty-four 20 s views over a 360◦ elliptical orbit taken using a three-headed gamma camera and reformatted into a matrix of 128×128. 99 mTc-HMPAO fixation was analysed regionally for frontal, parietal, temporal and occipital regions on the left and right. According to the pattern of 99mTc-HMPAO fixation, results were classified in four categories: Hypoperfusion of the AD type (temporoparietal hypoperfusion, whatever the perfusion of the frontal								

Boutoleau-Bretonniere C, Lebouviera T, Delaroche O, Lamy E, Evrard C, Charriau T, et al. Value of neuropsychological testing, imaging, and CSF biomarkers for the differential diagnosis and prognosis of clinically ambiguous dementia. Journal of Alzheimer's Disease 2012; 28(2):323-36.								
lobes); hypoperfusion of the FTD type (frontal±temporal hypoperfusion, no posterior defect); hypoperfusion of another type; normal SPECT. FTD type pattern used for analysis here.								
Results	**True positives:**	14	**False negatives:**	4	**False positives:**	3	**True negatives:**	8
Additional comments	Patients tested at baseline and formal reference diagnosis made at 24 months follow up.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Boutoleau-Bretonniere C, Lebouviera T, Delaroche O, Lamy E, Evrard C, Charriau T, et al. Value of neuropsychological testing, imaging, and CSF biomarkers for the differential diagnosis and prognosis of clinically ambiguous dementia. Journal of Alzheimer's Disease 2012; 28: 323-36.	
Study type	prospective cohort
Country	France
Setting	Neurological memory Centre
Inclusion criteria	Based on CAD criteria: 1) dementia according to DSM-IV criteria; 2) cognitive changes of moderate severity (MMSE ≥ 18); 3) clinical symptoms at inclusion not fulfilling existing criteria for FTD, VaD, PD, LBD, progressive supranuclear palsy/corticobasal degeneration spectrum ; 4) presence of ≥1 "atypical feature" for AD listed in criteria III to V of NINCDS-ADRDA criteria
Exclusion criteria	1) Clinical symptoms at inclusion fulfilling existing criteria for FTD, VaD, PD, LBD, progressive supranuclear palsy/corticobasal degeneration spectrum; 2) a major depressive disorder based on DSM-IV-TR criteria that is not being treated; 3) rapidly progressing dementia (<1 year since symptoms onset); 4) neoplastic, inflammatory, infectious, toxic or metabolic causes as evidenced by imaging and routine blood tests; 5) abnormal CSF (>5.109 leukocytes/mL and/or total protein level >1g/L); 6) advanced or unstable disease; 7) contraindications to MRI or SPECT imaging; 8) investigators unable to obtain

Boutoleau-Bretonniere C, Lebouviera T, Delaroche O, Lamy E, Evrard C, Charriau T, et al. Value of neuropsychological testing, imaging, and CSF biomarkers for the differential diagnosis and prognosis of clinically ambiguous dementia. Journal of Alzheimer's Disease 2012; 28: 323-36.								
	CSF.							
Sex	61.7% male							
Age	Mean age 63.9 years (SD 9.4)							
Presentation	Clinically ambiguous dementia (CAD) as defined by CAD criteria at baseline							
Reference standard	Clinician diagnosis at 24 month follow up based on: Neary 1998 (FTD); NINCDS-ADRDA (AD); NINDS-AIREN (VaD); McKeith consensus criteria (DLB); psychiatric disorders using DSM-IV-TR; AD based on 4 criteria. AD criteria: 1) patients did not fit into either of the aforementioned criteria for non-AD dementia; 2) patients fulfilled NINCDS-ADRDA criteria I and II for probable AD; 3) 2-years follow-up evidenced a deterioration in memory impairment (drop in FCSRT total recall score ≥4) and in global cognitive functioning (drop in MMSE score ≥3); 4) initial atypical features did not appear meaningful in retrospect (i.e., gait disturbances that did not evolve into overt parkinsonism, or initial psychiatric, cognitive and/or behavioural symptoms that were relegated to the background in hindsight).							
AD versus non-AD dementia plus unclassifiable group								
Index Test: MRI MRI scans were made on different 1.0 and 1.5 Tesla scanners across several clinics. MTLA was rated visually when a coronal T1-weighted gradient echo sequence was available (55/60 patients), using Scheltens score ranging from 0 (no atrophy) to 4 (severe atrophy). Scores of the left and right side were averaged. The degree of white matter hyperintensities severity was rated visually on axial T2-weighted or fluid-attenuated inversion recovery (FLAIR) images using the Fazekas scale, ranging from grade 0 (no lesion) to grade 3 (confluent lesions).								
Results	**True positives:**	6	**False negatives:**	12	**False positives:**	13	**True negatives:**	25
Additional comments	Patients tested at baseline and formal reference diagnosis made at 24 months follow up.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus non-AD dementia not including unclassifiable group								

Boutoleau-Bretonniere C, Lebouviera T, Delaroche O, Lamy E, Evrard C, Charriau T, et al. Value of neuropsychological testing, imaging, and CSF biomarkers for the differential diagnosis and prognosis of clinically ambiguous dementia. Journal of Alzheimer's Disease 2012; 28: 323-36.								
Index Test: MRI MRI scans were made on different 1.0 and 1.5 Tesla scanners across several clinics. MTLA was rated visually when a coronal T1-weighted gradient echo sequence was available (55/60 patients), using Scheltens score ranging from 0 (no atrophy) to 4 (severe atrophy). Scores of the left and right side were averaged. The degree of white matter hyperintensities severity was rated visually on axial T2-weighted or fluid-attenuated inversion recovery (FLAIR) images using the Fazekas scale, ranging from grade 0 (no lesion) to grade 3 (confluent lesions).								
Results	**True positives:**	10	**False negatives:**	8	**False positives:**	4	**True negatives:**	22
Additional comments	Patients tested at baseline and formal reference diagnosis made at 24 months follow up.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
FTD versus non-FTD dementia plus unclassifiable group								
Index Test: MRI MRI scans were made on different 1.0 and 1.5 Tesla scanners across several clinics. MTLA was rated visually when a coronal T1-weighted gradient echo sequence was available (55/60 patients), using Scheltens score ranging from 0 (no atrophy) to 4 (severe atrophy). Scores of the left and right side were averaged. The degree of white matter hyperintensities severity was rated visually on axial T2-weighted or fluid-attenuated inversion recovery (FLAIR) images using the Fazekas scale, ranging from grade 0 (no lesion) to grade 3 (confluent lesions).								
Results	**True positives:**	2	**False negatives:**	9	**False positives:**	17	**True negatives:**	28
Additional comments	Patients tested at baseline and formal reference diagnosis made at 24 months follow up.							
Risk of bias	**Patient**	Unclear	**Index test:**	Low	**Reference**	Low	**Flow and**	High

Boutoleau-Bretonniere C, Lebouviera T, Delaroche O, Lamy E, Evrard C, Charriau T, et al. Value of neuropsychological testing, imaging, and CSF biomarkers for the differential diagnosis and prognosis of clinically ambiguous dementia. Journal of Alzheimer's Disease 2012; 28: 323-36.								
	selection:				**standard:**		**timing:**	
Overall risk of bias	Serious (Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
VaD versus non-VaD dementia plus unclassifiable group								
Index Test: MRI MRI scans were made on different 1.0 and 1.5 Tesla scanners across several clinics. MTLA was rated visually when a coronal T1-weighted gradient echo sequence was available (55/60 patients), using Scheltens score ranging from 0 (no atrophy) to 4 (severe atrophy). Scores of the left and right side were averaged. The degree of white matter hyperintensities severity was rated visually on axial T2-weighted or fluid-attenuated inversion recovery (FLAIR) images using the Fazekas scale, ranging from grade 0 (no lesion) to grade 3 (confluent lesions).								
Results	**True positives:**	7	**False negatives:**	1	**False positives:**	12	**True negatives:**	36
Additional comments	Patients tested at baseline and formal reference diagnosis made at 24 months follow up.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus non AD dementia (FTD, VaD, psychiatric disease)								
Index Test: Amyloid Beta 1-42 CSF Amyloid Beta 1-42 measured by commercially available sandwich ELISAs (Innotest, Innogenetics,Ghent, Belgium). Cut off <500 pg/ml.								
Results	**True positives:**	14	**False**	4	**False positives:**	9	**True negatives:**	17

Boutoleau-Bretonniere C, Lebouviera T, Delaroche O, Lamy E, Evrard C, Charriau T, et al. Value of neuropsychological testing, imaging, and CSF biomarkers for the differential diagnosis and prognosis of clinically ambiguous dementia. Journal of Alzheimer's Disease 2012; 28: 323-36.								
			negatives:					
Additional comments	Patients tested at baseline and formal reference diagnosis made at 24 months follow up.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Total tau CSF Total tau measured by commercially available sandwich ELISAs (Innotest, Innogenetics,Ghent, Belgium). Usual test cut off >350 pg/ml prespecified,								
Results	**True positives:**	18	**False negatives:**	0	**False positives:**	7	**True negatives:**	19
Additional comments	Patients tested at baseline and formal reference diagnosis made at 24 months follow up.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Total tau CSF Total tau measured by commercially available sandwich ELISAs (Innotest, Innogenetics, Ghent, Belgium). Optimised test cut off of > 480pg/ml here								
Results	**True positives:**	16	**False**	2	**False positives:**	3	**True negatives:**	23

Boutoleau-Bretonniere C, Lebouviera T, Delaroche O, Lamy E, Evrard C, Charriau T, et al. Value of neuropsychological testing, imaging, and CSF biomarkers for the differential diagnosis and prognosis of clinically ambiguous dementia. Journal of Alzheimer's Disease 2012; 28: 323-36.								
			negatives:					
Additional comments	Patients tested at baseline and formal reference diagnosis made at 24 months follow up.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: p-tau 181 CSF P- tau measured by commercially available sandwich ELISAs (Innotest, Innogenetics, Ghent, Belgium). Usual test cut off >50 pg/ml.								
Results	**True positives:**	18	**False negatives:**	0	**False positives:**	9	**True negatives:**	17
Additional comments	Patients tested at baseline and formal reference diagnosis made at 24 months follow up.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: p-tau 181 CSF P- tau measured by commercially available sandwich ELISAs (Innotest, Innogenetics, Ghent, Belgium). Optimised test cut off >68 pg/ml.								
Results	**True positives:**	17	**False**	1	**False positives:**	4	**True negatives:**	22

Boutoleau-Bretonniere C, Lebouviera T, Delaroche O, Lamy E, Evrard C, Charriau T, et al. Value of neuropsychological testing, imaging, and CSF biomarkers for the differential diagnosis and prognosis of clinically ambiguous dementia. Journal of Alzheimer's Disease 2012; 28: 323-36.								
			negatives:					
Additional comments	Patients tested at baseline and formal reference diagnosis made at 24 months follow up.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Amyloid Beta 1-42 The INNOTEST Amyloid Tau Index (IATI) was calculated using Amyloid Beta 42/(240 + [1.18×T-tau]) ratio. Measured by commercially available sandwich ELISAs (Innotest, Innogenetics, Ghent, Belgium). Cut off <0.8.								
Results	**True positives:**	17	**False negatives:**	1	**False positives:**	8	**True negatives:**	18
Additional comments	Patients tested at baseline and formal reference diagnosis made at 24 months follow up.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: CSF 14-3-3, total Tau and p-tau ≥2 abnormal CSF biomarkers, conventional cut offs, Amyloid beta 1-42 500pg/ml, total tau 350pg/ml, P-tau 50pg/ml								

Boutoleau-Bretonniere C, Lebouviera T, Delaroche O, Lamy E, Evrard C, Charriau T, et al. Value of neuropsychological testing, imaging, and CSF biomarkers for the differential diagnosis and prognosis of clinically ambiguous dementia. Journal of Alzheimer's Disease 2012; 28: 323-36.								
Results	**True positives:**	18	**False negatives:**	0	**False positives:**	8	**True negatives:**	18
Additional comments	Patients tested at baseline and formal reference diagnosis made at 24 months follow up.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: CSF 14-3-3, total Tau and p-tau ≥2 abnormal CSF biomarkers, optimised cut offs Amyloid beta 1-42 500pg/ml, total tau 480pg/ml, P-tau 68pg/ml								
Results	**True positives:**	17	**False negatives:**	1	**False positives:**	3	**True negatives:**	23
Additional comments	Patients tested at baseline and formal reference diagnosis made at 24 months follow up.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Brandel JP, Delasnerie-Laupretre N, Laplanche JL, Hauw JJ, Alperovitch A. Diagnosis of Creutzfeldt-Jakob disease: effect of clinical criteria on incidence estimates. Neurology 2000; 54: 1095–1099.								
Study type	Retrospective cohort							
Country	France							
Setting	Not stated, but samples provided by the French national CJD surveillance network							
Inclusion criteria	Suspicion of sporadic CJD							
Exclusion criteria	Genetic or iatrogenic CJD							
Sex	Not stated							
Age	Not stated							
Presentation	Not reported							
Reference standard	Histopathological examination of autopsy samples							
CJD versus not CJD								
Index Test: Master's criteria for CJD Master's criteria for CJD (Masters, 1979).								
Results	**True positives:**	193	**False negatives:**	3	**False positives:**	36	**True negatives:**	4
Additional comments	Data for the non-autopsy cases was excluded as the clinician diagnosis used the index test							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: French criteria for CJD French criteria for CJD (Cathala, 1979)								
Results	**True positives:**	173	**False negatives:**	23	**False positives:**	20	**True negatives:**	20

Brandel JP, Delasnerie-Laupretre N, Laplanche JL, Hauw JJ, Alperovitch A. Diagnosis of Creutzfeldt-Jakob disease: effect of clinical criteria on incidence estimates. Neurology 2000; 54: 1095–1099.								
Additional comments	Data for the non-autopsy cases was excluded as the clinician diagnosis used the index test							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: European criteria for CJD European criteria for CJD								
Results	**True positives:**	179	**False negatives:**	17	**False positives:**	29	**True negatives:**	11
Additional comments	Data for the non-autopsy cases was excluded as the clinician diagnosis used the index test							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
CJD probable versus not CJD (possible CJD excluded)								
Index Test: Master's criteria for CJD Master's criteria for CJD (Masters, 1979).								
Results	**True positives:**	145	**False negatives:**	6	**False positives:**	18	**True negatives:**	4
Additional comments	Data for the non-autopsy cases was excluded as the clinician diagnosis used the index test							

Brandel JP, Delasnerie-Laupretre N, Laplanche JL, Hauw JJ, Alperovitch A. Diagnosis of Creutzfeldt-Jakob disease: effect of clinical criteria on incidence estimates. Neurology 2000; 54: 1095–1099.								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Unclear risk of bias for patient selection as we could only use data for autopsied patients; subgroup analysis that excluded >10% population.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: French criteria for CJD French criteria for CJD (Cathala, 1979)								
Results	**True positives:**	99	**False negatives:**	52	**False positives:**	1	**True negatives:**	21
Additional comments	Data for the non-autopsy cases was excluded as the clinician diagnosis used the index test							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Unclear risk of bias for patient selection as we could only use data for autopsied patients; subgroup analysis that excluded >10% population.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: European criteria for CJD European criteria for CJD								
Results	**True positives:**	99	**False negatives:**	52	**False positives:**	1	**True negatives:**	21
Additional comments	Data for the non-autopsy cases was excluded as the clinician diagnosis used the index test							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High

Brandel JP, Delasnerie-Laupretre N, Laplanche JL, Hauw JJ, Alperovitch A. Diagnosis of Creutzfeldt-Jakob disease: effect of clinical criteria on incidence estimates. Neurology 2000; 54: 1095–1099.								
Overall risk of bias	Serious (Unclear risk of bias for patient selection as we could only use data for autopsied patients; subgroup analysis that excluded >10% population.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Brandt C, Bahl JC, Heegaard NH, Waldemar G, Johannsen P. Usability of cerebrospinal fluidbiomarkers in a tertiary memoryclinic. Dement Geriatr Cogn Disord 2008; 25: 553-558.								
Study type	Retrospective cohort							
Country	Denmark							
Setting	Copenhagen Memory Clinic , Copenhagen University Hospital							
Inclusion criteria	Participants undergoing initial diagnosis for dementia, or referred from other dementia specialists for a second opinion							
Exclusion criteria	Not stated							
Sex	57.1% male							
Age	Mean age 63.1 years (no SD data provided, but ages of participants ranged from 27-86 years old)							
Presentation	suspected dementia							
Reference standard	AD was diagnosed according to NINCDS-ADRDA criteria; VaD was diagnosed using NINDS-AIREN; diagnosis of FTD use the FTD consensus criteria (Neary et al); DBL used the DLB consensus criteria (McKeith et al); MCI used the Peterson criteria; depression used the ICD-10 and other diagnostic criteria are not specified.							
AD versus non-AD (including depression, MCI, other forms of dementia and unspecified diagnoses)								
Index Test: Amyloid Beta 1-42 Beta Amyloid 1–42 in CSF, < 400pg/ml, determined using an ELISA assay (Innotest Beta Amyloid 1-42)								
Results	**True positives:**	32	**False negatives:**	16	**False positives:**	35	**True negatives:**	64
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		

Brandel JP, Delasnerie-Laupretre N, Laplanche JL, Hauw JJ, Alperovitch A. Diagnosis of Creutzfeldt-Jakob disease: effect of clinical criteria on incidence estimates. Neurology 2000; 54: 1095–1099.								
Overall indirectness	Not serious							
Index Test: Total Tau Total -tau in CSF, <51 years >300pg/ml, 51-70 years >450pg/ml, >70 years >530pg/ml, determined using an ELISA assay (Innotest hTau Ag)								
Results	**True positives:**	25	**False negatives:**	23	**False positives:**	11	**True negatives:**	88
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: p-tau 181 p-tau 181 in CSF, >80pg/ml, determined using an ELISA assay (Innotest Phospho-tau 181)								
Results	**True positives:**	16	**False negatives:**	32	**False positives:**	8	**True negatives:**	92
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: 2 out of 3 abnormal (Amyloid Beta 1–42, Total Tau, p-tau) 2 out of 3 abnormal (Beta Amyloid 1–42, Total- tau, p-tau). For total -tau cut offs were <51 years >300pg/ml, 51-70 years >450pg/ml, >70 years								

Brandel JP, Delasnerie-Laupretre N, Laplanche JL, Hauw JJ, Alperovitch A. Diagnosis of Creutzfeldt-Jakob disease: effect of clinical criteria on incidence estimates. Neurology 2000; 54: 1095–1099.								
>530pg/ml; Beta Amyloid 1–42 , < 400pg/ml; p-tau 181, >80pg/ml								
Results	**True positives:**	20	**False negatives:**	28	**False positives:**	10	**True negatives:**	89
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Amyloid Beta 1-42, Total Tau and p-tau abnormal 3 out of 3 abnormal (Beta Amyloid 1–42, Total- tau, p-tau). For total -tau cut offs were <51 years >300pg/ml, 51-70 years >450pg/ml, >70 years >530pg/ml; Beta Amyloid 1–42 , < 400pg/ml; p-tau 181, >80pg/ml								
Results	**True positives:**	13	**False negatives:**	35	**False positives:**	1	**True negatives:**	98
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Burkhard PR; Sanchez JC; Landis T; Hochstrasser DF. CSF detection of the 14-3-3 protein in unselected patients with dementia.Neurology. 2001; 56: 1528-33	
Study type	Prospective cohort

Burkhard PR; Sanchez JC; Landis T; Hochstrasser DF. CSF detection of the 14-3-3 protein in unselected patients with dementia.Neurology. 2001; 56: 1528-33								
Country	Switzerland							
Setting	Not stated							
Inclusion criteria	Patients with ongoing cognitive impairment referred for further investigation							
Exclusion criteria	Not stated							
Sex	59.0% male							
Age	Mean age 66 years (range 17-85)							
Presentation	Patients with ongoing cognitive impairment							
Reference standard	Criteria not specified							
CJD versus not CJD								
Index Test: CSF 14-3-3 immunoblotting CSF 14-3-3 protein, immunoblotting								
Results	**True positives:**	2	**False negatives:**	0	**False positives:**	12	**True negatives:**	86
Risk of bias	**Patient selection:**	Low	**Index test:**	Yes	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (Patients do not have suspected CJD at baseline)							

P.1.3 C

Callahan CM, Unverzagt FW, Hui SL, et al. Six-item screener to identify cognitive impairment among potential subjects for clinical research. Med Care. 2002;40(9):771-81. PMID: 12218768.	
Study type	Prospective cohort
Country	USA
Setting	Indiana Alzheimer's Disease Centre

Callahan CM, Unverzagt FW, Hui SL, et al. Six-item screener to identify cognitive impairment among potential subjects for clinical research. Med Care. 2002;40(9):771-81. PMID: 12218768.								
Inclusion criteria	People referred to the Indiana Alzheimer's Disease Centre for evaluation for dementia.							
Exclusion criteria	Inability to complete assessments due to severe cognitive impairment.							
Sex	42.9% male							
Age	Mean age 69.6 years (SD not provided)							
Presentation	Suspected dementia							
Reference standard	Dementia diagnosed using DSM-III-R and ICD-10 criteria. Patients were diagnosed as cognitive impairment-no dementia if: (1) the informant reported a clinically significant decline in cognition; (2) the physician detected a clinically significant impairment in cognition; or (3) the participant's scores on cognitive testing fell below the 7th percentile; and if there was no clinically important impairment in the performance of activities of daily living.17 The 7th percentile is approximately equivalent to 1.5 standard deviations (SD) below the mean, the level of impairment specified by Mayo Clinic in their criteria for mild cognitive impairment.							
Dementia versus no dementia								
Index Test: 6 item screener (≥0) 6 item screener, ≥ 0								
Results	**True positives:**	345	**False negatives:**	0	**False positives:**	306	**True negatives:**	0
Additional comments	The data for cohort one was excluded as the people consisted of a community- based sample screened for dementia and did not have suspected dementia at baseline. For the analysis presented the paper does not state whether the comparator group includes no dementia and cognitive impairment no dementia or if it is just the non-dementia group alone.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: 6 item screener (≥1) 6 item screener, ≥ 1								

Callahan CM, Unverzagt FW, Hui SL, et al. Six-item screener to identify cognitive impairment among potential subjects for clinical research. Med Care. 2002;40(9):771-81. PMID: 12218768.								
Results	**True positives:**	334	**False negatives:**	11	**False positives:**	143	**True negatives:**	163
Additional comments	The data for cohort one was excluded as the people consisted of a community- based sample screened for dementia and did not have suspected dementia at baseline. For the analysis presented the paper does not state whether the comparator group includes no dementia and cognitive impairment no dementia or if it is just the non-dementia group alone.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: 6 item screener (≥2) 6 item screener, ≥ 2								
Results	**True positives:**	309	**False negatives:**	36	**False positives:**	63	**True negatives:**	243
Additional comments	The data for cohort one was excluded as the people consisted of a community- based sample screened for dementia and did not have suspected dementia at baseline. For the analysis presented the paper does not state whether the comparator group includes no dementia and cognitive impairment no dementia or if it is just the non-dementia group alone.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: 6 item screener (≥3) 6 item screener, ≥ 3								

Callahan CM, Unverzagt FW, Hui SL, et al. Six-item screener to identify cognitive impairment among potential subjects for clinical research. Med Care. 2002;40(9):771-81. PMID: 12218768.								
Results	**True positives:**	278	**False negatives:**	67	**False positives:**	28	**True negatives:**	278
Additional comments	The data for cohort one was excluded as the people consisted of a community- based sample screened for dementia and did not have suspected dementia at baseline. For the analysis presented the paper does not state whether the comparator group includes no dementia and cognitive impairment no dementia or if it is just the non-dementia group alone.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: 6 item screener (≥4) 6 item screener, ≥ 4								
Results	**True positives:**	233	**False negatives:**	112	**False positives:**	12	**True negatives:**	294
Additional comments	The data for cohort one was excluded as the people consisted of a community- based sample screened for dementia and did not have suspected dementia at baseline. For the analysis presented the paper does not state whether the comparator group includes no dementia and cognitive impairment no dementia or if it is just the non-dementia group alone.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: 6 item screener (≥5) 6 item screener, ≥ 5								

Callahan CM, Unverzagt FW, Hui SL, et al. Six-item screener to identify cognitive impairment among potential subjects for clinical research. Med Care. 2002;40(9):771-81. PMID: 12218768.								
Results	**True positives:**	169	**False negatives:**	176	**False positives:**	4	**True negatives:**	302
Additional comments	The data for cohort one was excluded as the people consisted of a community- based sample screened for dementia and did not have suspected dementia at baseline. For the analysis presented the paper does not state whether the comparator group includes no dementia and cognitive impairment no dementia or if it is just the non-dementia group alone.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: 6 item screener (≥6) 6 item screener, 6								
Results	**True positives:**	105	**False negatives:**	240	**False positives:**	2	**True negatives:**	304
Additional comments	The data for cohort one was excluded as the people consisted of a community- based sample screened for dementia and did not have suspected dementia at baseline. For the analysis presented the paper does not state whether the comparator group includes no dementia and cognitive impairment no dementia or if it is just the non-dementia group alone.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<28) MMSE, ≤ 27								

Callahan CM, Unverzagt FW, Hui SL, et al. Six-item screener to identify cognitive impairment among potential subjects for clinical research. Med Care. 2002;40(9):771-81. PMID: 12218768.							
Results	**True positives:**	338	**False negatives:**	7	**False positives:**	107	**True negatives:** 199
Additional comments	The data for cohort one was excluded as the people consisted of a community- based sample screened for dementia and did not have suspected dementia at baseline. For the analysis presented the paper does not state whether the comparator group includes no dementia and cognitive impairment no dementia or if it is just the non-dementia group alone.						
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Serious (It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: MMSE (<27) MMSE, ≤ 26							
Results	**True positives:**	326	**False negatives:**	19	**False positives:**	67	**True negatives:** 239
Additional comments	The data for cohort one was excluded as the people consisted of a community- based sample screened for dementia and did not have suspected dementia at baseline. For the analysis presented the paper does not state whether the comparator group includes no dementia and cognitive impairment no dementia or if it is just the non-dementia group alone.						
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Serious (It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: MMSE (<26) MMSE, ≤ 25							

Callahan CM, Unverzagt FW, Hui SL, et al. Six-item screener to identify cognitive impairment among potential subjects for clinical research. Med Care. 2002;40(9):771-81. PMID: 12218768.								
Results	**True positives:**	308	**False negatives:**	37	**False positives:**	49	**True negatives:**	257
Additional comments	The data for cohort one was excluded as the people consisted of a community- based sample screened for dementia and did not have suspected dementia at baseline. For the analysis presented the paper does not state whether the comparator group includes no dementia and cognitive impairment no dementia or if it is just the non-dementia group alone.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<25) MMSE, ≤ 24								
Results	**True positives:**	292	**False negatives:**	53	**False positives:**	30	**True negatives:**	276
Additional comments	The data for cohort one was excluded as the people consisted of a community- based sample screened for dementia and did not have suspected dementia at baseline. For the analysis presented the paper does not state whether the comparator group includes no dementia and cognitive impairment no dementia or if it is just the non-dementia group alone.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<24) MMSE, ≤ 23								

Callahan CM, Unverzagt FW, Hui SL, et al. Six-item screener to identify cognitive impairment among potential subjects for clinical research. Med Care. 2002;40(9):771-81. PMID: 12218768.							
Results	**True positives:**	281	**False negatives:**	64	**False positives:**	20	**True negatives:** 286
Additional comments	The data for cohort one was excluded as the people consisted of a community- based sample screened for dementia and did not have suspected dementia at baseline. For the analysis presented the paper does not state whether the comparator group includes no dementia and cognitive impairment no dementia or if it is just the non-dementia group alone.						
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Serious (It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: MMSE (<23) MMSE, ≤ 22							
Results	**True positives:**	265	**False negatives:**	80	**False positives:**	14	**True negatives:** 292
Additional comments	The data for cohort one was excluded as the people consisted of a community- based sample screened for dementia and did not have suspected dementia at baseline. For the analysis presented the paper does not state whether the comparator group includes no dementia and cognitive impairment no dementia or if it is just the non-dementia group alone.						
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Serious (It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: MMSE (<22) MMSE, ≤ 21							

Callahan CM, Unverzagt FW, Hui SL, et al. Six-item screener to identify cognitive impairment among potential subjects for clinical research. Med Care. 2002;40(9):771-81. PMID: 12218768.								
Results	**True positives:**	252	**False negatives:**	93	**False positives:**	9	**True negatives:**	297
Additional comments	The data for cohort one was excluded as the people consisted of a community- based sample screened for dementia and did not have suspected dementia at baseline. For the analysis presented the paper does not state whether the comparator group includes no dementia and cognitive impairment no dementia or if it is just the non-dementia group alone.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Carnero-Pardo C, Espejo-Martinez B, Lopez-Alcalde S, Espinosa-Garcia M, Saez-Zea C, Vilchez-Carrillo R, et al. Effectiveness and costs of phototest in dementia and cognitive impairment screening. BMC Neurology 2011; 11: 92.	
Study type	Prospective cohort
Country	Spain
Setting	Four primary care centres in the Metropolitan District of North Granada
Inclusion criteria	Suspicion of Cognitive impairment or Dementia, based on subjective complaints of memory loss or cognitive alteration, similar complaints made by a relative or informer, or observation by physicians of suspicious signs or symptoms.
Exclusion criteria	Previous enrolment in this study or previous diagnosis of cognitive or dementia.
Sex	27.9% male
Age	Mean age 72.5 years (SD 11.3)
Presentation	Memory loss complaints from the patient, the family or the person accompanying them, or suspected by the doctor on the basis of general observations
Reference standard	Clinician diagnosis based on the Cognitive-Behavioural Neurology Unit evaluations and a detailed clinical assessment using the DSM-IVR criteria for dementia.
Dementia versus no dementia	

Carnero-Pardo C, Espejo-Martinez B, Lopez-Alcalde S, Espinosa-Garcia M, Saez-Zea C, Vilchez-Carrillo R, et al. Effectiveness and costs of phototest in dementia and cognitive impairment screening. BMC Neurology 2011; 11: 92.							
Index Test: phototest (<27) phototest ≤ 26. Spanish version A.							
Results	**True positives:**	39	**False negatives:**	9	**False positives:**	10	**True negatives:** 82
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: Memory Impairment Screen, MIS (<4) MIS (Memory Impairment Screen), cut off 3/4. Spanish							
Results	**True positives:**	28	**False negatives:**	2	**False positives:**	17	**True negatives:** 70
Additional comments							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: Memory Impairment Screen, MIS (<5) MIS (Memory Impairment Screen), cut off 4/5. Spanish							
Results	**True positives:**	29	**False negatives:**	1	**False positives:**	25	**True negatives:** 62
Additional comme							

Carnero-Pardo C, Espejo-Martinez B, Lopez-Alcalde S, Espinosa-Garcia M, Saez-Zea C, Vilchez-Carrillo R, et al. Effectiveness and costs of phototest in dementia and cognitive impairment screening. BMC Neurology 2011; 11: 92.								
nts								
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Carnero-Pardo 2013 {published and unpublished data} Carnero-Pardo C, Espejo-Martinez B, Lopez-Alcalde S, Espinosa-Garcia M, Saez-Zea C, Vilchez-Carrillo R, et al. Effectiveness and costs of phototest in dementia and cognitive impairment screening. BMC Neurology 2011;11: 92.] Creavin S. Solicitud de información para la revisión Cochrane : Efectividad del Mini-Mental en la detección del deterioro cognitivo en Atención Primaria [personal communication to Creavin et al 2016 Cohrane Review authors]								
Study type	Prospective cohort							
Country	Spain							
Setting	Four primary care centres in the Metropolitan District of North Granada plus 1 health centre in Madrid							
Inclusion criteria	Suspicion of Cognitive impairment or Dementia, based on subjective complaints of memory loss or cognitive alteration, similar complaints made by a relative or informer, or observation by physicians of suspicious signs or symptoms.							
Exclusion criteria	Previous enrolment in this study or previous diagnosis of cognitive or dementia.							
Sex	29.2% male							
Age	Mean age 72.6 years (SD not stated)							
Presentation	Memory loss complaints from the patient, the family or the person accompanying them, or suspected by the doctor on the basis of general observations							
Reference standard	Clinician diagnosis based on the Cognitive-Behavioural Neurology Unit evaluations and a detailed clinical assessment using the DSM-IVR criteria for dementia.							
Dementia versus no dementia								
Index Test: MMSE (<25) MMSE (Folstein 1975 version), cut off 24/25, Spanish version								
Results	**True positives:**	77	**False**	0	**False positives:**	175	**True negatives:**	108

Carnero-Pardo 2013 {published and unpublished data} Carnero-Pardo C, Espejo-Martinez B, Lopez-Alcalde S, Espinosa-Garcia M, Saez-Zea C, Vilchez-Carrillo R, et al. Effectiveness and costs of phototest in dementia and cognitive impairment screening. BMC Neurology 2011;11: 92.] Creavin S. Solicitud de información para la revisión Cochrane : Efectividad del Mini-Mental en la detección del deterioro cognitivo en Atención Primaria [personal communication to Creavin et al 2016 Cohrane Review authors]								
			negatives:					
Additional comments	Includes unpublished data from Madrid (174 subjects) from 1 health centre between April 2000 and October 2002; published Granada data from February 2008 to January 2009. Additional data available for cut offs down to 14 as normal not presented here as these cut offs are not used in other studies.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Multiple test thresholds were used)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<24) MMSE (Folstein 1975 version), cut off 23/24, Spanish version								
Results	**True positives:**	77	**False negatives:**	0	**False positives:**	153	**True negatives:**	130
Additional comments	Includes unpublished data from Madrid (174 subjects) from 1 health centre between April 2000 and October 2002; published Granada data from February 2008 to January 2009. Additional data available for cut offs down to 14 as normal not presented here as these cut offs are not used in other studies.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Multiple test thresholds were used)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<23) MMSE (Folstein 1975 version), cut off 22/23, Spanish version								
Results	**True positives:**	76	**False**	1	**False positives:**	122	**True negatives:**	161

Carnero-Pardo 2013 {published and unpublished data} Carnero-Pardo C, Espejo-Martinez B, Lopez-Alcalde S, Espinosa-Garcia M, Saez-Zea C, Vilchez-Carrillo R, et al. Effectiveness and costs of phototest in dementia and cognitive impairment screening. BMC Neurology 2011;11: 92.] Creavin S. Solicitud de información para la revisión Cochrane : Efectividad del Mini-Mental en la detección del deterioro cognitivo en Atención Primaria [personal communication to Creavin et al 2016 Cohrane Review authors]								
			negatives:					
Additional comments	Includes unpublished data from Madrid (174 subjects) from 1 health centre between April 2000 and October 2002; published Granada data from February 2008 to January 2009. Additional data available for cut offs down to 14 as normal not presented here as these cut offs are not used in other studies.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Multiple test thresholds were used)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<22) MMSE (Folstein 1975 version), cut off 21/22, Spanish version								
Results	**True positives:**	74	**False negatives:**	3	**False positives:**	93	**True negatives:**	190
Additional comments	Includes unpublished data from Madrid (174 subjects) from 1 health centre between April 2000 and October 2002; published Granada data from February 2008 to January 2009. Additional data available for cut offs down to 14 as normal not presented here as these cut offs are not used in other studies.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Multiple test thresholds were used)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<21) MMSE (Folstein 1975 version), cut off 20/21, Spanish version								
Results	**True positives:**	73	**False**	4	**False positives:**	76	**True negatives:**	207

Carnero-Pardo 2013 {published and unpublished data} Carnero-Pardo C, Espejo-Martinez B, Lopez-Alcalde S, Espinosa-Garcia M, Saez-Zea C, Vilchez-Carrillo R, et al. Effectiveness and costs of phototest in dementia and cognitive impairment screening. BMC Neurology 2011;11: 92.] Creavin S. Solicitud de información para la revisión Cochrane : Efectividad del Mini-Mental en la detección del deterioro cognitivo en Atención Primaria [personal communication to Creavin et al 2016 Cohrane Review authors]								
			negatives:					
Additional comments	Includes unpublished data from Madrid (174 subjects) from 1 health centre between April 2000 and October 2002; published Granada data from February 2008 to January 2009. Additional data available for cut offs down to 14 as normal not presented here as these cut offs are not used in other studies.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Multiple test thresholds were used)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<20) MMSE (Folstein 1975 version), cut off 19/20, Spanish version.								
Results	**True positives:**	72	**False negatives:**	5	**False positives:**	51	**True negatives:**	232
Additional comments	Includes unpublished data from Madrid (174 subjects) from 1 health centre between April 2000 and October 2002; published Granada data from February 2008 to January 2009. Additional data available for cut offs down to 14 as normal not presented here as these cut offs are not used in other studies.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Multiple test thresholds were used)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<19) MMSE (Folstein 1975 version), cut off 18/19, Spanish version								
Results	**True positives:**	68	**False**	9	**False positives:**	37	**True negatives:**	246

Carnero-Pardo 2013 {published and unpublished data} Carnero-Pardo C, Espejo-Martinez B, Lopez-Alcalde S, Espinosa-Garcia M, Saez-Zea C, Vilchez-Carrillo R, et al. Effectiveness and costs of phototest in dementia and cognitive impairment screening. BMC Neurology 2011;11: 92.] Creavin S. Solicitud de información para la revisión Cochrane : Efectividad del Mini-Mental en la detección del deterioro cognitivo en Atención Primaria [personal communication to Creavin et al 2016 Cohrane Review authors]								
			negatives:					
Additional comments	Includes unpublished data from Madrid (174 subjects) from 1 health centre between April 2000 and October 2002; published Granada data from February 2008 to January 2009. Additional data available for cut offs down to 14 as normal not presented here as these cut offs are not used in other studies.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Multiple test thresholds were used)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<18) MMSE (Folstein 1975 version) , cut off 17/18, Spanish version								
Results	**True positives:**	62	**False negatives:**	15	**False positives:**	23	**True negatives:**	260
Additional comments	Includes unpublished data from Madrid (174 subjects) from 1 health centre between April 2000 and October 2002; published Granada data from February 2008 to January 2009. Additional data available for cut offs down to 14 as normal not presented here as these cut offs are not used in other studies.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Multiple test thresholds were used)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<17) MMSE (Folstein 1975 version), cut off 16/17, Spanish version								
Results	**True positives:**	54	**False**	23	**False positives:**	20	**True negatives:**	263

Carnero-Pardo 2013 {published and unpublished data} Carnero-Pardo C, Espejo-Martinez B, Lopez-Alcalde S, Espinosa-Garcia M, Saez-Zea C, Vilchez-Carrillo R, et al. Effectiveness and costs of phototest in dementia and cognitive impairment screening. BMC Neurology 2011;11: 92.] Creavin S. Solicitud de información para la revisión Cochrane : Efectividad del Mini-Mental en la detección del deterioro cognitivo en Atención Primaria [personal communication to Creavin et al 2016 Cohrane Review authors]								
			negatives:					
Additional comments	Includes unpublished data from Madrid (174 subjects) from 1 health centre between April 2000 and October 2002; published Granada data from February 2008 to January 2009. Additional data available for cut offs down to 14 as normal not presented here as these cut offs are not used in other studies.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Multiple test thresholds were used)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Carnero-Pardo C, Cruz-Orduña I, Espejo-Martínez B, Martos-Aparicio C, López-Alcalde S, Olazarán J. Utility of the Mini-Cog for detection of cognitive impairment in primary care: data from two spanish studies. International Journal of Alzheimer's Disease 2013; 2013: 1-7.	
Study type	Prospective cohort
Country	Spain
Setting	Three primary care centres in Granada
Inclusion criteria	People presenting at the primary care clinic with cognitive complaints or with cognitive impairment suspected by the family physician or an informant.
Exclusion criteria	People with a former diagnosis of cognitive impairment
Sex	28.5% male
Age	Mean age 71.9 years (SD 8.9)
Presentation	Complaints or suspicion (either by informant or by family physician) of cognitive dysfunction or cognitive deterioration
Reference standard	Mild cognitive impairment was diagnosed on the basis of a clinically relevant abnormal performance in at least one neuropsychological test; and absence of dementia. Dementia was diagnosed according to DSM-IV-TR.
Dementia versus no dementia (including MCI)	
Index Test: Mini-Cog (≤2)	

Carnero-Pardo C, Cruz-Orduña I, Espejo-Martínez B, Martos-Aparicio C, López-Alcalde S, Olazarán J. Utility of the Mini-Cog for detection of cognitive impairment in primary care: data from two spanish studies. International Journal of Alzheimer's Disease 2013; 2013: 1-7.								
Mini-Cog data extracted from MMSE and clock drawing test (Spanish version), ≤ 2 cut off								
Results	**True positives:**	49	**False negatives:**	0	**False positives:**	56	**True negatives:**	37
Additional comments	The data presented here was obtained from an unpublished Cochrane review using published and unpublished data from the primary study. The published primary study includes data from 2 study sites, but the Cochrane review authors used data confined to the Granada study sites as part of the Mini-Cog test (the CDT) was included as part of the reference standard in Madrid and was known by the individuals completing the reference standard. Also, the diagnosis of dementia separate from cognitive impairment was only available in the Granada sample and the data was made available to the CR group by the authors. The data for the CDT and MMSE were not extracted here as the primary study authors grouped mild cognitive impairment and dementia together in their analysis and we could not separate them with the information provided.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (The test threshold was not pre-specified, but was optimised based on the data obtained.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Chan Y, Yeung K-W, Ho H-F, Ho K-M, Lam ET-K, Leung W-L, Kam K-M. Use of cerebrospinal fluid enzyme immunoassay for diagnosis of neurosyphillis. International journal of STD and AIDs 2014; 25: 571-578.	
Study type	Prospective cohort
Country	Hong Kong
Setting	Social hygiene service, Hong Kong.
Inclusion criteria	Neurosyphilis workup from social hygiene clinic
Exclusion criteria	Previous known history of neurosphyilis, pregnancy, failed lumbar puncture, patients unable to give consent.
Sex	80.0% male
Age	Median age 42 years (range 19-79)
Presentation	Suspected neurosyphilis
Reference	Diagnosis by the IUSTI 2008 criteria. One of CSF-FTA-ABS or CSF-TPPA positive plus one of CSF mononuclear cell > 5/mm

Chan Y, Yeung K-W, Ho H-F, Ho K-M, Lam ET-K, Leung W-L, Kam K-M. Use of cerebrospinal fluid enzyme immunoassay for diagnosis of neurosyphillis. International journal of STD and AIDs 2014; 25: 571-578.							
standard	cubed or reactive CSF-VDRL.						
Neurosyphilis versus not neurosyphilis							
Index Test: CSF EIA CSF EIA, Enzyme imunoassay. Three recombinant T-pallodim antigent TpN15 TpN17 and TpN47. Cut-off 0.3 above the mean of the negative serum control.							
Results	**True positives:**	17	**False negatives:**	0	**False positives:**	15	**True negatives:** 13
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						

Chen C, Dong YH, Merchant R, Collinson S, Ting E, Quah SL et al. TTheMontreal Cognitive Assessment (MoCA) is superior to the Mini-Mental State Examination (MMSE) in detecting patients with moderate cognitive impairment, no dementia (CIND) and at high risk of dementia. Conference: Alzheimer's Association International Conference, Paris France. Conference Start: 20110716 Conference End: 20110721. 2011.	
Study type	Prospective cohort
Country	Singapore
Setting	Memory clinic
Inclusion criteria	Consecutive memory clinic patients
Exclusion criteria	Not stated
Sex	47.0% male
Age	Mean age 73.0 years (SD 10.0)
Presentation	Suspected dementia
Reference standard	Clinician diagnosis based on DSM-IV
Dementia vs no dementia	

Chen C, Dong YH, Merchant R, Collinson S, Ting E, Quah SL et al. TTheMontreal Cognitive Assessment (MoCA) is superior to the Mini-Mental State Examination (MMSE) in detecting patients with moderate cognitive impairment, no dementia (CIND) and at high risk of dementia. Conference: Alzheimer's Association International Conference, Paris France. Conference Start: 20110716 Conference End: 20110721. 2011.								
(normal + MCI)								
Index Test: Montreal Cognitive Assessment, MoCA (<19) Montreal Cognitive Assessment (MoCA), 18/19, Singaporean version								
Results	**True positives:**	162	**False negatives:**	10	**False positives:**	49	**True negatives:**	95
Additional comments	Data on test results for people with dementia versus non-dementia was obtained from Davis 2015 Cochrane review based on published and unpublished data from the Chen 2011 authors. Chen 2011 is a conference abstract and Dong 2012 does not present data for dementia versus no dementia participants so both studies were excluded.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Unclear	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Very serious (Unclear whether inappropriate exclusions were avoided or if a pre-specified test threshold was used; unclear whether index and reference tests were interpreted without knowledge of each other and whether all participants were included in the analysis.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Chohan G, Pennington C, Mackenzie JM, Andrews M, Everington D, Will RG, Knight RS, Green AJ. The role of cerebrospinal fluid 14-3-3 and other proteins in the diagnosis of sporadic Creutzfeldt-Jakob disease in the UK: a 10-year review. J Neurol Neurosurg Psychiatry. 2010; 81: 1243-8.	
Study type	Retrospective cohort
Country	UK
Setting	National CJD surveillance Unit, UK
Inclusion criteria	People referred to Surveillance unit with suspected CJD.
Exclusion criteria	Not stated
Sex	50.8% male
Age	Mean age 66.6 years (SD 10.2)

Chohan G, Pennington C, Mackenzie JM, Andrews M, Everington D, Will RG, Knight RS, Green AJ. The role of cerebrospinal fluid 14-3-3 and other proteins in the diagnosis of sporadic Creutzfeldt-Jakob disease in the UK: a 10-year review. J Neurol Neurosurg Psychiatry. 2010; 81: 1243-8.								
Presentation	Rapidly progressive dementia leading to suspected CJD							
Reference standard	Confirmed CJD based on neuropathological data, non-CJD diagnosis based on neuropathology or alternative clinical diagnosis, basis for probable CJD diagnosis is unclear.							
confirmed CJD versus not CJD								
Index Test: CSF 14-3-3 immunoblotting Presence of a detectable 14-3-3 band in CSF sample								
Results	**True positives:**	210	**False negatives:**	35	**False positives:**	44	**True negatives:**	127
Additional comments	Age range was 28-89 years old. Analysis excludes people diagnosed with probable CJD, but lacking neuropathological confirmation.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Total Tau CSF Total Tau (Innotest h-TAU -Ag assay), >1260pg/ml								
Results	**True positives:**	175	**False negatives:**	41	**False positives:**	20	**True negatives:**	115
Additional comments	Age range was 28-89 years old. Analysis excludes people diagnosed with probable CJD, but lacking neuropathological confirmation.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.)							
Indirectness	**Patient**	Low	**Index test:**	Low	**Reference**	Low		

Chohan G, Pennington C, Mackenzie JM, Andrews M, Everington D, Will RG, Knight RS, Green AJ. The role of cerebrospinal fluid 14-3-3 and other proteins in the diagnosis of sporadic Creutzfeldt-Jakob disease in the UK: a 10-year review. J Neurol Neurosurg Psychiatry. 2010; 81: 1243-8.								
	selection:				**standard:**			
Overall indirectness	Not serious							
Index Test: S100B, 1.0ng/ml CSF S100b assayed using an ELISA, >1.0ng/ml								
Results	**True positives:**	158	**False negatives:**	85	**False positives:**	17	**True negatives:**	152
Additional comments	Age range was 28-89 years old. Analysis excludes people diagnosed with probable CJD, but lacking neuropathological confirmation.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: CSF 14-3-3 (presence) and S100b (>1.0ng/ml) Presence of a detectable 14-3-3 band in CSF sample and CSF S100b assayed using an ELISA, >1.0ng/ml								
Results	**True positives:**	151	**False negatives:**	91	**False positives:**	9	**True negatives:**	160
Additional comments	Age range was 28-89 years old. Analysis excludes people diagnosed with probable CJD, but lacking neuropathological confirmation.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		

Chohan G, Pennington C, Mackenzie JM, Andrews M, Everington D, Will RG, Knight RS, Green AJ. The role of cerebrospinal fluid 14-3-3 and other proteins in the diagnosis of sporadic Creutzfeldt-Jakob disease in the UK: a 10-year review. J Neurol Neurosurg Psychiatry. 2010; 81: 1243-8.								
Overall indirectness	Not serious							
Index Test: Total Tau and S100b CSF Total Tau (Innotest h-TAU -Ag assay), >1260pg/ml and CSF S100b assayed using an ELISA, >1.0ng/ml.								
Results	**True positives:**	127	**False negatives:**	89	**False positives:**	7	**True negatives:**	128
Additional comments	Age range was 28-89 years old. Analysis excludes people diagnosed with probable CJD, but lacking neuropathological confirmation.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: CSF 14-3-3 and total Tau CSF Total Tau (Innotest h-TAU -Ag assay), >1260pg/ml and presence of a detectable 14-3-3 band in CSF sample.								
Results	**True positives:**	162	**False negatives:**	54	**False positives:**	16	**True negatives:**	119
Additional comments	Age range was 28-89 years old. Analysis excludes people diagnosed with probable CJD, but lacking neuropathological confirmation.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall	Not serious							

Chohan G, Pennington C, Mackenzie JM, Andrews M, Everington D, Will RG, Knight RS, Green AJ. The role of cerebrospinal fluid 14-3-3 and other proteins in the diagnosis of sporadic Creutzfeldt-Jakob disease in the UK: a 10-year review. J Neurol Neurosurg Psychiatry. 2010; 81: 1243-8.								
indirectness								
Index Test: CSF 14-3-3, total Tau and S100b CSF Total Tau (Innotest h-TAU -Ag assay), >1260pg/ml; presence of a detectable 14-3-3 band in CSF sample and CSF S100b assayed using an ELISA, >1.0ng/ml.								
Results	**True positives:**	123	**False negatives:**	93	**False positives:**	6	**True negatives:**	129
Additional comments	Age range was 28-89 years old. Analysis excludes people diagnosed with probable CJD, but lacking neuropathological confirmation.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Christensen IT, Larsson E-M, Holm IE, Nielsen OBF, Andersen S. Olfactory testing in consecutive patients referred with suspected dementia. BMC Geriatrics 2017; 17: 129- 135.								
Study type	Prospective cohort							
Country	Denmark							
Setting	Aalborg University Hospital geriatric outpatient clinic							
Inclusion criteria	Patients referred to the geriatric outpatient clinic at Aalborg University Hospital for evaluation of cognitive decline.							
Exclusion criteria	A history of nose-throat pathology with increasing sinusitis or chronic sinusitis, a flue condition, previous brain trauma, concussion of the brain with unconsciousness, and cerebral surgery.							
Sex	52% male							
Age	Mean age 79.1 years (no SD provided)							
Presentation	Suspected dementia							
Reference	Clinician diagnosis of probable AD according to the ICD-10 criteria suported by other criteria							

Chohan G, Pennington C, Mackenzie JM, Andrews M, Everington D, Will RG, Knight RS, Green AJ. The role of cerebrospinal fluid 14-3-3 and other proteins in the diagnosis of sporadic Creutzfeldt-Jakob disease in the UK: a 10-year review. J Neurol Neurosurg Psychiatry. 2010; 81: 1243-8.								
standard								
AD versus non-AD								
Index Test: Olfactory test, ≥ 3 errors Olfactory test, ≥ 3 errors. Using Pocket Smell Test pads that released odours when scratched. Each included three different scents, with each patient exposed to 6 different scents. In the case of uncertainty the test was repeated and the patient was given one additional opportunity to complete the test. The patient had to match the scent to one of four named choices.								
Results	**True positives:**	19	**False negatives:**	5	**False positives:**	14	**True negatives:**	12
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious (Although the threshold was not pre-specified data was presented for all possible cut offs.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Olfactory test, ≥ 4 errors Olfactory test, ≥ 4 errors. Using Pocket Smell Test pads that released odours when scratched. Each included three different scents, with each patient exposed to 6 different scents. In the case of uncertainty the test was repeated and the patient was given one additional opportunity to complete the test. The patient had to match the scent to one of four named choices								
Results	**True positives:**	12	**False negatives:**	12	**False positives:**	7	**True negatives:**	19
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious (Although the threshold was not pre-specified data was presented for all possible cut offs.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Olfactory test, ≥ 5 errors								

Chohan G, Pennington C, Mackenzie JM, Andrews M, Everington D, Will RG, Knight RS, Green AJ. The role of cerebrospinal fluid 14-3-3 and other proteins in the diagnosis of sporadic Creutzfeldt-Jakob disease in the UK: a 10-year review. J Neurol Neurosurg Psychiatry. 2010; 81: 1243-8.								
Olfactory test, ≥ 5 errors. Using Pocket Smell Test pads that released odours when scratched. Each included three different scents, with each patient exposed to 6 different scents. In the case of uncertainty the test was repeated and the patient was given one additional opportunity to complete the test. The patient had to match the scent to one of four named choices.								
Results	**True positives:**	5	**False negatives:**	19	**False positives:**	4	**True negatives:**	22
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious (Although the threshold was not pre-specified data was presented for all possible cut offs.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Coulthart M, Jansen GH, Olsen E, Godal D, Connolly, T, Choi BCK, Wang Z, Cashman NR. Diagnostic accuracy of cerebrospinal fluid protein markers for sporadic Creutzfeldt-Jakob disease in Canada: a 6-year prospective study. BMC Neurology 2011, 11:133.	
Study type	Prospective cohort
Country	Canada
Setting	CJD surveillance system laboratory
Inclusion criteria	People with suspected CJD.
Exclusion criteria	Not stated
Sex	51.4% male
Age	Median age ranged from 63-66 years across CJD and not CJD groups.
Presentation	Rapidly progressive dementia leading to suspected CJD
Reference standard	Neuropathology was carried out on 170/1000 participants, with clinician diagnosis of non-CJD for the remaining participants.
CJD versus not CJD	
Index Test: CSF 14-3-3 immunoblotting 14-3-3 in CSF, detection by immunoblotting at threshold of approximately 1.5ng control 14-3-3 protein per lane.	

Coulthart M, Jansen GH, Olsen E, Godal D, Connolly, T, Choi BCK, Wang Z, Cashman NR. Diagnostic accuracy of cerebrospinal fluid protein markers for sporadic Creutzfeldt-Jakob disease in Canada: a 6-year prospective study. BMC Neurology 2011, 11:133.								
Results	**True positives:**	112	**False negatives:**	15	**False positives:**	244	**True negatives:**	629
Additional comments	Data analysis exclusion criteria consisted of situations where: i) the sample was technically inadequate for 14-3-3 testing; (ii) duplicate samples; (iii) unconfirmed suspected CJD at sample submission; (iv) the 14-3-3 assay result was indeterminate; (v) final diagnostic classification was genetic prion disease; (vi) final diagnostic classification was probable sCJD (as a positive 14-3-3 result was used as a criterion to classify such cases, they could not be included in the validation study for this marker); or (vii) the case remained open at study closure.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious (Not downgraded for exclusions during data analysis as <10% population excluded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Total Tau tau in CSF, INNOTEST hTau-Ag ELISA, cut off 976pg/ml								
Results	**True positives:**	109	**False negatives:**	11	**False positives:**	99	**True negatives:**	727
Additional comments	Data analysis exclusion criteria consisted of situations where: i) the sample was technically inadequate for 14-3-3 testing; (ii) duplicate samples; (iii) unconfirmed suspected CJD at sample submission; (iv) the 14-3-3 assay result was indeterminate; (v) final diagnostic classification was genetic prion disease; (vi) final diagnostic classification was probable sCJD (as a positive 14-3-3 result was used as a criterion to classify such cases, they could not be included in the validation study for this marker); or (vii) the case remained open at study closure.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Optimised threshold used to analyse Tau results; unclear whether the reference standards would correctly classify non-CJD cases as not specified; not downgraded for exclusions during data analysis as <10% population excluded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Coulthart M, Jansen GH, Olsen E, Godal D, Connolly, T, Choi BCK, Wang Z, Cashman NR. Diagnostic accuracy of cerebrospinal fluid protein markers for sporadic Creutzfeldt-Jakob disease in Canada: a 6-year prospective study. BMC Neurology 2011, 11:133.								
Index Test: Total Tau tau in CSF, INNOTEST hTau-Ag ELISA, cut off 1300pg/ml								
Results	**True positives:**	101	**False negatives:**	19	**False positives:**	66	**True negatives:**	760
Additional comments	Data analysis exclusion criteria consisted of situations where: i) the sample was technically inadequate for 14-3-3 testing; (ii) duplicate samples; (iii) unconfirmed suspected CJD at sample submission; (iv) the 14-3-3 assay result was indeterminate; (v) final diagnostic classification was genetic prion disease; (vi) final diagnostic classification was probable sCJD (as a positive 14-3-3 result was used as a criterion to classify such cases, they could not be included in the validation study for this marker); or (vii) the case remained open at study closure.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious (Unclear whether the reference standards would correctly classify non-CJD cases as not specified; not downgraded for exclusions during data analysis as <10% population excluded and standard threshold used to analyse Tau results.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: S100B, 2.5ng/ml S100B, Sangtec 100 ELISA kit, cut off 2.5ng/ml								
Results	**True positives:**	106	**False negatives:**	16	**False positives:**	104	**True negatives:**	698
Additional comments	Data analysis exclusion criteria consisted of situations where: i) the sample was technically inadequate for 14-3-3 testing; (ii) duplicate samples; (iii) unconfirmed suspected CJD at sample submission; (iv) the 14-3-3 assay result was indeterminate; (v) final diagnostic classification was genetic prion disease; (vi) final diagnostic classification was probable sCJD (as a positive 14-3-3 result was used as a criterion to classify such cases, they could not be included in the validation study for this marker); or (vii) the case remained open at study closure.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Optimised threshold used to analyse S100B results; unclear whether the reference standards would correctly classify non-CJD cases as not specified; not downgraded for exclusions during data analysis as <10% population excluded.)							

Coulthart M, Jansen GH, Olsen E, Godal D, Connolly, T, Choi BCK, Wang Z, Cashman NR. Diagnostic accuracy of cerebrospinal fluid protein markers for sporadic Creutzfeldt-Jakob disease in Canada: a 6-year prospective study. BMC Neurology 2011, 11:133.								
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: S100B, 4.2ng/ml S100B, Sangtec 100 ELISA kit, cut off 4.2ng/ml								
Results	**True positives:**	63	**False negatives:**	59	**False positives:**	24	**True negatives:**	778
Additional comments	Data analysis exclusion criteria consisted of situations where: i) the sample was technically inadequate for 14-3-3 testing; (ii) duplicate samples; (iii) unconfirmed suspected CJD at sample submission; (iv) the 14-3-3 assay result was indeterminate; (v) final diagnostic classification was genetic prion disease; (vi) final diagnostic classification was probable sCJD (as a positive 14-3-3 result was used as a criterion to classify such cases, they could not be included in the validation study for this marker); or (vii) the case remained open at study closure.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious (Unclear whether the reference standards would correctly classify non-CJD cases as not specified; not downgraded for exclusions during data analysis as <10% population excluded and standard threshold used to analyse S100B results.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Coutinho G, De Oliveira-Souzs R, Moll J, Tovar-Moll F, Mattos P. Is it possible to identify individuals with mild cognitive impairment and Alzheimer's disease using a 30-minute neuropsychological battery? Rev Psiq Clín. 2013;40:139-43	
Study type	Prospective cohort
Country	Brazil
Setting	Private clinic
Inclusion criteria	People referred by their physicians because of memory complaints.
Exclusion criteria	Not stated

Coutinho G, De Oliveira-Souzs R, Moll J, Tovar-Moll F, Mattos P. Is it possible to identify individuals with mild cognitive impairment and Alzheimer's disease using a 30-minute neuropsychological battery? Rev Psiq Clín. 2013;40:139-43								
Sex	38.2% male							
Age	Mean age 73.9 years (7.1)							
Presentation	Memory complaints							
Reference standard	Dementia diagnosis was made using DSM-IV criteria, neuroimaging (MRI), clinical data and the full neuropsychological battery (Logical Memory from WMS-III, the Brazilian version of RAVLT17-18, Family Pictures, Digit Span, Spatial Span, CDT, MMSE, Vocabulary from WAIS-III, Matrix Reasoning from WAIS-III, and verbal fluency, both semantic (animals and fruits) and letter). AD diagnoses were made based on NINCDS-ADRDA criteria.							
Dementia versus no dementia (including MCI)								
Index Test: Brief Neuropsychological Test Battery Brief battery of tests (The brief battery consists of Logical Memory from the Wechsler Memory Scale III, digit span, clock drawing, verbal category fluency (animals) and MMSE)								
Results	**True positives:**	48	**False negatives:**	5	**False positives:**	13	**True negatives:**	65
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Cruz-Orduna I, Bellon JM, Torrero P, Aparicio E, Sanz A, Mula N, et al. Detecting MCI and dementia in primary care: effectiveness of the MMS, the FAQ and the IQCODE. Family Practice 2012; 29: 401-6.	
Study type	prospective cohort
Country	Spain
Setting	Seven medical clinics of the Pena Prieta Primary Care Centre (Health District 1, Autonomous Community of Madrid).
Inclusion criteria	Age >49 years; any complaint or suspicion raised by the patient, an informant or primary care physician related to cognition; a reliable informant

Cruz-Orduna I, Bellon JM, Torrero P, Aparicio E, Sanz A, Mula N, et al. Detecting MCI and dementia in primary care: effectiveness of the MMS, the FAQ and the IQCODE. Family Practice 2012; 29: 401-6.								
Exclusion criteria	Not stated							
Sex	29.1% male							
Age	Mean age 72.2 years (SD 8.9)							
Presentation	Complaint or suspicion of cognitive impairment							
Reference standard	Formal neuropsychological workup, with clinical examination and history; diagnosed by senior neurologist using DSM-IV-R criteria for dementia.							
Dementia versus no dementia								
Index Test: MMSE (<19) MMSE, cut point =18/19, Spanish version.								
Results	**True positives:**	12	**False negatives:**	3	**False positives:**	20	**True negatives:**	125
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Thresholds were not pre-specified but were calculated to give optimum sensitivity and specificity.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Informant Questionnaire on Cognitive Decline, IQCODE (26 item, >3.6) Informant Questionnaire on Cognitive Decline, IQCODE (26 item, 95/96). Spanish								
Results	**True positives:**	12	**False negatives:**	3	**False positives:**	34	**True negatives:**	111
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Thresholds were not pre-specified but were calculated to give optimum sensitivity and specificity.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		

Cruz-Orduna I, Bellon JM, Torrero P, Aparicio E, Sanz A, Mula N, et al. Detecting MCI and dementia in primary care: effectiveness of the MMS, the FAQ and the IQCODE. Family Practice 2012; 29: 401-6.								
Overall indirectness	Not serious							
Index Test: Functional Activities Questionnaire, FAQ (<9) FAQ (Functional Activities Questionnaire), scored 0 to 33 (total dependence). Spanish. Cut off 8/9.								
Results	**True positives:**	13	**False negatives:**	2	**False positives:**	26	**True negatives:**	119
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Thresholds were not pre-specified but were calculated to give optimum sensitivity and specificity.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Cuadrado-Corrales N, Jiménez-Huete A, Albo C, Hortigüela R, Vega L, Cerrato L, Sierra-Moros M, Rábano A, de Pedro-Cuesta J, Calero M. Impact of the clinical context on the 14-3-3 test for the diagnosis of sporadic CJD.BMC Neurology 2006, 6: 25	
Study type	Retrospective cohort
Country	Spain
Setting	The Spanish National Referral and Surveillance system diagnostic laboratory
Inclusion criteria	WHO criteria for sporadic CJD
Exclusion criteria	Haemolytic CSF, genetic aetiology, insufficient follow-up information, possible sCJD at final classification
Sex	51.2% male
Age	Median age 69.5 years (range 27.9-86.9)
Presentation	Rapidly progressive dementia leading to suspected CJD
Reference standard	WHO criteria for CJD

Cuadrado-Corrales N, Jiménez-Huete A, Albo C, Hortigüela R, Vega L, Cerrato L, Sierra-Moros M, Rábano A, de Pedro-Cuesta J, Calero M. Impact of the clinical context on the 14-3-3 test for the diagnosis of sporadic CJD.BMC Neurology 2006, 6: 25								
CJD versus not CJD								
Index Test: CSF 14-3-3 immunoblotting CSF 14-3-3 protein, immunoblotting								
Results	**True positives:**	155	**False negatives:**	22	**False positives:**	15	**True negatives:**	480
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (20% drop out due to problems with samples; <10 % excluded from analysis for possible CJD so not downgraded for this issue.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

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Davis HF, Skolasky RL, Selnes OA, Burgess DM, McArthur JC. Assessing HIV-associated dementia: modified HIV dementia scale versus the grooved pegboard. The AIDS reader 2002; 12: 29-31.	
Study type	Prospective cohort
Country	USA
Setting	Johns Hopkins neurology clinic
Inclusion criteria	Peolple with HIV, aged 18 years or older who were refererred to the Johns Hopkins neurology clinic for neurological assesssment
Exclusion criteria	A history of head trauma or loss of consciousness; curent diagnosis of active brain neoplasm or infection.
Sex	66.7% male
Age	Median age 39 years (range 33-47)
Presentation	Neurological issues
Reference standard	Clinician diagnosis using the American Academy of Neurology criteria
HAND versus other neurological disorder in HIV+ people	

Davis HF, Skolasky RL, Selnes OA, Burgess DM, McArthur JC. Assessing HIV-associated dementia: modified HIV dementia scale versus the grooved pegboard. The AIDS reader 2002; 12: 29-31.								
Index Test: Modified HIV dementia scale (m-HDS) (<7.5) Modified HIV dementia scale (m-HDS), cut-off <7.5								
Results	**True positives:**	101	**False negatives:**	43	**False positives:**	90	**True negatives:**	221
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Optimised test cut-offs used; unclear whether the index test was interpreted without knowledge of the reference test; unclear whether consecutive or random patients were enrolled.)							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (Study participants were aged from 33-47 years, median 39 years.)							
Index Test: Grooved pegboard test Grooved pegboard test, cut-off 1.5SD below the expected age-and education- adjusted mean.								
Results	**True positives:**	102	**False negatives:**	42	**False positives:**	168	**True negatives:**	143
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Unclear whether the index test was interpreted without knowledge of the reference test; unclear whether consecutive or random patients were enrolled.)							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (Study participants were aged from 33-47 years, median 39 years.)							
Index Test: Modified HIV dementia scale (m-HDS) and grooved pegboard combined. Modified HIV dementia scale (m-HDS) and grooved pegboard combined. A score of <7.5 on the m-HDS or 1.5SD below the expected age-and education-adjusted mean for the pegboard test.								
Results	**True positives:**	111	**False**	33	**False positives:**	187	**True negatives:**	124

Davis HF, Skolasky RL, Selnes OA, Burgess DM, McArthur JC. Assessing HIV-associated dementia: modified HIV dementia scale versus the grooved pegboard. The AIDS reader 2002; 12: 29-31.								
			negatives:					
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Optimised test cut-offs used; unclear whether the index test was interpreted without knowledge of the reference test; unclear whether consecutive or random patients were enrolled.)							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (Study participants were aged from 33-47 years, median 39 years.)							

Dobert N, Pantel J, Frolich L, Hamscho N, Menzel C, Grunwald F. Diagnostic value of FDG-PET and HMPAO-SPET in patients with mild dementia and mild cognitive impairment: Metabolic index and perfusion index. Dement Geriatr Cogn Disord 2005; 20: 63-70.	
Study type	Prospective cohort
Country	Germany
Setting	Memory clinic of the Department of Psychiatry of the University of Frankfurt.
Inclusion criteria	People with suspected early dementia presenting at the memory clinic
Exclusion criteria	Not stated
Sex	45.8% male
Age	Mean age 69.0 (SD 6.8 years)
Presentation	Suspected dementia
Reference standard	Dementia diagnosed based on all available information apart from PET and SPET index test results and using NINCDS-ADRDA for AD diagnosis, NINDS-AIREN for VaD
AD (including mixed AD and VaD) versus not AD	
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT. Transaxial, saggital and coronal images were reconstructed by a filtered back projection method using a Butterworth filter. Scans assess qualitatively by 2 experienced nuclear medicine physicians and for quantitative analysis a perfusion index was measured based on a standardised ROI analysis. The qualitative image patterns are described in detail the methods. AD pattern.	

Dobert N, Pantel J, Frolich L, Hamscho N, Menzel C, Grunwald F. Diagnostic value of FDG-PET and HMPAO-SPET in patients with mild dementia and mild cognitive impairment: Metabolic index and perfusion index. Dement Geriatr Cogn Disord 2005; 20: 63-70.								
Results	**True positives:**	102	**False negatives:**	41.76	**False positives:**	167.94	**True negatives:**	143.06
Additional comments	Additional subgroup analyses were not carried out as the numbers of study participants was very small (n=24)							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: FDG-PET FDG-PET. Carried out using a whole body scanner using a mean dose of 190M Bq with acquisition starting 45 min post injection. Transaxial, saggital and coronal images were reconstructed with an iterative reconstruction algorithm (slice thickness 3.49mm, pixel size 1.03mm). Scans assess qualitatively by by 2 experienced nuclear medicine physicians and for quantitative analysis the MI was measure based on a standardized region of interest (ROI) analysis consisting of 16 ROIs. The qualitative image patterns are described in detail the methods.								
Results	**True positives:**	111	**False negatives:**	33.12	**False positives:**	186.6	**True negatives:**	124.4
Additional comments	Additional subgroup analyses were not carried out as the numbers of study participants was very small (n=24)							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Dementia versus no dementia								

Dobert N, Pantel J, Frolich L, Hamscho N, Menzel C, Grunwald F. Diagnostic value of FDG-PET and HMPAO-SPET in patients with mild dementia and mild cognitive impairment: Metabolic index and perfusion index. Dement Geriatr Cogn Disord 2005; 20: 63-70.								
Index Test: FDG-PET (all dementia patterns) FDG-PET. Carried out using a whole body scanner using a mean dose of 190M Bq with acquisition starting 45 min post injection. Transaxial, saggital and coronal images were reconstructed with an iterative reconstruction algorithm (slice thickness 3.49mm, pixel size 1.03mm). Scans assess qualitatively by by 2 experienced nuclear medicine physicians and for quantitative analysis the MI was measure based on a standardized region of interest (ROI) analysis consisting of 16 ROIs. The qualitative image patterns are described in detail the methods.								
Results	**True positives:**	18	**False negatives:**	0	**False positives:**	1	**True negatives:**	5
Additional comments	Additional subgroup analyses were not carried out as the numbers of study participants was very small (n=24)							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: 99mTc-HMPAO SPECT (all dementia patterns) 99mTc-HMPAO SPECT. Transaxial, saggital and coronal images were reconstructed by a filtered back projection method using a Butterworth filter. Scans assess qualitatively by 2 experienced nuclear medicine physicians and for quantitative analysis a perfusion index was measured based on a standardised ROI analysis. The qualitative image patterns are described in detail the methods.								
Results	**True positives:**	16	**False negatives:**	2	**False positives:**	4	**True negatives:**	2
Additional comments	Subgroup analysis was not carried out as the numbers of study participants was very small (n=24)							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		

Dobert N, Pantel J, Frolich L, Hamscho N, Menzel C, Grunwald F. Diagnostic value of FDG-PET and HMPAO-SPET in patients with mild dementia and mild cognitive impairment: Metabolic index and perfusion index. Dement Geriatr Cogn Disord 2005; 20: 63-70.	
Overall indirectness	Not serious

Duits FH, Teunissen CE, Bouwman FH, Visser P-J, Mattsson N, Zetterberg H, Blennow K et al. The cerebrospinal fluid "Alzheimer profile": Easily said, but what does it mean?Alzheimer's & Dementia 2014; 10: 713–723.							
Study type	Prospective cohort						
Country	The Netherlands						
Setting	Memory clinic						
Inclusion criteria	Patients from the Amsterdam Dementia Cohort who had received a diagnosis of subjective memory complaints, MCI, AD, or other dementia and had baseline CSF collected between October 1999 and November 2011.						
Exclusion criteria	Not stated						
Sex	54.4% male						
Age	Mean age 67.1 years (SD 7.5)						
Presentation	Suspected dementia						
Reference standard	Probable AD was diagnosed according to the NINCDS-ADRDA criteria, and all patients met the core clinical National Institute of Aging– Alzheimer's Association (NIA-AA) criteria. Other criteria include: the consensus criteria for frontotemporal lobar degeneration (Neary, 1998), McKeith criteria (2005) for DLB, NINDS-AIREN for VaD; criteria by Boeve (2003) for corticobasal degeneration, and NINDS–Society for Progressive Supranuclear Palsy (Litvan, 1996) for progressive supranuclear palsy.						
AD versus no dementia (SMC, excludes MCI)							
Index Test: Amyloid Beta 1-42 Amyloid Beta 1-42, INNOTEST ELISA, cut-off < 550 pg/ml							
Results	**True positives:**	517	**False negatives:**	114	**False positives:**	33	**True negatives:** 218
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)						
Indirectness	**Patient**	Low	**Index test:**	Low	**Reference**	Low	

Duits FH, Teunissen CE, Bouwman FH, Visser P-J, Mattsson N, Zetterberg H, Blennow K et al. The cerebrospinal fluid "Alzheimer profile": Easily said, but what does it mean?Alzheimer's & Dementia 2014; 10: 713–723.								
	selection:				**standard:**			
Overall indirectness	Not serious							
AD versus other dementias (excluding MCI)								
Index Test: Amyloid Beta 1-42 Amyloid Beta 1-42, INNOTEST ELISA, cut-off < 550 pg/ml								
Results	**True positives:**	517	**False negatives:**	114	**False positives:**	75	**True negatives:**	192
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus not AD (SMC and other dementias, excluding MCI)								
Index Test: Amyloid Beta 1-42 Amyloid Beta 1-42, INNOTEST ELISA, cut-off < 550 pg/ml								
Results	**True positives:**	517	**False negatives:**	114	**False positives:**	107	**True negatives:**	411
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus no dementia (SMC, excludes MCI)								

Duits FH, Teunissen CE, Bouwman FH, Visser P-J, Mattsson N, Zetterberg H, Blennow K et al. The cerebrospinal fluid "Alzheimer profile": Easily said, but what does it mean?Alzheimer's & Dementia 2014; 10: 713–723.								
Index Test: Total tau t-tau, INNOTEST ELISA, cut-off > 375 pg/ml								
Results	**True positives:**	517	**False negatives:**	114	**False positives:**	48	**True negatives:**	203
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus other dementias (excluding MCI)								
Index Test: Total tau t-tau, INNOTEST ELISA, cut-off > 375 pg/ml								
Results	**True positives:**	517	**False negatives:**	114	**False positives:**	99	**True negatives:**	168
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus not AD (SMC and other dementias, excluding MCI)								
Index Test: Total tau Total tau, INNOTEST ELISA, cut-off > 375 pg/ml								
Results	**True positives:**	517	**False**	114	**False positives:**	146	**True negatives:**	372

Duits FH, Teunissen CE, Bouwman FH, Visser P-J, Mattsson N, Zetterberg H, Blennow K et al. The cerebrospinal fluid "Alzheimer profile": Easily said, but what does it mean?Alzheimer's & Dementia 2014; 10: 713–723.								
			negatives:					
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus no dementia (SMC, excludes MCI)								
Index Test: p-tau 181 p-tau 181, INNOTEST ELISA, cut-off > 52 pg/ml								
Results	**True positives:**	543	**False negatives:**	88	**False positives:**	98	**True negatives:**	153
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus other dementias (excluding MCI)								
Index Test: p-tau 181 p-tau 181, INNOTEST ELISA, cut-off > 52 pg/ml								
Results	**True positives:**	543	**False negatives:**	88	**False positives:**	109	**True negatives:**	158
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or							

Duits FH, Teunissen CE, Bouwman FH, Visser P-J, Mattsson N, Zetterberg H, Blennow K et al. The cerebrospinal fluid "Alzheimer profile": Easily said, but what does it mean?Alzheimer's & Dementia 2014; 10: 713–723.								
	whether inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus not AD (SMC and other dementias, excluding MCI)								
Index Test: p-tau 181 p-tau 181, INNOTEST ELISA, cut-off > 52 pg/ml								
Results	**True positives:**	543	**False negatives:**	88	**False positives:**	207	**True negatives:**	311
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus no dementia (SMC, excludes MCI)								
Index Test: Amyloid Beta 1-42 and t-tau and/or p-tau abnormal Amyloid Beta 1-42 and t-tau and/or p-tau 181 abnormal. Amyloid Beta 1-42, INNOTEST ELISA, cut-off < 550 pg/ml; t-tau, INNOTEST ELISA, cut-off > 375 pg/ml; p-tau 181, INNOTEST ELISA, cut-off > 52 pg/ml.								
Results	**True positives:**	467	**False negatives:**	164	**False positives:**	20	**True negatives:**	231
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		

Duits FH, Teunissen CE, Bouwman FH, Visser P-J, Mattsson N, Zetterberg H, Blennow K et al. The cerebrospinal fluid "Alzheimer profile": Easily said, but what does it mean?Alzheimer's & Dementia 2014; 10: 713–723.							
Overall indirectness	Not serious						
AD versus other dementias (excluding MCI)							
Index Test: Amyloid Beta 1-42 and t-tau and/or p-tau abnormal Amyloid Beta 1-42 and t-tau and/or p-tau 181 abnormal. Amyloid Beta 1-42, INNOTEST ELISA, cut-off < 550 pg/ml; t-tau, INNOTEST ELISA, cut-off > 375 pg/ml; p-tau 181, INNOTEST ELISA, cut-off > 52 pg/ml.							
Results	**True positives:**	467	**False negatives:**	164	**False positives:**	51	**True negatives:** 216
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
AD versus not AD (SMC and other dementias, excluding MCI)							
Index Test: Amyloid Beta 1-42 and t-tau and/or p-tau abnormal Amyloid Beta 1-42 and t-tau and/or p-tau 181 abnormal. Amyloid Beta 1-42, INNOTEST ELISA, cut-off < 550 pg/ml; t-tau, INNOTEST ELISA, cut-off > 375 pg/ml; p-tau 181, INNOTEST ELISA, cut-off > 52 pg/ml.							
Results	**True positives:**	467	**False negatives:**	164	**False positives:**	71	**True negatives:** 447
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
AD versus no dementia (SMC, excludes MCI)							

Duits FH, Teunissen CE, Bouwman FH, Visser P-J, Mattsson N, Zetterberg H, Blennow K et al. The cerebrospinal fluid "Alzheimer profile": Easily said, but what does it mean?Alzheimer's & Dementia 2014; 10: 713–723.							
Index Test: ≥ 2 of 3 biomarkers abnormal (Amyloid Beta 1-42, t-tau, p-tau) ≥ 2 of 3 biomarkers abnormal (Amyloid Beta 1-42, t-tau, p-tau 181). Amyloid Beta 1-42, INNOTEST ELISA, cut-off < 550 pg/ml; t-tau, INNOTEST ELISA, cut-off > 375 pg/ml; p-tau 181, INNOTEST ELISA, cut-off > 52 pg/ml.							
Results	**True positives:**	543	**False negatives:**	88	**False positives:**	50	**True negatives:** 201
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
AD versus other dementias (excluding MCI)							
Index Test: ≥ 2 of 3 biomarkers abnormal (Amyloid Beta 1-42, t-tau, p-tau) ≥ 2 of 3 biomarkers abnormal (Amyloid Beta 1-42, t-tau, p-tau 181). Amyloid Beta 1-42, INNOTEST ELISA, cut-off < 550 pg/ml; t-tau, INNOTEST ELISA, cut-off > 375 pg/ml; p-tau 181, INNOTEST ELISA, cut-off > 52 pg/ml.							
Results	**True positives:**	543	**False negatives:**	88	**False positives:**	93	**True negatives:** 174
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
AD versus not AD (SMC and other dementias, excluding MCI)							
Index Test: ≥ 2 of 3 biomarkers abnormal (Amyloid Beta 1-42, t-tau, p-tau) ≥ 2 of 3 biomarkers abnormal (Amyloid Beta 1-42, t-tau, p-tau 181). Amyloid Beta 1-42, INNOTEST ELISA, cut-off < 550 pg/ml; t-tau, INNOTEST ELISA,							

Duits FH, Teunissen CE, Bouwman FH, Visser P-J, Mattsson N, Zetterberg H, Blennow K et al. The cerebrospinal fluid "Alzheimer profile": Easily said, but what does it mean?Alzheimer's & Dementia 2014; 10: 713–723.							
cut-off > 375 pg/ml; p-tau 181, INNOTEST ELISA, cut-off > 52 pg/ml.							
Results	**True positives:**	543	**False negatives:**	88	**False positives:**	144	**True negatives:** 374
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
AD versus no dementia (SMC, excludes MCI)							
Index Test: Total Tau/Amyloid Beta 1-42 t-tau/ Amyloid Beta 1-42, cut-off 0.71. Amyloid Beta 1-42, INNOTEST ELISA; t-tau, INNOTEST ELISA.							
Results	**True positives:**	536	**False negatives:**	95	**False positives:**	25	**True negatives:** 226
Additional comments	Cut-off determined for sensitivity set at 85%.						
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
AD versus other dementias (excluding MCI)							
Index Test: Total Tau/Amyloid Beta 1-42 t-tau/ Amyloid Beta 1-42, cut-off 0.71. Amyloid Beta 1-42, INNOTEST ELISA; t-tau, INNOTEST ELISA.							
Results	**True positives:**	536	**False**	95	**False positives:**	67	**True negatives:** 200

Duits FH, Teunissen CE, Bouwman FH, Visser P-J, Mattsson N, Zetterberg H, Blennow K et al. The cerebrospinal fluid "Alzheimer profile": Easily said, but what does it mean?Alzheimer's & Dementia 2014; 10: 713–723.								
			negatives:					
Additional comments	Cut-off determined for sensitivity set at 85%.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus not AD (SMC and other dementias, excluding MCI)								
Index Test: Total Tau/Amyloid Beta 1-42 Total tau/ Amyloid Beta 1-42, cut-off 0.71. Amyloid Beta 1-42, INNOTEST ELISA; t-tau, INNOTEST ELISA.								
Results	**True positives:**	536	**False negatives:**	95	**False positives:**	92	**True negatives:**	426
Additional comments	Cut-off determined for sensitivity set at 85%.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus no dementia (SMC, excludes MCI)								
Index Test: Total Tau/Amyloid Beta 1-42 t-tau/ Amyloid Beta 1-42, cut-off 0.52. Amyloid Beta 1-42, INNOTEST ELISA; t-tau, INNOTEST ELISA.								
Results	**True positives:**	587	**False**	44	**False positives:**	43	**True negatives:**	208

Duits FH, Teunissen CE, Bouwman FH, Visser P-J, Mattsson N, Zetterberg H, Blennow K et al. The cerebrospinal fluid "Alzheimer profile": Easily said, but what does it mean?Alzheimer's & Dementia 2014; 10: 713–723.								
			negatives:					
Additional comments	Cut-off determined for sensitivity set at 93%.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus other dementias (excluding MCI)								
Index Test: Total Tau/Amyloid Beta 1-42 t-tau/ Amyloid Beta 1-42, cut-off 0.52. Amyloid Beta 1-42, INNOTEST ELISA; t-tau, INNOTEST ELISA.								
Results	**True positives:**	587	**False negatives:**	44	**False positives:**	91	**True negatives:**	176
Additional comments	Cut-off determined for sensitivity set at 93%.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus not AD (SMC and other dementias, excluding MCI)								
Index Test: Total Tau/Amyloid Beta 1-42 Total tau/ Amyloid Beta 1-42, cut-off 0.52. Amyloid Beta 1-42, INNOTEST ELISA; t-tau, INNOTEST ELISA.								

Duits FH, Teunissen CE, Bouwman FH, Visser P-J, Mattsson N, Zetterberg H, Blennow K et al. The cerebrospinal fluid "Alzheimer profile": Easily said, but what does it mean?Alzheimer's & Dementia 2014; 10: 713–723.								
Results	**True positives:**	587	**False negatives:**	44	**False positives:**	133	**True negatives:**	385
Additional comments	Cut-off determined for sensitivity set at 93%.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus no dementia (SMC, excludes MCI)								
Index Test: p-tau/Amyloid Beta 1-42 p-tau 181/ Amyloid Beta 1-42, cut-off 0.11. Amyloid Beta 1-42, INNOTEST ELISA; p-tau 181, INNOTEST ELISA.								
Results	**True positives:**	536	**False negatives:**	95	**False positives:**	30	**True negatives:**	221
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus other dementias (excluding MCI)								
Index Test: p-tau/Amyloid Beta 1-42 p-tau 181/ Amyloid Beta 1-42, cut-off 0.11. Amyloid Beta 1-42, INNOTEST ELISA; p-tau 181, INNOTEST ELISA.								
Results	**True positives:**	536	**False negatives:**	95	**False positives:**	53	**True negatives:**	214

Duits FH, Teunissen CE, Bouwman FH, Visser P-J, Mattsson N, Zetterberg H, Blennow K et al. The cerebrospinal fluid "Alzheimer profile": Easily said, but what does it mean?Alzheimer's & Dementia 2014; 10: 713–723.								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus not AD (SMC and other dementias, excluding MCI)								
Index Test: p-tau/Amyloid Beta 1-42 p-tau 181/ Amyloid Beta 1-42, cut-off 0.11. Amyloid Beta 1-42, INNOTEST ELISA; p-tau 181, INNOTEST ELISA.								
Results	**True positives:**	536	**False negatives:**	95	**False positives:**	84	**True negatives:**	834
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus no dementia (SMC, excludes MCI)								
Index Test: p-tau/Amyloid Beta 1-42 p-tau 181/ Amyloid Beta 1-42, cut-off 0.08. Amyloid Beta 1-42, INNOTEST ELISA; p-tau 181, INNOTEST ELISA.								
Results	**True positives:**	587	**False negatives:**	44	**False positives:**	48	**True negatives:**	203
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)							

Duits FH, Teunissen CE, Bouwman FH, Visser P-J, Mattsson N, Zetterberg H, Blennow K et al. The cerebrospinal fluid "Alzheimer profile": Easily said, but what does it mean?Alzheimer's & Dementia 2014; 10: 713–723.								
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus other dementias (excluding MCI)								
Index Test: p-tau/Amyloid Beta 1-42 p-tau 181/ Amyloid Beta 1-42, cut-off 0.08. Amyloid Beta 1-42, INNOTEST ELISA; p-tau 181, INNOTEST ELISA.								
Results	**True positives:**	587	**False negatives:**	44	**False positives:**	88	**True negatives:**	179
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus not AD (SMC and other dementias, excluding MCI)								
Index Test: p-tau/Amyloid Beta 1-42 p-tau 181/ Amyloid Beta 1-42, cut-off 0.08. Amyloid Beta 1-42, INNOTEST ELISA; p-tau 181, INNOTEST ELISA.								
Results	**True positives:**	587	**False negatives:**	44	**False positives:**	136	**True negatives:**	382
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Duits FH, Teunissen CE, Bouwman FH, Visser P-J, Mattsson N, Zetterberg H, Blennow K et al. The cerebrospinal fluid "Alzheimer profile": Easily said, but what does it mean?Alzheimer's & Dementia 2014; 10: 713–723.								
AD versus no dementia (SMC, excludes MCI)								
Index Test: Formula Hulstaert (biomarkers) Formula Hulstaert, 1999. 240 +1.18 x tau = Ab42								
Results	**True positives:**	587	**False negatives:**	44	**False positives:**	43	**True negatives:**	208
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus other dementias (excluding MCI)								
Index Test: Formula Hulstaert (biomarkers) Formula Hulstaert, 1999. 240 +1.18 x tau = Ab42								
Results	**True positives:**	587	**False negatives:**	44	**False positives:**	93	**True negatives:**	174
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus not AD (SMC and other dementias, excluding MCI)								
Index Test: Formula Hulstaert (biomarkers) Formula Hulstaert, 1999. 240 +1.18 x tau = Ab42								

Duits FH, Teunissen CE, Bouwman FH, Visser P-J, Mattsson N, Zetterberg H, Blennow K et al. The cerebrospinal fluid "Alzheimer profile": Easily said, but what does it mean?Alzheimer's & Dementia 2014; 10: 713–723.								
Results	**True positives:**	587	**False negatives:**	44	**False positives:**	136	**True negatives:**	382
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus no dementia (SMC, excludes MCI)								
Index Test: Formula Mulder (biomarkers) Formula Mulder, 373 + 0.82x tau =Ab42								
Results	**True positives:**	587	**False negatives:**	44	**False positives:**	45	**True negatives:**	206
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus other dementias (excluding MCI)								
Index Test: Formula Mulder (biomarkers) Formula Mulder, 373 + 0.82x tau =Ab42								
Results	**True positives:**	587	**False negatives:**	44	**False positives:**	93	**True negatives:**	158
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High

Duits FH, Teunissen CE, Bouwman FH, Visser P-J, Mattsson N, Zetterberg H, Blennow K et al. The cerebrospinal fluid "Alzheimer profile": Easily said, but what does it mean?Alzheimer's & Dementia 2014; 10: 713–723.								
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus not AD (SMC and other dementias, excluding MCI)								
Index Test: Formula Mulder (biomarkers) Formula Mulder, 373 + 0.82x tau =Ab42								
Results	**True positives:**	587	**False negatives:**	44	**False positives:**	138	**True negatives:**	364
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus no dementia (SMC, excludes MCI)								
Index Test: Formula Mattson (biomarkers) Formula Mattson, 3.694 + 0.0105 x tau = Ab42/p-tau								
Results	**True positives:**	505	**False negatives:**	126	**False positives:**	25	**True negatives:**	226
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		

Duits FH, Teunissen CE, Bouwman FH, Visser P-J, Mattsson N, Zetterberg H, Blennow K et al. The cerebrospinal fluid "Alzheimer profile": Easily said, but what does it mean?Alzheimer's & Dementia 2014; 10: 713–723.								
Overall indirectness	Not serious							
AD versus other dementias (excluding MCI)								
Index Test: Formula Mattson (biomarkers) Formula Mattson, 3.694 + 0.0105 x tau = Ab42/p-tau								
Results	**True positives:**	505	**False negatives:**	126	**False positives:**	53	**True negatives:**	214
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus not AD (SMC and other dementias, excluding MCI)								
Index Test: Formula Mattson (biomarkers) Formula Mattson, 3.694 + 0.0105 x tau = Ab42/p-tau								
Results	**True positives:**	505	**False negatives:**	26	**False positives:**	79	**True negatives:**	440
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus no dementia (SMC, excludes MCI)								
Index Test: Formula Schoonenboom (biomarkers)								

Duits FH, Teunissen CE, Bouwman FH, Visser P-J, Mattsson N, Zetterberg H, Blennow K et al. The cerebrospinal fluid "Alzheimer profile": Easily said, but what does it mean?Alzheimer's & Dementia 2014; 10: 713–723.								
Formula Schoonenboom, 152+8.25x p-tau = Ab42								
Results	**True positives:**	574	**False negatives:**	57	**False positives:**	40	**True negatives:**	211
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus other dementias (excluding MCI)								
Index Test: Formula Schoonenboom (biomarkers) Formula Schoonenboom, 152+8.25x p-tau = Ab42								
Results	**True positives:**	574	**False negatives:**	57	**False positives:**	75	**True negatives:**	192
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or whether inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus not AD (SMC and other dementias, excluding MCI)								
Index Test: Formula Schoonenboom (biomarkers) Formula Schoonenboom, 152+8.25x p-tau = Ab42								
Results	**True positives:**	574	**False negatives:**	57	**False positives:**	115	**True negatives:**	403

Duits FH, Teunissen CE, Bouwman FH, Visser P-J, Mattsson N, Zetterberg H, Blennow K et al. The cerebrospinal fluid "Alzheimer profile": Easily said, but what does it mean?Alzheimer's & Dementia 2014; 10: 713–723.								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Dummaresq J, Langevin S, Gagnon S, Serhir B, Deligne B, Tremblay C, Tsang RSW et al. Clinical Prediction and Diagnosis of Neurosyphilis in HIV-Infected Patients with Early Syphilis. Journal of Clinical Microbiology 2013; 51: 4060–4066.								
Study type	Retrospective cohort							
Country	Canada							
Setting	Centre Hospitalier de l' Universite de Montreal (CHUM)							
Inclusion criteria	Early syphilis plus one of blood serum RPR titre ≥ 1:32, neurological and/or ophthalmic signs or symptoms of neurosyphilis or CD4 cell count of < 350 cells/microlitre.							
Exclusion criteria	Syphilis of unknown duration, history of neurosyphilis, treatment with penicillin prior to lumbar puncture.							
Sex	99.2% male							
Age	Median age 42 years (range 22-66)							
Presentation	Suspected neurosyphilis							
Reference standard	CSF-VDRL test reactive							
Neurosyphilis versus not neurosyphilis								
Index Test: PCR for T. pallidum genes: polA, Tpp47, and bmp. PCR for T. pallidum genes: polA, Tpp47, and bmp.								
Results	**True positives:**	6	**False negatives:**	9	**False positives:**	36	**True negatives:**	57
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							

Dummaresq J, Langevin S, Gagnon S, Serhir B, Deligne B, Tremblay C, Tsang RSW et al. Clinical Prediction and Diagnosis of Neurosyphilis in HIV-Infected Patients with Early Syphilis. Journal of Clinical Microbiology 2013; 51: 4060–4066.								
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (>99% men who have sex with men)							
Index Test: FTA-ABS FTA-ABS, fluorescent treponemal antibody absorption assay.								
Results	**True positives:**	15	**False negatives:**	0	**False positives:**	76	**True negatives:**	9
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (>99% men who have sex with men)							
Index Test: TPPA TPPA, Treponema pallidum particle agglutination assay.								
Results	**True positives:**	10	**False negatives:**	5	**False positives:**	45	**True negatives:**	40
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (>99% men who have sex with men)							

Dummaresq J, Langevin S, Gagnon S, Serhir B, Deligne B, Tremblay C, Tsang RSW et al. Clinical Prediction and Diagnosis of Neurosyphilis in HIV-Infected Patients with Early Syphilis. Journal of Clinical Microbiology 2013; 51: 4060–4066.								
Index Test: INNO-LIA INNO-LIA Syphilis assay.								
Results	**True positives:**	12	**False negatives:**	0	**False positives:**	63	**True negatives:**	8
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (>99% men who have sex with men)							

Dumurgier J, Schraen S, Gabelle A, Vercruysse O, Bombois S, Laplanche J-L, Peoc'h K et al. Cerebrospinal fluid amyloid-β 42/40 ratio in clinical setting of memory centers: a multicentric study. Alzheimer's Research & Therapy 2015; 7:30-38.	
Study type	Prospective cohort
Country	France
Setting	French clinical and research memory centres specializing in the care of patients with cognitive disorders- data merged for 3 centres
Inclusion criteria	Patients with cognitive impairment attending the memory clinic
Exclusion criteria	Patients with unknown clinical diagnoses or MCI
Sex	48.1% male
Age	mean age 65.9 years (SD 10.7)
Presentation	Suspected dementia
Reference standard	AD was diagnosed according to NINCDS-ADRDA using all available information including CSF biomarker results. Non-AD diagnostic criteria are not specified.
AD versus not AD	
Index Test: p-tau/Amyloid Beta 1-42	

Dumurgier J, Schraen S, Gabelle A, Vercruysse O, Bombois S, Laplanche J-L, Peoc'h K et al. Cerebrospinal fluid amyloid-β 42/40 ratio in clinical setting of memory centers: a multicentric study. Alzheimer's Research & Therapy 2015; 7:30-38.								
CSF p-tau181 and Amyloid Beta 1-42 combined								
Results	**True positives:**	114	**False negatives:**	12	**False positives:**	9	**True negatives:**	150
Additional comments	The study description of test timing is unclear: the reference standard diagnosis included consideration of the CSF results, but the CSF was taken 1 month after diagnosis. Data was only presented as the combined results of the 3 centres for the use of combinations of CSF biomarkers							
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	High	**Flow and timing:**	High
Overall risk of bias	Very Serious (The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study; the timing of the reference and index tests is unclear and a subgroup analysis was carried out that excluded >10% population (with indeterminate results).)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: p-tau and Amyloid Beta 42/40 CSF p-tau181 and Amyloid Beta 1-42/1-40 ratio combined								
Results	**True positives:**	118	**False negatives:**	17	**False positives:**	15	**True negatives:**	153
Additional comments	The study description of test timing is unclear: the reference standard diagnosis included consideration of the CSF results, but the CSF was taken 1 month after diagnosis. Data was only presented as the combined results of the 3 centres for the use of combinations of CSF biomarkers							
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	High	**Flow and timing:**	High
Overall risk of bias	Very Serious (The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study; the timing of the reference and index tests is unclear and a subgroup analysis was carried out that excluded >10% population (with indeterminate results).)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall	Not serious							

Dumurgier J, Schraen S, Gabelle A, Vercruysse O, Bombois S, Laplanche J-L, Peoc'h K et al. Cerebrospinal fluid amyloid-β 42/40 ratio in clinical setting of memory centers: a multicentric study. Alzheimer's Research & Therapy 2015; 7:30-38.								
indirectness								
Index Test: p-tau and Amyloid Beta 1-42 combined then in case of discrepancy between p-tau and Amyloid Beta 1-42 the Amyloid Beta 42/40 ratio was used in place of Amyloid Beta 1-42 CSF p-tau181 and Amyloid Beta 1-42 combined then in case of discrepancy between p-tau181 and Amyloid Beta 1-42 the Amyloid Beta 1-42/1-40 ratio was used in place of Amyloid Beta 1-42								
Results	**True positives:**	125	**False negatives:**	17	**False positives:**	16	**True negatives:**	171
Additional comments	The study description of test timing is unclear: the reference standard diagnosis included consideration of the CSF results, but the CSF was taken 1 month after diagnosis. Data was only presented as the combined results of the 3 centres for the use of combinations of CSF biomarkers							
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	High	**Flow and timing:**	High
Overall risk of bias	Very Serious (The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study; the timing of the reference and index tests is unclear and a subgroup analysis was carried out that excluded >10% population (with indeterminate results).)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Total Tau Total Tau in CSF measured using an INNOTEST ELISA kit, optimal cut off calculated as 389pg/ml								
Results	**True positives:**	63	**False negatives:**	10	**False positives:**	9	**True negatives:**	42
Additional comments	The study description of test timing is unclear: the reference standard diagnosis included consideration of the CSF results, but the CSF was taken 1 month after diagnosis.							
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	High	**Flow and timing:**	Low
Overall risk of bias	Very Serious (The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study and the timing of the reference and index tests is unclear.)							

Dumurgier J, Schraen S, Gabelle A, Vercruysse O, Bombois S, Laplanche J-L, Peoc'h K et al. Cerebrospinal fluid amyloid-β 42/40 ratio in clinical setting of memory centers: a multicentric study. Alzheimer's Research & Therapy 2015; 7:30-38.								
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: p-tau 181 p-tau 181 in CSF measured using an INNOTEST ELISA kit, optimal cut off calculated as 64pg/ml								
Results	**True positives:**	62	**False negatives:**	11	**False positives:**	7	**True negatives:**	44
Additional comments	The study description of test timing is unclear: the reference standard diagnosis included consideration of the CSF results, but the CSF was taken 1 month after diagnosis.							
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	High	**Flow and timing:**	Low
Overall risk of bias	Very Serious (The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study and the timing of the reference and index tests is unclear.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Amyloid Beta 1-42 Amyloid Beta 1–42 in CSF measured using an INNOTEST ELISA kit, optimal cut off calculated as 836pg/ml								
Results	**True positives:**	66	**False negatives:**	7	**False positives:**	15	**True negatives:**	36
Additional comments	The study description of test timing is unclear: the reference standard diagnosis included consideration of the CSF results, but the CSF was taken 1 month after diagnosis.							
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	High	**Flow and timing:**	Low
Overall risk of bias	Very Serious (The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study and the timing of the reference and index tests is unclear.)							

Dumurgier J, Schraen S, Gabelle A, Vercruysse O, Bombois S, Laplanche J-L, Peoc'h K et al. Cerebrospinal fluid amyloid-β 42/40 ratio in clinical setting of memory centers: a multicentric study. Alzheimer's Research & Therapy 2015; 7:30-38.								
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Amyloid Beta 42/40 Amyloid Beta 1-42/1-40 in CSF measured using an INNOTEST ELISA kit, optimal cut off calculated as 0.082.								
Results	**True positives:**	66	**False negatives:**	7	**False positives:**	17	**True negatives:**	34
Additional comments	The study description of test timing is unclear: the reference standard diagnosis included consideration of the CSF results, but the CSF was taken 1 month after diagnosis.							
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	High	**Flow and timing:**	Low
Overall risk of bias	Very Serious (The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study and the timing of the reference and index tests is unclear.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Total Tau Total Tau in CSF measured using an INNOTEST ELISA kit, optimal cut off calculated as 343pg/ml								
Results	**True positives:**	37	**False negatives:**	13	**False positives:**	26	**True negatives:**	85
Additional comments	The study description of test timing is unclear: the reference standard diagnosis included consideration of the CSF results, but the CSF was taken 1 month after diagnosis.							
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	High	**Flow and timing:**	Low
Overall risk of bias	Very Serious (The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study and the timing of the reference and index tests is unclear.)							

Dumurgier J, Schraen S, Gabelle A, Vercruysse O, Bombois S, Laplanche J-L, Peoc'h K et al. Cerebrospinal fluid amyloid-β 42/40 ratio in clinical setting of memory centers: a multicentric study. Alzheimer's Research & Therapy 2015; 7:30-38.								
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: p-tau 181 p-tau 181 in CSF measured using an INNOTEST ELISA kit, optimal cut off calculated as 62pg/ml								
Results	**True positives:**	36	**False negatives:**	14	**False positives:**	9	**True negatives:**	102
Additional comments	The study description of test timing is unclear: the reference standard diagnosis included consideration of the CSF results, but the CSF was taken 1 month after diagnosis.							
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	High	**Flow and timing:**	Low
Overall risk of bias	Very Serious (The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study and the timing of the reference and index tests is unclear.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Amyloid Beta 1-42 Amyloid Beta 1–42 in CSF measured using an INNOTEST ELISA kit, optimal cut off calculated as 737pg/ml								
Results	**True positives:**	35	**False negatives:**	15	**False positives:**	22	**True negatives:**	89
Additional comments	The study description of test timing is unclear: the reference standard diagnosis included consideration of the CSF results, but the CSF was taken 1 month after diagnosis.							
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	High	**Flow and timing:**	Low
Overall risk of bias	Very Serious (The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study and the timing of the reference and index tests is unclear.)							

Dumurgier J, Schraen S, Gabelle A, Vercruysse O, Bombois S, Laplanche J-L, Peoc'h K et al. Cerebrospinal fluid amyloid-β 42/40 ratio in clinical setting of memory centers: a multicentric study. Alzheimer's Research & Therapy 2015; 7:30-38.								
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Amyloid Beta 42/40 Amyloid Beta 1-42/1-40 in CSF measured using an INNOTEST ELISA kit, optimal cut off calculated as 0.050.								
Results	**True positives:**	32	**False negatives:**	18	**False positives:**	23	**True negatives:**	88
Additional comments	The study description of test timing is unclear: the reference standard diagnosis included consideration of the CSF results, but the CSF was taken 1 month after diagnosis.							
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	High	**Flow and timing:**	Low
Overall risk of bias	Very Serious (The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study and the timing of the reference and index tests is unclear.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Total Tau Total Tau in CSF measured using an INNOTEST ELISA kit, optimal cut off calculated as 300pg/ml								
Results	**True positives:**	35	**False negatives:**	2	**False positives:**	2	**True negatives:**	43
Additional comments								
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	High	**Flow and timing:**	Low
Overall risk of bias	Very Serious (The reference standard diagnosis included consideration of the CSF results; the test cut-offs were optimised; patients with unknown clinical diagnoses or MCI were excluded from the study and the timing of the reference and index tests is unclear and it is unclear whether a consecutive or random sample of patients was enrolled.)							

Dumurgier J, Schraen S, Gabelle A, Vercruysse O, Bombois S, Laplanche J-L, Peoc'h K et al. Cerebrospinal fluid amyloid-β 42/40 ratio in clinical setting of memory centers: a multicentric study. Alzheimer's Research & Therapy 2015; 7:30-38.								
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: p-tau 181 p-tau 181 in CSF measured using an INNOTEST ELISA kit, optimal cut off calculated as 58pg/ml								
Results	**True positives:**	32	**False negatives:**	5	**False positives:**	4	**True negatives:**	41
Additional comments								
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	High	**Flow and timing:**	Low
Overall risk of bias	Very Serious (The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study and the timing of the reference and index tests is unclear.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Amyloid Beta 1-42 Amyloid Beta 1–42 in CSF measured using an INNOTEST ELISA kit, optimal cut off calculated as 814pg/ml								
Results	**True positives:**	31	**False negatives:**	6	**False positives:**	9	**True negatives:**	36
Additional comments								
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	High	**Flow and timing:**	Low
Overall risk of bias	Very Serious (The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study and the timing of the reference and index tests is unclear.)							

Dumurgier J, Schraen S, Gabelle A, Vercruysse O, Bombois S, Laplanche J-L, Peoc'h K et al. Cerebrospinal fluid amyloid-β 42/40 ratio in clinical setting of memory centers: a multicentric study. Alzheimer's Research & Therapy 2015; 7:30-38.								
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Amyloid Beta 42/40 Amyloid Beta 1-42/1-40 in CSF measured using an INNOTEST ELISA kit, optimal cut off calculated as 0.065.								
Results	**True positives:**	33	**False negatives:**	4	**False positives:**	7	**True negatives:**	38
Additional comments	The study description of test timing is unclear: the reference standard diagnosis included consideration of the CSF results, but the CSF was taken 1 month after diagnosis.							
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	High	**Flow and timing:**	Low
Overall risk of bias	Very Serious (The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study and the timing of the reference and index tests is unclear.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

P.1.5 E

Engedal K, Snaedal J, Hoegh P, Jelic V, Bo Andersen B, Naik M, Wahlund LO, Oeksengaard AR. Quantitative EEG applying the statistical recognition pattern method: a useful tool in dementia diagnostic workup. Dement Geriatr Cogn Disord 2015;40:1–12.	
Study type	Prospective cohort
Country	Norway
Setting	6 Nordic memory clinics that are members of the Nordic Network in Dementia Diagnostics.
Inclusion criteria	Patients attending their first assessment at the memory clinic
Exclusion criteria	Significant neurological disorder with dementia other than AD, PDD and LBD, major psychiatric disorders and alcohol or drug abuse.

Engedal K, Snaedal J, Hoegh P, Jelic V, Bo Andersen B, Naik M, Wahlund LO, Oeksengaard AR. Quantitative EEG applying the statistical recognition pattern method: a useful tool in dementia diagnostic workup. Dement Geriatr Cogn Disord 2015;40:1–12.								
Sex	46.0% male							
Age	Mean age 71.7 years (SD 8.6)							
Presentation	Memory impairment							
Reference standard	Clinical diagnosis based the use of DSM-IV-R and the McKhann criteria for the diagnosis of AD, the NINDS-AIREN criteria for vascular dementia, the revised consensus criteria for LBD and the Lund-Manchester criteria for frontotemporal dementia.							
AD versus non-AD								
Index Test: EEG EEGs were recorded using NicoletOne EEG Systems (Natus).For each EEG channel, 20 spectral features were extracted; coherence was estimated for 37 chosen channel pairs, and the same spectral features were extracted as for each individual channel. All EEGs in this study were resampled to 256 Hz in order to make them comparable. The data are analysed applying the statistical pattern recognition technique, which is used to construct a classifier from two diagnostic groups of qEEGs. Three classifiers derived from the data gathered in a previous study were used: 'healthy control index'; 'Alzheimer's disease index', 'diffuse Lewy body/Parkinson's disease index'. Each of the recordings gathered in this study was classified by the three indices described above.								
Results	**True positives:**	94	**False negatives:**	41	**False positives:**	142	**True negatives:**	95
Additional comments	We excluded the healthy individuals that were recruited separately from our analysis as they do not match the research question population of interest							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
DLB versus non-DLB								
Index Test: EEG EEGs were recorded using NicoletOne EEG Systems (Natus).For each EEG channel, 20 spectral features were extracted; coherence was estimated for 37 chosen channel pairs, and the same spectral features were extracted as for each individual channel. All EEGs in this study were resampled to 256 Hz in order to make them comparable. The data are analysed applying the statistical pattern recognition technique, which is used to construct a classifier								

Engedal K, Snaedal J, Hoegh P, Jelic V, Bo Andersen B, Naik M, Wahlund LO, Oeksengaard AR. Quantitative EEG applying the statistical recognition pattern method: a useful tool in dementia diagnostic workup. Dement Geriatr Cogn Disord 2015;40:1–12.								
from two diagnostic groups of qEEGs. Three classifiers derived from the data gathered in a previous study were used: 'healthy control index'; 'Alzheimer's disease index', 'diffuse Lewy body/Parkinson's disease index'. Each of the recordings gathered in this study was classified by the three indices described above.								
Results	**True positives:**	13	**False negatives:**	2	**False positives:**	46	**True negatives:**	326
Additional comments	We excluded the healthy individuals that were recruited separately from our analysis as they do not match the research question population of interest							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Estorch M, Camacho V, Paredes P, et al. Cardiac (123)I-metaiodobenzylguanidine imaging allows early identification of dementia with Lewy bodies during life. Eur J Nucl Med Mol Imaging 2008; 35: 1636-1641.	
Study type	Prospective cohort
Country	Spain
Setting	Memory Unit in a Department of Neurology
Inclusion criteria	All patients with neurodegenerative diseases and cognitive impairment, and meeting the clinical international criteria of probable DLB
Exclusion criteria	None stated
Sex	46.2% male
Age	Mean age 77 years (range 60-89)
Presentation	People have previously been diagnosed with a neurodegenerative disease and meet the International Consensus Criteria for probable DLB (when two of fluctuating cognition, well-structured visual hallucinations and/or motor symptoms of parkinsonism are present)
Reference standard	Final clinical diagnosis 4 years after MIBG imaging

Estorch M, Camacho V, Paredes P, et al. Cardiac (123)I-metaiodobenzylguanidine imaging allows early identification of dementia with Lewy bodies during life. Eur J Nucl Med Mol Imaging 2008; 35: 1636-1641.								
DLB vs no-DLB								
Index Test: 123I-MIBG cardiac scintigraphy Myocardial 123I-MIBG activity was semi-quantified, obtaining the heart-to-mediastinuim ratio (HMR) and myocardial washout rate. Normal HMR defined for patients older than 60 years as >1.56								
Results	**True positives:**	18	**False negatives:**	1	**False positives:**	1	**True negatives:**	24
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Significant proportion of people not given a final reference standard diagnosis)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

P.1.6 F

Ferman TJ, Boeve BF, Smith GE, Lin S-C, Silber MH, Wszolek Z et al. Inclusion of RBD improves the diagnostic classification of dementia with Lewy bodies. Neurology200; 77: 876-882.	
Study type	Prospective cohort
Country	USA
Setting	Alzheimer's disease research centre, Maine.
Inclusion criteria	Autopsy at the centre; DSM-III diagnosis of dementia; clinically probable REM sleep behaviour disorder (RBD)
Exclusion criteria	None stated
Sex	57.7% male
Age	Not stated
Presentation	Suspected DLB
Reference standard	Braak criteria for DLB
DLB versus not DLB	

Ferman TJ, Boeve BF, Smith GE, Lin S-C, Silber MH, Wszolek Z et al. Inclusion of RBD improves the diagnostic classification of dementia with Lewy bodies. Neurology200; 77: 876-882.							
Index Test: Two or more of fluctuating attention and concentration, visual hallucinations and Parkinsonism Two or more of fluctuating attention and concentration, visual hallucinations and Parkinsonism							
Results	**True positives:**	83	**False negatives:**	15	**False positives:**	37	**True negatives:** 99
Additional comments	Features are very similar to the DLB consensus criteria, 2004.						
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: Two or more of visual hallucinations, Parkinsonism, fluctuating attention and concentration or RBD Two or more of visual hallucinations, Parkinsonism, fluctuating attention and concentration or RBD							
Results	**True positives:**	86	**False negatives:**	12	**False positives:**	37	**True negatives:** 99
Additional comments							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: RBD or two or more of visual hallucinations, Parkinsonism, and fluctuating attention and concentration RBD or two or more of visual hallucinations, Parkinsonism, and fluctuating attention and concentration							
Results	**True positives:**	88	**False**	10	**False positives:**	37	**True negatives:** 99

Ferman TJ, Boeve BF, Smith GE, Lin S-C, Silber MH, Wszolek Z et al. Inclusion of RBD improves the diagnostic classification of dementia with Lewy bodies. Neurology200; 77: 876-882.								
			negatives:					
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Two or more of visual hallucinations, Parkinsonism or RBD Two or more of visual hallucinations, Parkinsonism or RBD								
Results	**True positives:**	81	**False negatives:**	17	**False positives:**	21	**True negatives:**	115
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Flicker L, Logiudice D, Carlin JB, Ames D. The predictive value of dementia screening instruments in clinical populations. International Journal of Geriatric Psychiatry 1997; 12: 203–9.	
Study type	prospective cohort
Country	Australia
Setting	Memory clinic

Flicker L, Logiudice D, Carlin JB, Ames D. The predictive value of dementia screening instruments in clinical populations. International Journal of Geriatric Psychiatry 1997; 12: 203–9.							
Inclusion criteria	Patients attending the memory clinic who were able to complete the 3 assessments (MMSE, IQCODE and AMT) without an interpreter.						
Exclusion criteria	Not stated						
Sex	37.8% male						
Age	Mean age 73.4 years (SD 9.3)						
Presentation	Memory problems						
Reference standard	Clinician diagnosis based on DSM -III-R criteria.						
Dementia versus no dementia							
Index Test: Informant Questionnaire on Cognitive Decline, IQCODE (26 item, >3.5) Informant Questionnaire on Cognitive Decline, IQCODE (26 item, 3.6)							
Results	**True positives:**	188	**False negatives:**	28	**False positives:**	35	**True negatives:** 48
Additional comments	The random group of patients referred to the aged care assessment team were excluded from analysis as they did not have suspected dementia at baseline.						
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:** High
Overall risk of bias	Very serious (Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: Informant Questionnaire on Cognitive Decline, IQCODE (26 item, >3.6) IQCODE (26 item, 3.7)							
Results	**True positives:**	176	**False negatives:**	40	**False positives:**	32	**True negatives:** 51
Additional comme	The random group of patients referred to the aged care assessment team were excluded from analysis as they did not have						

Flicker L, Logiudice D, Carlin JB, Ames D. The predictive value of dementia screening instruments in clinical populations. International Journal of Geriatric Psychiatry 1997; 12: 203–9.								
nts	suspected dementia at baseline.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Informant Questionnaire on Cognitive Decline, IQCODE (26 item, >3.7) IQCODE (26 item, 3.8)								
Results	**True positives:**	168	**False negatives:**	48	**False positives:**	29	**True negatives:**	54
Additional comme nts	The random group of patients referred to the aged care assessment team were excluded from analysis as they did not have suspected dementia at baseline.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Informant Questionnaire on Cognitive Decline, IQCODE (26 item, >3.8) IQCODE (26 item, 3.9)								
Results	**True positives:**	161	**False negatives:**	55	**False positives:**	24	**True negatives:**	59
Additional comme	The random group of patients referred to the aged care assessment team were excluded from analysis as they did not have							

Flicker L, Logiudice D, Carlin JB, Ames D. The predictive value of dementia screening instruments in clinical populations. International Journal of Geriatric Psychiatry 1997; 12: 203–9.								
nts	suspected dementia at baseline.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Informant Questionnaire on Cognitive Decline, IQCODE (26 item, >3.9) IQCODE (26 item, 4.0)								
Results	**True positives:**	152	**False negatives:**	64	**False positives:**	21	**True negatives:**	62
Additional comments	The random group of patients referred to the aged care assessment team were excluded from analysis as they did not have suspected dementia at baseline.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Informant Questionnaire on Cognitive Decline, IQCODE (26 item, >4.0) IQCODE (26 item, 4.1)								
Results	**True positives:**	140	**False negatives:**	76	**False positives:**	17	**True negatives:**	66
Additional comme	The random group of patients referred to the aged care assessment team were excluded from analysis as they did not have							

Flicker L, Logiudice D, Carlin JB, Ames D. The predictive value of dementia screening instruments in clinical populations. International Journal of Geriatric Psychiatry 1997; 12: 203–9.								
nts	suspected dementia at baseline.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Informant Questionnaire on Cognitive Decline, IQCODE (26 item, >4.1) IQCODE (26 item, 4.2)								
Results	**True positives:**	126	**False negatives:**	90	**False positives:**	14	**True negatives:**	69
Additional comments	The random group of patients referred to the aged care assessment team were excluded from analysis as they did not have suspected dementia at baseline.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<18) MMSE (17/18)								
Results	**True positives:**	108	**False negatives:**	108	**False positives:**	8	**True negatives:**	75
Additional comme	The random group of patients referred to the aged care assessment team were excluded from analysis as they did not have							

Flicker L, Logiudice D, Carlin JB, Ames D. The predictive value of dementia screening instruments in clinical populations. International Journal of Geriatric Psychiatry 1997; 12: 203–9.								
nts	suspected dementia at baseline.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<19) MMSE (18/19)								
Results	**True positives:**	120	**False negatives:**	96	**False positives:**	11	**True negatives:**	72
Additional comments	The random group of patients referred to the aged care assessment team were excluded from analysis as they did not have suspected dementia at baseline.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<20) MMSE (19/20)								
Results	**True positives:**	134	**False negatives:**	82	**False positives:**	13	**True negatives:**	70
Additional comme	The random group of patients referred to the aged care assessment team were excluded from analysis as they did not have							

Flicker L, Logiudice D, Carlin JB, Ames D. The predictive value of dementia screening instruments in clinical populations. International Journal of Geriatric Psychiatry 1997; 12: 203–9.								
nts	suspected dementia at baseline.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<21) MMSE (20/21)								
Results	**True positives:**	149	**False negatives:**	67	**False positives:**	20	**True negatives:**	63
Additional comments	The random group of patients referred to the aged care assessment team were excluded from analysis as they did not have suspected dementia at baseline.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<22) MMSE (21/22)								
Results	**True positives:**	162	**False negatives:**	54	**False positives:**	24	**True negatives:**	59
Additional comme	The random group of patients referred to the aged care assessment team were excluded from analysis as they did not have							

Flicker L, Logiudice D, Carlin JB, Ames D. The predictive value of dementia screening instruments in clinical populations. International Journal of Geriatric Psychiatry 1997; 12: 203–9.								
nts	suspected dementia at baseline.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<23) MMSE (22/23)								
Results	**True positives:**	172	**False negatives:**	44	**False positives:**	26	**True negatives:**	57
Additional comments	The random group of patients referred to the aged care assessment team were excluded from analysis as they did not have suspected dementia at baseline.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<24) MMSE (23/24)								
Results	**True positives:**	183	**False negatives:**	33	**False positives:**	33	**True negatives:**	50
Additional comme	The random group of patients referred to the aged care assessment team were excluded from analysis as they did not have							

Flicker L, Logiudice D, Carlin JB, Ames D. The predictive value of dementia screening instruments in clinical populations. International Journal of Geriatric Psychiatry 1997; 12: 203–9.								
nts	suspected dementia at baseline.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<25) MMSE (24/25)								
Results	**True positives:**	194	**False negatives:**	22	**False positives:**	39	**True negatives:**	44
Additional comments	The random group of patients referred to the aged care assessment team were excluded from analysis as they did not have suspected dementia at baseline.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<26) MMSE (25/26)								
Results	**True positives:**	199	**False negatives:**	17	**False positives:**	45	**True negatives:**	38
Additional comme	The random group of patients referred to the aged care assessment team were excluded from analysis as they did not have							

Flicker L, Logiudice D, Carlin JB, Ames D. The predictive value of dementia screening instruments in clinical populations. International Journal of Geriatric Psychiatry 1997; 12: 203–9.								
nts	suspected dementia at baseline.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Abbreviated Mental Test, AMT (<7) AMT (6/7)								
Results	**True positives:**	126	**False negatives:**	90	**False positives:**	11	**True negatives:**	72
Additional comme nts	The random group of patients referred to the aged care assessment team were excluded from analysis as they did not have suspected dementia at baseline.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Abbreviated Mental Test, AMT (<8) AMT (7/8)								
Results	**True positives:**	157	**False negatives:**	59	**False positives:**	24	**True negatives:**	59
Additional comme	The random group of patients referred to the aged care assessment team were excluded from analysis as they did not have							

Flicker L, Logiudice D, Carlin JB, Ames D. The predictive value of dementia screening instruments in clinical populations. International Journal of Geriatric Psychiatry 1997; 12: 203–9.								
nts	suspected dementia at baseline.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Abbreviated Mental Test, AMT (<9) AMT (8/9)								
Results	**True positives:**	189	**False negatives:**	27	**False positives:**	39	**True negatives:**	44
Additional comments	The random group of patients referred to the aged care assessment team were excluded from analysis as they did not have suspected dementia at baseline.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Abbreviated Mental Test, AMT (<10) Abbreviated Mental Test, AMT (9/10)								
Results	**True positives:**	210	**False negatives:**	6	**False positives:**	60	**True negatives:**	23
Additional comme	The random group of patients referred to the aged care assessment team were excluded from analysis as they did not have							

Flicker L, Logiudice D, Carlin JB, Ames D. The predictive value of dementia screening instruments in clinical populations. International Journal of Geriatric Psychiatry 1997; 12: 203–9.								
nts	suspected dementia at baseline.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Fourier A, Dorey A, Perret-Liauder A, Quadro I. Detection of CSF 14-3-3 Protein in Sporadic Creutzfeldt-Jakob Disease Patients Using a New Automated Capillary Western Assay.Mol Neurobiol, [epub ahead of print]	
Study type	Retrospective cohort
Country	France
Setting	Neurochemistry Laboratory (Hospices Civils de Lyon, France)
Inclusion criteria	Patients undergoing a lumbar puncture for the evaluation of CSF 14-3- 3 protein who have suspected CJD.
Exclusion criteria	None stated
Sex	47.3% male
Age	Median age sCJD 71.0 years, non-CJD 72.0 years (range 54.1-86.7)
Presentation	Rapidly progressive dementia leading to suspected CJD
Reference standard	Clinician diagnosis using WHO criteria, with definite sCJD confirmed using neuropathology. For non-CJD patients the probable clinical diagnosis was proposed by neurologists based on clinical data, imaging/biological markers, and disease evolution.
CJD versus not CJD	
Index Test: CSF 14-3-3 Automated Capillary Western Assay CSF 14-3-3 Automated Capillary Western Assay. Positive if composite criterion areas ratio >235. Carried out using Peggy Sue® 12–230 k Dalton (kDa) size assays. The determination of the size, areas, heights, and signal to noise (S/N) ratios of 14-3-3 protein and 10× System Control protein (used as internal standard) was automatically calculated on Compass for Simple Western® software. A composite criterion, called areas ratio, was also calculated to introduce the use of 10xSC protein as an internal standard. The formula of areas ratio was (area of 14-3-3 protein/area of 10× SC protein) × 10,000.	

Fourier A, Dorey A, Perret-Liauder A, Quadro I. Detection of CSF 14-3-3 Protein in Sporadic Creutzfeldt-Jakob Disease Patients Using a New Automated Capillary Western Assay.Mol Neurobiol, [epub ahead of print]								
Results	**True positives:**	72	**False negatives:**	5	**False positives:**	9	**True negatives:**	182
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious (Unclear whether the threshold was pre-specified)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: CSF 14-3-3 immunoblotting 14-3-3 detected by immunoblotting. The 14-3-3 protein band in CSF samples was optically observed and compared to known specimen to permit a characterization as negative or positive sample								
Results	**True positives:**	71	**False negatives:**	6	**False positives:**	29	**True negatives:**	162
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Foutz A, Appleby BS, Hamlin C, Liu X, Yang S, Cohen Y, Chen W, Blevins J et al. Diagnostic and prognostic value of human prion detection in cerebrospinal fluid. Ann Neurol 2017; 81: 79-92.	
Study type	Prospective cohort
Country	USA
Setting	National Prion disease pathology surveillance centre
Inclusion criteria	WHO diagnosis of CJD or non-CJD, methionine or valine at codon 129 or hPrP gene, unequivocal classification of pathology
Exclusion criteria	None stated

Foutz A, Appleby BS, Hamlin C, Liu X, Yang S, Cohen Y, Chen W, Blevins J et al. Diagnostic and prognostic value of human prion detection in cerebrospinal fluid. Ann Neurol 2017; 81: 79-92.							
Sex	Not stated						
Age	Nor stated						
Presentation	Suspected CJD						
Reference standard	Neuropathology						
CJD versus not CJD							
Index Test: Real-time quaking-induced prion conversion, RT-QuIC. Real-time quaking-induced prion conversion (RT-QuIC), (second generation assay). Samples considered positive if >1 well in the first round or > 2 wells total (in first and repeat rounds) were positive and exceeded the diagnostic cut-off stated.							
Results	**True positives:**	62	**False negatives:**	3	**False positives:**	0	**True negatives:** 14
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: CSF 14-3-3 immunoblotting 14-3-3 detected by immunoblotting.							
Results	**True positives:**	53	**False negatives:**	12	**False positives:**	8	**True negatives:** 6
Additional comments							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	

Foutz A, Appleby BS, Hamlin C, Liu X, Yang S, Cohen Y, Chen W, Blevins J et al. Diagnostic and prognostic value of human prion detection in cerebrospinal fluid. Ann Neurol 2017; 81: 79-92.								
Overall indirectness	Not serious							
Index Test: Total Tau Total tau, ELISA, cut-off > 1150 pg/ml.								
Results	**True positives:**	62	**False negatives:**	3	**False positives:**	4	**True negatives:**	10
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Frisoni GB, Prestia A, Zanetti O, Galluzzi S, Romano M, Cotelli M, Gennarelli M, Binetti G, Bocchio L, Paghera B, Amicucci G,Bonetti M,Benussi L, Ghidoni R, Geroldi C. Markers of Alzheimer's disease in a population attending a memory clinic. Alzheimers Dement 2009; 5: 307-317.	
Study type	Prospective cohort
Country	Italy
Setting	Translational out-patient memory clinic at the Scientific Institute for the Research and Care of Alzheimer's disease
Inclusion criteria	Patients referred to the memory clinic with memory complaints or other cognitive disturbances unaccounted for by focal cerebral, physical, psychiatric, or metabolic diseases.
Exclusion criteria	Patients whose cognitive deficit reverted (regarded as primarily depressed with secondary cognitive impairment)
Sex	37.0% male
Age	Mean age 73.1 years (SD 7.4)
Presentation	Memory complaints or other cognitive disturbances unaccounted for by focal cerebral, physical, psychiatric, or metabolic diseases.
Reference	AD was diagnosed according to NINCDS-ADRDA criteria; LDLB using the consensus criteria reported in McKeith et al. 2006, FTD

Frisoni GB, Prestia A, Zanetti O, Galluzzi S, Romano M, Cotelli M, Gennarelli M, Binetti G, Bocchio L, Paghera B, Amicucci G,Bonetti M,Benussi L, Ghidoni R, Geroldi C. Markers of Alzheimer's disease in a population attending a memory clinic. Alzheimers Dement 2009; 5: 307-317.								
standard	based on Knopman et al. 2003, VaD according to NINDS-AIREN.							
Dementia versus no dementia (MCI included)								
Index Test: MRI Medial temporal-lobe atrophy on MRI scan. Atrophy score R2 on left or right hippocampus on visual rating scale of Scheltens et al. In each hippocampus, atrophy is rated 0 to 1 for normal, 2 for mild, 3 for moderate, and 4 for severe.								
Results	**True positives:**	59	**False negatives:**	26	**False positives:**	20	**True negatives:**	28
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus non-AD dementia (excluding MCI)								
Index Test: MRI Medial temporal-lobe atrophy on MRI scan. Atrophy score R2 on left or right hippocampus on visual rating scale of Scheltens et al. In each hippocampus, atrophy is rated 0 to 1 for normal, 2 for mild, 3 for moderate, and 4 for severe.								
Results	**True positives:**	41	**False negatives:**	6	**False positives:**	18	**True negatives:**	20
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with >10% population excluded; patients whose cognitive deficit reverted (regarded as primarily depressed with secondary cognitive impairment) were excluded from the study; unclear whether reference test was interpreted without knowledge of index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Frisoni GB, Prestia A, Zanetti O, Galluzzi S, Romano M, Cotelli M, Gennarelli M, Binetti G, Bocchio L, Paghera B, Amicucci G,Bonetti M,Benussi L, Ghidoni R, Geroldi C. Markers of Alzheimer's disease in a population attending a memory clinic. Alzheimers Dement 2009; 5: 307-317.								
AD versus non-AD (including other dementias and MCI)								
Index Test: MRI Medial temporal-lobe atrophy on MRI scan. Atrophy score R2 on left or right hippocampus on visual rating scale of Scheltens et al. In each hippocampus, atrophy is rated 0 to 1 for normal, 2 for mild, 3 for moderate, and 4 for severe.								
Results	**True positives:**	41	**False negatives:**	6	**False positives:**	38	**True negatives:**	48
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Dementia versus no dementia (MCI included)								
Index Test: FDG-PET 24-ring, three dimensional PET/CT device with an isotropic resolution of 5.99 mm, a 15.7-cm axial field of view (FOV), a 70-cm transaxial FOV. Test assessed cortical hypometabolism on 18F-FDG-PET. Score of 8/36 or higher on visual rating scale assessing metabolism in six bilateral brain areas (frontal, temporal pole, medial temporal, superior parietal, inferior parietal, and posterior cingulate). For each area, glucose metabolism is rated as 0 for normal, 0.5 for uncertain, 1 for mild, 2 for moderate, and 3 for severe.								
Results	**True positives:**	27	**False negatives:**	23	**False positives:**	5	**True negatives:**	23
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Serious (Patients whose cognitive deficit reverted (regarded as primarily depressed with secondary cognitive impairment) were excluded from the study; unclear whether reference test was interpreted without knowledge of index test and unclear whether results of index test interpreted without knowledge of reference test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall	Not serious							

Frisoni GB, Prestia A, Zanetti O, Galluzzi S, Romano M, Cotelli M, Gennarelli M, Binetti G, Bocchio L, Paghera B, Amicucci G,Bonetti M,Benussi L, Ghidoni R, Geroldi C. Markers of Alzheimer's disease in a population attending a memory clinic. Alzheimers Dement 2009; 5: 307-317.								
indirectness								
AD versus non-AD dementia (excluding MCI)								
Index Test: FDG-PET 24-ring, three dimensional PET/CT device with an isotropic resolution of 5.99 mm, a 15.7-cm axial field of view (FOV), a 70-cm transaxial FOV. Test assessed cortical hypometabolism on 18F-FDG-PET. Score of 8/36 or higher on visual rating scale assessing metabolism in six bilateral brain areas (frontal, temporal pole, medial temporal, superior parietal, inferior parietal, and posterior cingulate). For each area, glucose metabolism is rated as 0 for normal, 0.5 for uncertain, 1 for mild, 2 for moderate, and 3 for severe.								
Results	**True positives:**	22	**False negatives:**	12	**False positives:**	5	**True negatives:**	11
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Very serious (Subgroup analysis with >10% population excluded; patients whose cognitive deficit reverted (regarded as primarily depressed with secondary cognitive impairment) were excluded from the study; unclear whether reference test was interpreted without knowledge of index test and unclear whether results of index test interpreted without knowledge of reference test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus non-AD (including other dementias and MCI)								
Index Test: FDG-PET 24-ring, three dimensional PET/CT device with an isotropic resolution of 5.99 mm, a 15.7-cm axial field of view (FOV), a 70-cm transaxial FOV. Test assessed cortical hypometabolism on 18F-FDG-PET. Score of 8/36 or higher on visual rating scale assessing metabolism in six bilateral brain areas (frontal, temporal pole, medial temporal, superior parietal, inferior parietal, and posterior cingulate). For each area, glucose metabolism is rated as 0 for normal, 0.5 for uncertain, 1 for mild, 2 for moderate, and 3 for severe.								
Results	**True positives:**	22	**False negatives:**	12	**False positives:**	10	**True negatives:**	34
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Serious (Patients whose cognitive deficit reverted (regarded as primarily depressed with secondary cognitive impairment) were							

Frisoni GB, Prestia A, Zanetti O, Galluzzi S, Romano M, Cotelli M, Gennarelli M, Binetti G, Bocchio L, Paghera B, Amicucci G,Bonetti M,Benussi L, Ghidoni R, Geroldi C. Markers of Alzheimer's disease in a population attending a memory clinic. Alzheimers Dement 2009; 5: 307-317.								
	excluded from the study; unclear whether reference test was interpreted without knowledge of index test and unclear whether results of index test interpreted without knowledge of reference test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Dementia versus no dementia (MCI included)								
Index Test: Amyloid Beta 1-42 and total tau Amyloid Beta 1-42, <500 pg/mL and total tau > 450 pg/mL in 51–70-year-old subjects, and >500pg/ml in 71–93-year-old subjects. Assayed using INNOTEST ELISAs.								
Results	**True positives:**	28	**False negatives:**	38	**False positives:**	6	**True negatives:**	22
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Serious (Patients whose cognitive deficit reverted (regarded as primarily depressed with secondary cognitive impairment) were excluded from the study; unclear whether reference test was interpreted without knowledge of index test and unclear whether results of index test interpreted without knowledge of reference test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus non-AD dementias (excluding MCI)								
Index Test: Amyloid Beta 1-42 and total tau Amyloid Beta 1-42, <500 pg/mL and total tau > 450 pg/mL in 51–70-year-old subjects, and >500pg/ml in 71–93-year-old subjects. Assayed using INNOTEST ELISAs.								
Results	**True positives:**	27	**False negatives:**	11	**False positives:**	1	**True negatives:**	27
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	High

Frisoni GB, Prestia A, Zanetti O, Galluzzi S, Romano M, Cotelli M, Gennarelli M, Binetti G, Bocchio L, Paghera B, Amicucci G,Bonetti M,Benussi L, Ghidoni R, Geroldi C. Markers of Alzheimer's disease in a population attending a memory clinic. Alzheimers Dement 2009; 5: 307-317.								
Overall risk of bias	Very serious (Subgroup analysis with >10% population excluded; patients whose cognitive deficit reverted (regarded as primarily depressed with secondary cognitive impairment) were excluded from the study; unclear whether reference test was interpreted without knowledge of index test and unclear whether results of index test interpreted without knowledge of reference test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus non-AD (including other dementias and MCI)								
Index Test: Amyloid Beta 1-42 and total tau Amyloid Beta 1-42, <500 pg/mL and total tau > 450 pg/mL in 51–70-year-old subjects, and >500pg/ml in 71–93-year-old subjects. Assayed using INNOTEST ELISAs.								
Results	**True positives:**	27	**False negatives:**	11	**False positives:**	7	**True negatives:**	49
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Serious (Patients whose cognitive deficit reverted (regarded as primarily depressed with secondary cognitive impairment) were excluded from the study; unclear whether reference test was interpreted without knowledge of index test and unclear whether results of index test interpreted without knowledge of reference test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

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Gabelle A, Dumurgier J, Vercruysse O, Paquet C, Bombois S, Laplanche J-L., et al.Impact of the 2008-2012 French Alzheimer plan on the use of cerebrospinal fluid biomarkers in research memory center: the PLM Study. J. Alzheimers Dis. 2013; 34: 7–305.	
Study type	Prospective cohort
Country	France
Setting	Memory centres in Lille and Paris-North

Gabelle A, Dumurgier J, Vercruysse O, Paquet C, Bombois S, Laplanche J-L., et al.Impact of the 2008-2012 French Alzheimer plan on the use of cerebrospinal fluid biomarkers in research memory center: the PLM Study. J. Alzheimers Dis. 2013; 34: 7–305.								
Inclusion criteria	People with cognitive or behavioural disorders attending the participating clinics.							
Exclusion criteria	People with unclear, unknown or postponed clinical diagnosis							
Sex	44.2% male							
Age	Median age varies from 61-73 years across diagnostic groups.							
Presentation	Suspected dementia							
Reference standard	AD was diagnosed using NINCDS-ADRDA; patients with MCI had to meet the Petersen criteria, McKhann and Neary consensus criteria was used for FTLD; McKeith criteria for LBD.							
AD versus non-AD (MCI excluded from analysis)								
Index Test: Amyloid Beta 1-42 Amyloid Beta 1-42, INNOTEST Amyloid Beta 1-42 ELISA, cut off <440pg/ml								
Results	**True positives:**	262	**False negatives:**	87	**False positives:**	76	**True negatives:**	133
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Test thresholds were not pre-specified, but optimised based on the data; it was unclear whether the study enrolled random or consecutive people or avoided inappropriate exclusions. A subgroup analysis was carried out but as < 10% population was excluded the study was not downgraded for this.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Total Tau Total tau, INNOTEST hTau-Ag ELISA, cut off >301pg/ml								
Results	**True positives:**	283	**False negatives:**	66	**False positives:**	48	**True negatives:**	161
Additional comments								
Risk of bias	**Patient**	Unclear	**Index test:**	High	**Reference**	Low	**Flow and**	Low

Gabelle A, Dumurgier J, Vercruysse O, Paquet C, Bombois S, Laplanche J-L., et al.Impact of the 2008-2012 French Alzheimer plan on the use of cerebrospinal fluid biomarkers in research memory center: the PLM Study. J. Alzheimers Dis. 2013; 34: 7–305.								
	selection:				**standard:**		**timing:**	
Overall risk of bias	Serious (Test thresholds were not pre-specified, but optimised based on the data; it was unclear whether the study enrolled random or consecutive people or avoided inappropriate exclusions. A subgroup analysis was carried out but as < 10% population was excluded the study was not downgraded for this.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: p-tau 181 p-tau, INNOTEST tau 181, cut off >59pg/ml								
Results	**True positives:**	293	**False negatives:**	56	**False positives:**	40	**True negatives:**	169
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Test thresholds were not pre-specified, but optimised based on the data; it was unclear whether the study enrolled random or consecutive people or avoided inappropriate exclusions. A subgroup analysis was carried out but as < 10% population was excluded the study was not downgraded for this.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Amyloid Beta 1-42/Total Tau Amyloid Beta 1-42/total tau, ≤ 1.43								
Results	**True positives:**	292	**False negatives:**	57	**False positives:**	51	**True negatives:**	158
Additional comments								
Risk of bias	**Patient**	Unclear	**Index test:**	High	**Reference**	Low	**Flow and**	Low

Gabelle A, Dumurgier J, Vercruysse O, Paquet C, Bombois S, Laplanche J-L., et al.Impact of the 2008-2012 French Alzheimer plan on the use of cerebrospinal fluid biomarkers in research memory center: the PLM Study. J. Alzheimers Dis. 2013; 34: 7–305.								
	selection:				**standard:**		**timing:**	
Overall risk of bias	Serious (Test thresholds were not pre-specified, but optimised based on the data; it was unclear whether the study enrolled random or consecutive people or avoided inappropriate exclusions. A subgroup analysis was carried out but as < 10% population was excluded the study was not downgraded for this.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Amyloid Beta 1-42/p-tau 181 Amyloid Beta 1-42/p- tau, cut off ≤ 6.53								
Results	**True positives:**	282	**False negatives:**	67	**False positives:**	41	**True negatives:**	168
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Test thresholds were not pre-specified, but optimised based on the data; it was unclear whether the study enrolled random or consecutive people or avoided inappropriate exclusions. A subgroup analysis was carried out but as < 10% population was excluded the study was not downgraded for this.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Amyloid Beta 1-42 Amyloid Beta 1-42, INNOTEST Amyloid Beta 1-42 ELISA, cut off <519pg/ml								
Results	**True positives:**	222	**False negatives:**	50	**False positives:**	106	**True negatives:**	264
Additional comments								
Risk of bias	**Patient**	Unclear	**Index test:**	High	**Reference**	Low	**Flow and**	Low

Gabelle A, Dumurgier J, Vercruysse O, Paquet C, Bombois S, Laplanche J-L., et al.Impact of the 2008-2012 French Alzheimer plan on the use of cerebrospinal fluid biomarkers in research memory center: the PLM Study. J. Alzheimers Dis. 2013; 34: 7–305.								
	selection:				**standard:**		**timing:**	
Overall risk of bias	Serious (Test thresholds were not pre-specified, but optimised based on the data; it was unclear whether the study enrolled random or consecutive people or avoided inappropriate exclusions. A subgroup analysis was carried out but as < 10% population was excluded the study was not downgraded for this.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Total Tau Total tau, INNOTEST hTau-Ag ELISA, cut off >362pg/ml								
Results	**True positives:**	221	**False negatives:**	51	**False positives:**	80	**True negatives:**	290
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Test thresholds were not pre-specified, but optimised based on the data; it was unclear whether the study enrolled random or consecutive people or avoided inappropriate exclusions. A subgroup analysis was carried out but as < 10% population was excluded the study was not downgraded for this.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: p-tau 181 p-tau 181, INNOTEST ELISA, cut off >61pg/ml								
Results	**True positives:**	209	**False negatives:**	63	**False positives:**	43	**True negatives:**	327
Additional comments								
Risk of bias	**Patient**	Unclear	**Index test:**	High	**Reference**	Low	**Flow and**	Low

Gabelle A, Dumurgier J, Vercruysse O, Paquet C, Bombois S, Laplanche J-L., et al.Impact of the 2008-2012 French Alzheimer plan on the use of cerebrospinal fluid biomarkers in research memory center: the PLM Study. J. Alzheimers Dis. 2013; 34: 7–305.								
	selection:				**standard:**		**timing:**	
Overall risk of bias	Serious (Test thresholds were not pre-specified, but optimised based on the data; it was unclear whether the study enrolled random or consecutive people or avoided inappropriate exclusions. A subgroup analysis was carried out but as < 10% population was excluded the study was not downgraded for this.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Amyloid Beta 1-42/Total Tau Amyloid Beta 1-42/total tau, ≤ 2.48								
Results	**True positives:**	236	**False negatives:**	36	**False positives:**	79	**True negatives:**	291
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Test thresholds were not pre-specified, but optimised based on the data; it was unclear whether the study enrolled random or consecutive people or avoided inappropriate exclusions. A subgroup analysis was carried out but as < 10% population was excluded the study was not downgraded for this.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Amyloid Beta 1-42/p-tau 181 Amyloid Beta 1-42/ p- tau 181, cut off ≤ 15.10								
Results	**True positives:**	232	**False negatives:**	40	**False positives:**	59	**True negatives:**	311
Additional comments								
Risk of bias	**Patient**	Unclear	**Index test:**	High	**Reference**	Low	**Flow and**	Low

Gabelle A, Dumurgier J, Vercruysse O, Paquet C, Bombois S, Laplanche J-L., et al.Impact of the 2008-2012 French Alzheimer plan on the use of cerebrospinal fluid biomarkers in research memory center: the PLM Study. J. Alzheimers Dis. 2013; 34: 7–305.								
	selection:				**standard:**		**timing:**	
Overall risk of bias	Serious (Test thresholds were not pre-specified, but optimised based on the data; it was unclear whether the study enrolled random or consecutive people or avoided inappropriate exclusions. A subgroup analysis was carried out but as < 10% population was excluded the study was not downgraded for this.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Galvin JE. Improving the clinical detection of Lewy body dementia with the Lewy body composite risk score. Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring, 2015; 1: 316-324.	
Study type	Prospective cohort
Country	USA
Setting	Pearl I. Barlow Centre for Memory Evaluation and Treatment, a dementia specialty practice at NYU Medical Center.
Inclusion criteria	Consecutive memory clinic referrals
Exclusion criteria	Not stated
Sex	47.0% male
Age	Mean age 77.8 years (8.2)
Presentation	Suspected dementia
Reference standard	AD was diagnosed according to the NINCDS-ADRDA criteria; FTD according to Rascovsky (2011) revised diagnostic criteria for the behavioural variant of frontotemporal dementia; PPA according to Gorno-Tempini (2011); VaD according to the VASCOG statement (Sachdev 2014).
DLB versus AD	
Index Test: Lewy body composite risk score, LBCRS, ≥3 Lewy body composite risk score (LBCRS) which consists of items from Movement Disorders Society-Unified Parkinson's Disease Rating Scale, motor subscale part III (UPDRS), the neuropsychiatric inventory (NPI), Mayo fluctuation questionnaire (MFQ), Epworth Sleepiness Scale (EES), the Mayo sleep questionnaire (MSQ) and from physical findings and complaints of the patient. The operationalization of physical findings as being present for at least 6 months or symptoms permitted the scoring of the LBCRS by totalling the sum of signs and symptoms rated as present occurring at least three times over the past 6 months. Cut off ≥3.	

Galvin JE. Improving the clinical detection of Lewy body dementia with the Lewy body composite risk score. Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring, 2015; 1: 316-324.							
Results	**True positives:**	50	**False negatives:**	3	**False positives:**	22	**True negatives:** 78
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:** High
Overall risk of bias	Serious (Subgroup analysis was carried out excluding >30% study population.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
DLB versus non-DLB dementias							
Index Test: Lewy body composite risk score, LBCRS, ≥3 Lewy body composite risk score (LBCRS) which consists of items from Movement Disorders Society-Unified Parkinson's Disease Rating Scale, motor subscale part III (UPDRS), the neuropsychiatric inventory (NPI), Mayo fluctuation questionnaire (MFQ), Epworth Sleepiness Scale (EES), the Mayo sleep questionnaire (MSQ) and from physical findings and complaints of the patient. The operationalization of physical findings as being present for at least 6 months or symptoms permitted the scoring of the LBCRS by totalling the sum of signs and symptoms rated as present occurring at least three times over the past 6 months. Cut off ≥3.							
Results	**True positives:**	52	**False negatives:**	1	**False positives:**	17	**True negatives:** 107
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:** High
Overall risk of bias	Serious (Subgroup analysis was carried out excluding >30% study population.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						

Forcano Garcia M, Perlado Ortiz de Pinedo F. Cognitive deterioration: use of the short version of the Informant Test (IQCODE) in the geriatrics consultations. Revista Española de Geriatria y Gerontolgia 2002; 37: 81–5.	
Study type	Prospective cohort

Forcano Garcia M, Perlado Ortiz de Pinedo F. Cognitive deterioration: use of the short version of the Informant Test (IQCODE) in the geriatrics consultations. Revista Española de Geriatria y Gerontolgia 2002; 37: 81–5.								
Country	Spain							
Setting	Geriatric external facility							
Inclusion criteria	People referred to the facility due to memory loss, behavioural disorder and/or cognitive deterioration.							
Exclusion criteria	People with previously diagnosed dementia. The Cochrane Review has marked this study as having inappropriate exclusions at the patient selection stage so there may be other additional excluded groups.							
Sex	Not stated in Cochrane Review							
Age	Not stated in Cochrane Review							
Presentation	Memory loss, behavioural disorder and/or cognitive deterioration.							
Reference standard	Clinician diagnosis based on DSM -III-R							
Dementia versus no dementia								
Index Test: Informant Questionnaire on Cognitive Decline, IQCODE (16 item, >3.5) IQCODE (Spanish, 16 item, 3.6 primary threshold for study								
Results	**True positives:**	83	**False negatives:**	7	**False positives:**	4	**True negatives:**	19
Additional comments	The random group of patients referred to the aged care assessment team were excluded from analysis as they did not have suspected dementia at baseline.							
Risk of bias	**Patient selection:**	High	**Index test:**	Unclear	**Reference standard:**	Unclear	**Flow and timing:**	Unclear
Overall risk of bias	Serious (Inappropriate exclusions at patient selection stage.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Gold G, Bouras C, Canuto A, Bergallo M, Herrmann FR, Hof PR, Mayor P-A, Michel J-P, Giannakopoulos P. Clinicopathological Validation Study of Four Sets of Clinical Criteria for Vascular Dementia. Am J Psychiatry 2002; 159:82–87.	
Study type	Retrospective cohort

Gold G, Bouras C, Canuto A, Bergallo M, Herrmann FR, Hof PR, Mayor P-A, Michel J-P, Giannakopoulos P. Clinicopathological Validation Study of Four Sets of Clinical Criteria for Vascular Dementia. Am J Psychiatry 2002; 159:82–87.							
Country	Switzerland						
Setting	University of Geneva Hospitals Belle-Idée						
Inclusion criteria	Diagnosis of dementia and subsequent autopsy examination; clinically evaluated, including neurological and mental status examinations and head computerized tomography (CT) or magnetic resonance imaging (MRI), within 6 months of their death.						
Exclusion criteria	Patients with major neuropsychiatric illness, alcoholism, or Parkinson's disease were excluded.						
Sex	61.8% male						
Age	Mean age 84.7 years (SD 6.4)						
Presentation	Dementia						
Reference standard	Cases of Alzheimer's disease were confirmed by using the National Institute on Aging-Reagan criteria. VaD was assessed based on the presence of both macroscopic and microscopic vascular pathology. Cases that satisfied both neuropathological criteria for AD and the study autopsy criteria for VaD were classified as having mixed dementias.						
VaD versus AD and mixed dementia (AD plus VaD)							
Index Test: NINDS-AIREN (possible) NINDS-AIREN, possible diagnosis							
Results	**True positives:**	11	**False negatives:**	9	**False positives:**	11	**True negatives:** 58
Additional comments	The data for the ICD-10 and DSM-IV was not extracted as updated versions of these criteria exist.						
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: NINDS-AIREN (probable) NINDS-AIREN, probable diagnosis							
Results	**True positives:**	4	**False negatives:**	16	**False positives:**	5	**True negatives:** 64

Gold G, Bouras C, Canuto A, Bergallo M, Herrmann FR, Hof PR, Mayor P-A, Michel J-P, Giannakopoulos P. Clinicopathological Validation Study of Four Sets of Clinical Criteria for Vascular Dementia. Am J Psychiatry 2002; 159:82–87.								
Additional comments	The data for the ICD-10 and DSM-IV was not extracted as updated versions of these criteria exist.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: ADDTC (possible) ADDTC, possible diagnosis								
Results	**True positives:**	14	**False negatives:**	6	**False positives:**	15	**True negatives:**	54
Additional comments	The data for the ICD-10 and DSM-IV was not extracted as updated versions of these criteria exist.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: ADDTC (probable) ADDTC, probable diagnosis								
Results	**True positives:**	5	**False negatives:**	15	**False positives:**	6	**True negatives:**	63
Additional comments	The data for the ICD-10 and DSM-IV was not extracted as updated versions of these criteria exist.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low

Gold G, Bouras C, Canuto A, Bergallo M, Herrmann FR, Hof PR, Mayor P-A, Michel J-P, Giannakopoulos P. Clinicopathological Validation Study of Four Sets of Clinical Criteria for Vascular Dementia. Am J Psychiatry 2002; 159:82–87.						
Overall risk of bias	Not serious					
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low
Overall indirectness	Not serious					

Goldstein FC, Ashley A, Miller E, Alexeeva O, Zanders L, King V. Validity of the Montreal Cognitive Assessment as a screen for mild cognitive impairment and dementia in African Americans. Journal of Geriatr Psych and Neurol 2014; 27; 199-203.								
Study type	Prospective cohort							
Country	USA							
Setting	Memory disorders clinic at Grady memorial Hospital, Atlanta.							
Inclusion criteria	African American, ≥ 50 years old, cognitive assessment at the clinic.							
Exclusion criteria	Pre-existing conditions such as intellectual disabilities, drug and/or substance abuse, and severe psychiatric illness that could affect their performance on the cognitive measures apart from a primary neurodegenerative aetiology.							
Sex	30.1% male							
Age	Mean age 70.2 (SD 9.5)							
Presentation	Suspected dementia							
Reference standard	Clinician diagnosis based on neuropsychological battery							
Dementia versus no dementia (MCI included								
Index Test: Montreal Cognitive Assessment, MoCA (<24) MoCA ≤23								
Results	**True positives:**	26	**False negatives:**	1	**False positives:**	37	**True negatives:**	17
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		

Goldstein FC, Ashley A, Miller E, Alexeeva O, Zanders L, King V. Validity of the Montreal Cognitive Assessment as a screen for mild cognitive impairment and dementia in African Americans. Journal of Geriatr Psych and Neurol 2014; 27; 199-203.							
Overall indirectness	Serious (Study only recruited African Americans ≥ 50 years old.)						
Index Test: Montreal Cognitive Assessment, MoCA (<25) MoCA ≤24							
Results	**True positives:**	27	**False negatives:**	0	**False positives:**	42	**True negatives:** 12
Additional comments							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Serious (Study only recruited African Americans ≥ 50 years old.)						

Goncalves DC, Arnold E, Appadurai K, Byrne GJ. Case finding in dementia: comparative utility of three brief instruments in the memory clinic setting. International Psychogeriatrics 2011; 23: 788–96.	
Study type	Prospective cohort
Country	Australia
Setting	Memory clinic in a city hospital
Inclusion criteria	Participants were referred by their primary care physicians.
Exclusion criteria	Patients lacking an informant to complete the IQCODE for them.
Sex	44.0% male
Age	Mean age 76.9 years (SD 8.9)
Presentation	Memory problems.
Reference standard	Clinician diagnosis based on DSM-IV-TR criteria plus all available information (including index tests)
Dementia versus no dementia (includes MCI)	

Goncalves DC, Arnold E, Appadurai K, Byrne GJ. Case finding in dementia: comparative utility of three brief instruments in the memory clinic setting. International Psychogeriatrics 2011; 23: 788–96.								
Index Test: Informant Questionnaire on Cognitive Decline, IQCODE (16 item, >4.1) IQCODE (16 item), optimised threshold for study > 4.1								
Results	**True positives:**	109	**False negatives:**	43	**False positives:**	17	**True negatives:**	35
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	High	**Flow and timing:**	Low
Overall risk of bias	Serious (The reference diagnosis was not independent of the index tests; optimised test thresholds were used.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<24) SMMSE (Molloy, 1991 version of MMSE). Optimised threshold for study <24								
Results	**True positives:**	126	**False negatives:**	26	**False positives:**	14	**True negatives:**	38
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	High	**Flow and timing:**	Low
Overall risk of bias	Serious (The reference diagnosis was not independent of the index tests; optimised test thresholds were used.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Goncalves DC, Arnold E, Appadurai K, Byrne GJ. Case finding in dementia: comparative utility of three brief instruments in the memory clinic setting. International Psychogeriatrics 2011;23: 788–96.	
Study type	Prospective cohort
Country	Australia

Goncalves DC, Arnold E, Appadurai K, Byrne GJ. Case finding in dementia: comparative utility of three brief instruments in the memory clinic setting. International Psychogeriatrics 2011;23: 788–96.								
Setting	Memory clinic in a city hospital							
Inclusion criteria	Participants were referred by their primary care physicians.							
Exclusion criteria	Patients lacking an informant to complete the IQCODE for them.							
Sex	44.0% male							
Age	Mean age 76.9 years (SD 8.9)							
Presentation	Memory problems							
Reference standard	DSM-IV-TR criteria plus all available information (including index tests)							
Dementia verus no dementia (incluldes MCI)								
Index Test: Rowland Universal Dementia Assessment Scale, RUDAS (<21) Rowland Universal Dementia Assessment Scale, RUDAS (<21)								
Results	**True positives:**	100	**False negatives:**	52	**False positives:**	5	**True negatives:**	47
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	High	**Flow and timing:**	Low
Overall risk of bias	Serious (The reference diagnosis was not independent of the index tests; optimised test thresholds were used.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Goodman I, Golden G,Flitman S, Xie K, McConville M, Levy S ,Zimmerman E, Lebedeva Z, Richter R, Minagar A, Averback P. A multi-center blinded prospective study of urine neural thread protein measurements in patients with suspected Alzheimer's disease. J Am Med Dir Assoc 2007; 8: 21-30.	
Study type	
Country	USA
Setting	8 speciality memory/ dementia/ cognitive impairment clinics across 8 US states.
Inclusion criteria	New referrals to the specialist clinics with cognitive impairment, memory problems or suspected dementia for the diagnosis of dementia; ≥ 45 years old; subsequent clinical diagnosis.

Goodman I, Golden G,Flitman S, Xie K, McConville M, Levy S ,Zimmerman E, Lebedeva Z, Richter R, Minagar A, Averback P. A multi-center blinded prospective study of urine neural thread protein measurements in patients with suspected Alzheimer's disease. J Am Med Dir Assoc 2007; 8: 21-30.							
Exclusion criteria	Inability to provide a suitable first morning urine sample (contaminated sample with bacteria etc., renal disease or not the first morning urine).						
Sex	61.0% male						
Age	Mean age 69.6 years (SD 11.7)						
Presentation	People had cognitive impairment, memory impairment or suspected dementia						
Reference standard	AD diagnosed using the NINCDS-ARDRA criteria, MCI using the Quality Standards Subcommittee of the AAN (AAN MCI criteria).						
AD (probable and possible) versus non-AD (including MCI)							
Index Test: Urinary AD7c-NTP (22ug/ml) Urinary AD7c-NTP (22ug/ml)							
Results	**True positives:**	52	**False negatives:**	36	**False positives:**	22	**True negatives:** 58
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Probable AD versus non-AD (including MCI)							
Index Test: Urinary AD7c-NTP (22ug/ml) Urinary AD7c-NTP (22ug/ml)							
Results	**True positives:**	32	**False negatives:**	3	**False positives:**	22	**True negatives:** 58
Additional comments	The probable AD group was excluded from this subgroup analysis (n= 35).						
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** High

Goodman I, Golden G,Flitman S, Xie K, McConville M, Levy S ,Zimmerman E, Lebedeva Z, Richter R, Minagar A, Averback P. A multi-center blinded prospective study of urine neural thread protein measurements in patients with suspected Alzheimer's disease. J Am Med Dir Assoc 2007; 8: 21-30.								
Overall risk of bias	Serious (Subgroup analysis excluding >10% population; it is unclear whether the reference test was carried out without knowledge of the index test results.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Possible AD versus non-AD (including MCI)								
Index Test: Urinary AD7c-NTP (22ug/ml) Urinary AD7c-NTP (22ug/ml)								
Results	**True positives:**	20	**False negatives:**	33	**False positives:**	22	**True negatives:**	58
Additional comments	The possible AD group was excluded from this subgroup analysis (n= 53).							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis excluding >10% population; it is unclear whether the reference test was carried out without knowledge of the index test results.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Gustafson L, Englund E, Brunnstrom H, Brun A, Erikson C, Warkentin S, Passant U. The Accuracy of Short Clinical Rating Scales in Neuropathologically Diagnosed Dementia. The American Journal of Geriatric Psychiatry 2010; 18: 810- 820.	
Study type	Prospective cohort
Country	Sweden
Setting	Psychogeriatric and Psychiatric Departments at the University of Lund
Inclusion criteria	Individuals with DSM-III and ICD-10 diagnosed dementia who were referred to the department and followed up for subtype diagnosis.

Gustafson L, Englund E, Brunnstrom H, Brun A, Erikson C, Warkentin S, Passant U. The Accuracy of Short Clinical Rating Scales in Neuropathologically Diagnosed Dementia. The American Journal of Geriatric Psychiatry 2010; 18: 810- 820.								
Exclusion criteria	Chronic psychosis and epilepsy, severe somatic disease, severe head injury, addiction, stroke with remaining gross focal neurological symptoms and a condition that did not allow the application of the three clinical rating scales.							
Sex	41.1% male							
Age	Mean age at onset 64.0 years (no SD stated)							
Presentation	Dementia with subtype diagnosis required							
Reference standard	Neuoropathology using standardised procedures optimised over time with reference to the Swedish Consensus on Dementia Diseases (Wallin, 1994) and in accordance with criteria for AD (Braak, 1991; CERAD), DLB (McKeith, 2005) and FTD (The Lund and Manchester groups criteria, 1994; Neary, 1998).							
AD (including mixed VaD and AD) versus FTD and VaD alone								
Index Test: AD scale (≥6) AD scale, cut-off ≥ 6								
Results	**True positives:**	84	**False negatives:**	21	**False positives:**	11	**True negatives:**	74
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious (The study was not downgraded for subgroup analysis as <10% population was excluded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
FTD versus AD and VaD								
Index Test: FTD scale (≥6) FTD scale, cut- off ≥ 6.								
Results	**True positives:**	48	**False negatives:**	4	**False positives:**	11	**True negatives:**	127
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious (The study was not downgraded for subgroup analysis as <10% population was excluded.)							
Indirectness	**Patient**	Low	**Index test:**	Low	**Reference**	Low		

Gustafson L, Englund E, Brunnstrom H, Brun A, Erikson C, Warkentin S, Passant U. The Accuracy of Short Clinical Rating Scales in Neuropathologically Diagnosed Dementia. The American Journal of Geriatric Psychiatry 2010; 18: 810- 820.								
	selection:				**standard:**			
Overall indirectness	Not serious							
VaD (including mixed VaD and AD) versus AD alone and FTD								
Index Test: Hachinski Ischemic score, HIS (≥7) Hachinski Ischemic score (HIS), cut-off ≥ 7.								
Results	**True positives:**	36	**False negatives:**	16	**False positives:**	11	**True negatives:**	127
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious (The study was not downgraded for subgroup analysis as <10% population was excluded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

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Hamlin C, Puoti G, Berri S, Sting E, Harris C et al. A comparison of tau and 14-3-3 protein in the diagnosis of Creutzfeldt-Jakob disease. Neurology, 2012; 79:547-552.	
Study type	Retrospective cohort
Country	USA
Setting	National Prion Disease Pathology Surveillance Centre
Inclusion criteria	People with suspected CJD or prion disease referred to the surveillance centre for diagnosis with results for 14-3-3 protein analysis, measured tau, and a neuropathology examination.
Exclusion criteria	Not stated
Sex	42.0% male
Age	Median age 48 years (range 16-91)
Presentation	Suspected CJD/prion disease

Hamlin C, Puoti G, Berri S, Sting E, Harris C et al. A comparison of tau and 14-3-3 protein in the diagnosis of Creutzfeldt-Jakob disease. Neurology, 2012; 79:547-552.								
Reference standard	Criteria not specified							
Prion disease versus no prion disease								
Index Test: Total Tau Tau, >1000 pg/ml (Invitrogen ELISA)								
Results	**True positives:**	218	**False negatives:**	27	**False positives:**	63	**True negatives:**	112
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Multiple thresholds were tested and unclear whether researchers were blind to reference test results or that the reference test was interpreted without knowledge of index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Total Tau Tau, >1150 pg/ml (Invitrogen ELISA)								
Results	**True positives:**	213	**False negatives:**	32	**False positives:**	57	**True negatives:**	118
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Multiple thresholds were tested and unclear whether researchers were blind to reference test results or that the reference test was interpreted without knowledge of index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: CSF 14-3-3 immunoblotting								

Hamlin C, Puoti G, Berri S, Sting E, Harris C et al. A comparison of tau and 14-3-3 protein in the diagnosis of Creutzfeldt-Jakob disease. Neurology, 2012; 79:547-552.								
14-3-4, Immunoblotting with ambiguous results ignored								
Results	**True positives:**	183	**False negatives:**	10	**False positives:**	76	**True negatives:**	30
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (> 28% population excluded as 14-3-3 results were ambiguous; multiple thresholds were tested and unclear whether researchers were blind to reference test results or that the reference test was interpreted without knowledge of index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Hancock P, Larner AJ. Diagnostic utility of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) and its combination with the Addenbrooke's Cognitive Examination-Revised (ACE-R) in a memory clinic-based population. International Psychogeriatrics 2009; 21: 526–30.								
Study type	Prospective cohort							
Country	UK							
Setting	Memory clinics in a psychiatric hospital and cognitive function clinic based in a regional neuroscience centre							
Inclusion criteria	Patients attending memory/cognitive function clinics with an informant.							
Exclusion criteria	Patients lacking an informant to complete the IQCODE for them.							
Sex	49.0% male							
Age	Median age 67 years (range 29-94)							
Presentation	Memory problems.							
Reference standard	Clinician diagnosis based on DSM-IV criteria							
Dementia versus no dementia								
Index Test: Informant Questionnaire on Cognitive Decline, IQCODE (26 item, >3.5)								

Hamlin C, Puoti G, Berri S, Sting E, Harris C et al. A comparison of tau and 14-3-3 protein in the diagnosis of Creutzfeldt-Jakob disease. Neurology, 2012; 79:547-552.								
IQCODE (26 item) optimised threshold for study 3.6								
Results	**True positives:**	73	**False negatives:**	12	**False positives:**	36	**True negatives:**	23
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (An optimised test threshold was used.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Hancock P and Larner L. Test your memory test: diagnostic utility in a memory clinic population. Int. Journal Geriatr Psych 2011; 25: 976-980.								
Study type	Prospective cohort							
Country	UK							
Setting	A memory clinic in a psychiatric hospital and a cognitive functional clinic in a regional neuroscience centre.							
Inclusion criteria	People referred to the memory clinics over a 23- month period (February 2008- December 2009).							
Exclusion criteria	Not stated							
Sex	58.0% male							
Age	Mean age 63.3 years (SD 12.6)							
Presentation	Suspected dementia							
Reference standard	Clinician diagnosis using DSM-IV for dementia and established criteria for dementia subtypes (McKhann, 1984, 2001; Roman, 1993; McKeith 1996, 1999; Neary, 1998 and Petersen 1999.)							
Dementia versus not dementia (including MCI)								
Index Test: Test Your Memory, TYM (≤42) Test your memory (TYM), index paper cut-off ≤ 42/50								
Results	**True positives:**	74	**False negatives:**	4	**False positives:**	80	**True negatives:**	66
Risk of bias	**Patient**	Low	**Index test:**	Low	**Reference**	Low	**Flow and**	Low

Hancock P and Larner L. Test your memory test: diagnostic utility in a memory clinic population. Int. Journal Geriatr Psych 2011; 25: 976-980.								
	selection:				**standard:**		**timing:**	
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Test Your Memory, TYM (≤30) Test your memory (TYM), cut-off ≤ 30/50								
Results	**True positives:**	57	**False negatives:**	21	**False positives:**	18	**True negatives:**	128
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Optimised test threshold.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<24) MMSE, ≤ 23/30 (Folstein version)								
Results	**True positives:**	56	**False negatives:**	15	**False positives:**	7	**True negatives:**	132
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Optimised test threshold.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		

Hancock P and Larner L. Test your memory test: diagnostic utility in a memory clinic population. Int. Journal Geriatr Psych 2011; 25: 976-980.							
Overall indirectness	Not serious						
Index Test: Addenbrooke's Cognitive Examination-Revised, ACE-R (<74) Addenbrooke's Cognitive Examination-Revised, ACE-R (<74)							
Results	**True positives:**	35	**False negatives:**	4	**False positives:**	7	**True negatives:** 94
Additional comments							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Serious (Optimised test threshold.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						

Hanyu H, Shimizu S, Hirao K, Sakurai H, Iwamoto T, Chikamori T, Hida S et al. The role of 123-I Metaiodobenzylguanidine myocardial scintigraphy in the diagnosis of Lew Body Disease in patients with dementia in a memory clinic. Dementia Geriatr Cogn Disord 2006; 22: 379-384.	
Study type	Prospective cohort
Country	Japan
Setting	Memory clinic of the Department of Geriatric Medicine, Tokyo Medical University Hospital.
Inclusion criteria	People referred to the memory clinic who fulfilled the DSM-IV criteria for dementia and had one or more of the following symptoms: parkinsonian-like features; autonomic symptoms and hallucinations or systematized delusions.
Exclusion criteria	Ischemic or chronic heart disease, cardiomyopathy, diabetes mellitus, thyroid disease or taking drugs known to affect MIBG accumulation.
Sex	47.9% male
Age	Mean age 77.6 years (SD 6.4)
Presentation	Dementia with suspected DLB.

Hanyu H, Shimizu S, Hirao K, Sakurai H, Iwamoto T, Chikamori T, Hida S et al. The role of 123-I Metaiodobenzylguanidine myocardial scintigraphy in the diagnosis of Lew Body Disease in patients with dementia in a memory clinic. Dementia Geriatr Cogn Disord 2006; 22: 379-384.								
Reference standard	Clinician diagnosis based on NINCDS-ADRDA for AD, the consortium for DLB international criteria (McKeith, 1996) for DLB, NINDS-AIREN for VaD and PDD according to the UK Brain Bank (Hughes, 1992) and McKeith (1996). Other diagnoses made using the DSM-IV.							
PDD and DLB versus other dementias								
Index Test: 123I-MIBG cardiac scintigraphy MIBG scintigraphy, heart-to-mediastinum (H/M) ratio. Early and delayed SPECT was performed 20 min and 4 hr after injection, respectively. Planar scan and SPECT were performed with a double-headed camera equipped with a low -energy, high resolution parallel hole collimator (PRISM 2000VP, Pickers). After scatter correction, relative organ uptake was determined by setting the region of interest (ROI) on the anterior view. The H/M ratio was calculated by dividing the count density of the left ventricle ROI by the mediastinal ROI according to standard methods. Values were compared to those from normal controls obtained at the Institute.								
Results	**True positives:**	39	**False negatives:**	2	**False positives:**	7	**True negatives:**	48
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard and whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Harris JM, Gall C, Thompson JC, Richardson AMT, Neary D et al. Sensitivity and specificity of FTDC criteria for behavioural frontotemporal dementia. Neurology 2013; 20: 1881-1887.	
Study type	Retrospective cohort
Country	UK
Setting	Cerebral function unit, Greater Manchester Neuroscience Centre
Inclusion criteria	Assessed at centre for early onset dementia and then undergoing subsequent autopsy.
Exclusion criteria	Predominant PPA, extra pyramidal disorders, mixed frontotemporal and non-frontotemporal pathology.

Harris JM, Gall C, Thompson JC, Richardson AMT, Neary D et al. Sensitivity and specificity of FTDC criteria for behavioural frontotemporal dementia. Neurology 2013; 20: 1881-1887.							
Sex	58.2% male						
Age	Mean age 60.7 years (SD not calculable)						
Presentation	Early onset dementia						
Reference standard	Neuropathology - criteria not stated						
Probable bv FTD versus not bv FTD (including possible)							
Index Test: FTDC criteria for bv FTD FTDC criteria for bvFTD (Rascovsky, 2011)							
Results	**True positives:**	47	**False negatives:**	5	**False positives:**	8	**True negatives:** 79
Risk of bias	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Serious (Study excludes third of sample at initial screening)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Possible bv FTD versus not bv FTD							
Index Test: FTDC criteria for bv FTD FTDC criteria for bvFTD (Rascovsky, 2011)							
Results	**True positives:**	61	**False negatives:**	16	**False positives:**	3	**True negatives:** 67
Risk of bias	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Serious (Study excludes third of sample at initial screening)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						

Heath CA, Cooper SA, Murray K, Lowman A, Henry C, MacLeod MA et al. Validation of diagnostic criteria for variant Creutzfeldt-Jakob Disease. Annals of Neurology 2010; 6: 761-770.								
Study type	Retrospective cohort							
Country	UK							
Setting	National CJD Surveillance Unit							
Inclusion criteria	Cases of suspected CJD referred to the surveillance unit between 1995 and 2004 with subsequent autopsy/ biopsy confirmation of vCJD or an alternative diagnosis (non-CJD).							
Exclusion criteria	None stated							
Sex	58.9% male							
Age	Mean age at onset 32.0. years (SD not stated)							
Presentation	Suspected CJD							
Reference standard	Autopsy/cerebral biopsy							
CJD (probable and possible) versus not CJD								
Index Test: WHO CJD criteria Diagnostic criteria for CJD (WHO, 2002)								
Results	**True positives:**	94	**False negatives:**	12	**False positives:**	13	**True negatives:**	32
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether the index test was interpreted without knowledge of the results of the reference test; whether a consecutive or random sample of patients was enrolled or inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (Mean age at onset< 40 years old)							
CJD (probable) versus not CJD (including possible CJD)								
Index Test: WHO CJD criteria Diagnostic criteria for CJD (WHO, 2002)								
Results	**True positives:**	88	**False**	18	**False positives:**	0	**True negatives:**	45

Heath CA, Cooper SA, Murray K, Lowman A, Henry C, MacLeod MA et al. Validation of diagnostic criteria for variant Creutzfeldt-Jakob Disease. Annals of Neurology 2010; 6: 761-770.								
			negatives:					
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether the index test was interpreted without knowledge of the results of the reference test; whether a consecutive or random sample of patients was enrolled or inappropriate exclusions were avoided.)							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (Mean age at onset< 40 years old)							

Hentschel F, Kreis M, Damian M, Krumm B, Frolich L. The clinical utility of structural neuroimaging with MRI for diagnosis and differential diagnosis of dementia: a memory clinic study. Int J Geriatr Psychiatry. 2005; 20: 645-50.								
Study type	Prospective cohort							
Country	Germany							
Setting	Memory clinic of the Central Institute for Mental Health, University of Heidelberg							
Inclusion criteria	People referred to the memory clinic with cognitive disturbances							
Exclusion criteria	Not stated							
Sex	Not stated							
Age	Mean age 68.6 years (SD8.6)							
Presentation	Suspected dementia							
Reference standard	AD diagnosed according to the NINCDS-ADRDA criteria; VD according to NINDS-AIREN criteria; criteria for DLB and FTD not specified. No dementia group included people with MCI and no cognitive disturbances. The MRI and CERAD battery results were available to clinicians during diagnosis.							
Dementia versus no dementia								
Index Test: MRI MRI using T1, double echo and FLAIR sequence.								
Results	**True positives:**	46	**False negatives:**	4	**False positives:**	23	**True negatives:**	28
Risk of bias	**Patient**	Low	**Index test:**	Unclear	**Reference**	High	**Flow and**	Low

Hentschel F, Kreis M, Damian M, Krumm B, Frolich L. The clinical utility of structural neuroimaging with MRI for diagnosis and differential diagnosis of dementia: a memory clinic study. Int J Geriatr Psychiatry. 2005; 20: 645-50.								
	selection:				**standard:**		**timing:**	
Overall risk of bias	Very serious (The index tests were carried out with knowledge of the primary care diagnosis and it is unclear whether pre-specified thresholds were used; the reference standard diagnosis used all available data including the index test results.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: CERAD battery CERAD battery. It consists of the following subtests: Verbal category fluency (animal naming); Modified Boston Naming Test (naming 15 drawn objects); MMSE; Word List Test (10 words – immediate and delayed recall and recognition); Constructional praxis (copying drawn figures and then reproducing them after a delay).								
Results	**True positives:**	37	**False negatives:**	13	**False positives:**	1	**True negatives:**	49
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	High	**Flow and timing:**	Low
Overall risk of bias	Very serious (The index tests were carried out with knowledge of the primary care diagnosis and it is unclear whether pre-specified thresholds were used; the reference standard diagnosis used all available data including the index test results)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Hoffman JM, Welsh-Bohmer KA ,Hanson M, Krain B, Hulette C, Earl N etal. FDG PET imaging in patients with pathologically verified dementia. J Nucl Med. 2000; 41: 1920-8.	
Study type	Prospective cohort
Country	USA
Setting	Memory Disorder Clinic of the Joseph and Kathleen Bryan Alzheimer's Disease Research Centre at Duke University.
Inclusion criteria	Patients at the Memory Disorder Clinic with diagnostically challenging or difficult to identify dementia (using clinical criteria).

Hoffman JM, Welsh-Bohmer KA ,Hanson M, Krain B, Hulette C, Earl N etal. FDG PET imaging in patients with pathologically verified dementia. J Nucl Med. 2000; 41: 1920-8.								
Exclusion criteria	Not stated							
Sex	63.6% male							
Age	Mean age 67.5 years (SD 9.6)							
Presentation	Diagnostically challenging dementia							
Reference standard	Pathologic confirmation of diagnosis was obtained (biopsy, n =2; autopsy, n= 19; biopsy and autopsy, n= 1) using the CERAD criteria.							
AD versus non-AD dementias								
Index Test: FDG-PET FDG-PET. 370 MBq (10 mCi) FDG was administered followed by a 40-min uptake period. Transaxial imaging of the entire intracranial contents was obtained. The FDG PET images were displayed on film and graded for the confidence of the classic pattern of bilateral temporo-parietal hypometabolism. The grading scale was as follows: 0 5 definitely normal; 1 = probably normal; 2 = definitely abnormal with varying degree of bilateral temporo-parietal hypometabolism; 3 =classic bilateral temporo-parietal hypometabolism; and 4 = abnormal but not AD pattern (including frontal, focal, or only unilateral hypometabolism). For the purposes of statistical analysis, grades 2 and 3 FDG PET interpretations were grouped together as being metabolically diagnostic of AD.								
Results	**True positives:**	13	**False negatives:**	1	**False positives:**	3	**True negatives:**	5
Additional comments	Data was not extracted to examine the diagnostic test accuracy of the NINCDS-ADRDA clinical criteria compared to neuropathology as a newer version of NINCDS-ADRDA is now in use (2011).							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Holman BL, Johnson KA, Gerada B, Carvalho PA, Satlin A.The scintigraphic appearance of Alzheimer's disease: a prospective study using technetium-99m-HMPAO SPECT. J Nucl Med 1992; 33: 181–185.	
Study type	Prospective cohort
Country	USA

Holman BL, Johnson KA, Gerada B, Carvalho PA, Satlin A.The scintigraphic appearance of Alzheimer's disease: a prospective study using technetium-99m-HMPAO SPECT. J Nucl Med 1992; 33: 181–185.								
Setting	Nuclear medicine clinic							
Inclusion criteria	Referral to the nuclear medicine clinic with a complaint of memory or cognitive impairment.							
Exclusion criteria	Not stated							
Sex	Not stated							
Age	Not stated							
Presentation	Memory loss or cognitive abnormalities							
Reference standard	Diagnosis was carried out by a neurologist with experience of diagnosing dementia using NINDS-ADRDA for AD, other diagnostic criteria and CT and/or MRI data.							
AD versus non-AD								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT imaged using a X- headed camera (ASPECT), a digital SPECT system with a single-crystal sodium iodide ring detector and three collimators. Acquisition time was 30 min (15 sec per projection) in 120 projections with a 360-degree rotation of the collimators. Images were interpreted using a colour scale and classified into different perfusion pattern groups (A to F). A was considered normal.								
Results	**True positives:**	48	**False negatives:**	4	**False positives:**	44	**True negatives:**	17
Additional comments	In the absence of information about which pattern is considered diagnostic for AD we only analysed AD versus non-AD for not having pattern A (normal). The non-AD group consisted of patients diagnosed with other dementias and other non-dementia disorders including depression.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (People with uncertain clinical diagnoses (> 10% population) were excluded from analysis)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

P.1.9 I

Ibach B, Binder H, Dragon M, Poljansky S, Haen E, Schmitz E, et al. Cerebrospinal fluid tau and beta-amyloid in Alzheimer patients, disease controls and an age-matched random sample. Neurobiol Aging 2006; 27: 1202–11.

Ibach B, Binder H, Dragon M, Poljansky S, Haen E, Schmitz E, et al. Cerebrospinal fluid tau and beta-amyloid in Alzheimer patients, disease controls and an age-matched random sample. Neurobiol Aging 2006; 27: 1202–11.								
Study type	Prospective cohort							
Country	Germany							
Setting	In-patient service and/or memory disorders outpatient clinic at State Hospital for Psychiatry and Psychotherapy, Bezirksklinikum Regensburg, Germany.							
Inclusion criteria	Participants undergoing diagnostic procedure for suspected dementia or cognitive decline in a memory clinic or in-patient clinic at the Stste Hospital.							
Exclusion criteria	Not stated							
Sex	43.0% male							
Age	Mean age 65.5 years (SD 10.2)							
Presentation	Suspected cognitive decline or dementia.							
Reference standard	DSM-III-R, DSM-IV criteria for dementia with all other available test information apart from CSF index test results. AD diagnosed according to NINCDS-ADRDA; Newcastle criteria was used for DLB.							
AD versus other dementias								
Index Test: Amyloid Beta 1-42 Beta Amyloid 1–42 in CSF, INNOTEST ELISA, cut off 540pg/ml								
Results	**True positives:**	54	**False negatives:**	22	**False positives:**	21	**True negatives:**	27
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the test thresholds were not pre-specified and it is unclear whether the index test was interpreted without knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Total Tau Tau in CSF, INNOTEST hTAu-Ag ELISA, cut off 400pg/ml								
Results	**True positives:**	55	**False**	21	**False positives:**	14	**True negatives:**	34

Ibach B, Binder H, Dragon M, Poljansky S, Haen E, Schmitz E, et al. Cerebrospinal fluid tau and beta-amyloid in Alzheimer patients, disease controls and an age-matched random sample. Neurobiol Aging 2006; 27: 1202–11.								
			negatives:					
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the test thresholds were not pre-specified and it is unclear whether the index test was interpreted without knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: p-tau 181 p-tau 181 in CSF, INNOTEST p-tau 181, cut off 69pg/ml								
Results	**True positives:**	56	**False negatives:**	20	**False positives:**	12	**True negatives:**	36
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the test thresholds were not pre-specified and it is unclear whether the index test was interpreted without knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Total Tau/Amyloid Beta 1-42 Tau/Beta Amyloid 1-42, cut off 0.78								
Results	**True positives:**	57	**False**	19	**False positives:**	12	**True negatives:**	36

Ibach B, Binder H, Dragon M, Poljansky S, Haen E, Schmitz E, et al. Cerebrospinal fluid tau and beta-amyloid in Alzheimer patients, disease controls and an age-matched random sample. Neurobiol Aging 2006; 27: 1202–11.								
			negatives:					
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the test thresholds were not pre-specified and it is unclear whether the index test was interpreted without knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: p-tau/Amyloid Beta 1-42 p-tau 181/Beta Amyloid 1-42, cut off 0.131								
Results	**True positives:**	59	**False negatives:**	17	**False positives:**	12	**True negatives:**	36
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the test thresholds were not pre-specified and it is unclear whether the index test was interpreted without knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

P.1.10 J

Jagust W, Reed B,Mungas D,Ellis W, De Carli C.What does fluorodeoxyglucose PET imaging add to a clinical diagnosis of dementia? Neurology. 2007; 69: 871-7.							
Study type	Retrospective Cohort						
Country	USA						
Setting	Helen Wills Neuroscience Institute at California Berkeley.						
Inclusion criteria	Individuals with a clinical evaluation, pathological examination and FDG-PET scan.						
Exclusion criteria	Not stated						
Sex	63.0% male						
Age	Mean age 75.0 years (11)						
Presentation	suspected dementia						
Reference standard	Neuropthology using the CERAD criteria						
AD versus non-AD dementia							
Index Test: FDG-PET FDG-PET imaging was performed on either a Siemens-CTI ECAT EXACT or ECAT EXACT HR tomograph in two-dimensional mode. All images were corrected for attenuation with transmission scans obtained with a rotating external positron source. Images were reconstructed using standard two-dimensional filtered backprojection. Raters were asked to make a judgment about whether the image reflected the presence of AD or not. Images consistent with AD were agreed upon a priori to show bilateral temporal or parietal hypometabolism or both, highly asymmetric temporoparietal hypometabolism, or posterior cingulate hypometabolism. Frontal hypometabolism was thought to be consistent with a diagnosis of AD if it was accompanied by more severe temporoparietal hypometabolism.							
Results	**True positives:**	16	**False negatives:**	3	**False positives:**	7	**True negatives:** 19
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall	Not serious						

Jagust W, Reed B,Mungas D,Ellis W, De Carli C.What does fluorodeoxyglucose PET imaging add to a clinical diagnosis of dementia? Neurology. 2007; 69: 871-7.	
indirectness	

Jahn H, Wittke S, Zurbig P, Raedler TJ, Arlt S, Kellmn M, Mullen W, Eichenlaub M, Mischak H, Wiedmann K. Peptide Fingerprinting of Alzheimer's Disease in Cerebrospinal Fluid: Identification and Prospective Evaluation of New Synaptic Biomarkers. PLoS ONE 2011; 6: e26540.							
Study type	Prospective cohort						
Country	Germany						
Setting	University Hospital Hamburg- Eppendorf memory clinic						
Inclusion criteria	People referred to the memory clinic of the University Hospital Hamburg- Eppendorf.						
Exclusion criteria	Not stated						
Sex	49.0% male						
Age	Mean age 65.3 years (12.3)						
Presentation	Memory problems						
Reference standard	ICD-10 and the National Institute of Neurological and Communicative Disorders and the Stroke-Alzheimer's Disease and Related Disorders Association criteria (NINCDS-ADRDA) to identify patients with vascular dementia. MCI diagnoses were made according to the criteria of Petersen and FTD was diagnosed according to the Lund–Manchester criteria.						
AD versus non-AD (excluding MCI)							
Index Test: Mass spec(trometry) CE-MS analysis was performed as described using a P/ACEMDQ (Beckman Coulter, Fullerton, USA) system on-line coupled to a Micro- TOF MS (Bruker Daltonic).							
Results	**True positives:**	55	**False negatives:**	8	**False positives:**	4	**True negatives:** 19
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:** High
Overall risk of bias	Serious (>10% population excluded from analysis; unclear whether the patients were a random or consecutive sample or whether inappropriate exclusions were avoided; unclear whether the reference standard was interpreted without knowledge of the index tests results)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall	Not serious						

Jahn H, Wittke S, Zurbig P, Raedler TJ, Arlt S, Kellmn M, Mullen W, Eichenlaub M, Mischak H, Wiedmann K. Peptide Fingerprinting of Alzheimer's Disease in Cerebrospinal Fluid: Identification and Prospective Evaluation of New Synaptic Biomarkers. PLoS ONE 2011; 6: e26540.								
indirectness								
Index Test: Amyloid Beta 1-42, Total Tau and p-tau abnormal The CSF levels of Aß42, total tau, and phospho181-tau were measured using commercial ELISAs (Innogenetics). Cut-off values for AD suspicious biomarker concentrations were >540 pg/ml for total-tau, >61 pg/ml for phospho181-tau and beta-amyloid 1–42 values, <240+1.186 total-tau pg/ml.								
Results	**True positives:**	50	**False negatives:**	7	**False positives:**	7	**True negatives:**	14
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (>10% population excluded from analysis; unclear whether the patients were a random or consecutive sample or whether inappropriate exclusions were avoided; unclear whether the reference standard was interpreted without knowledge of the index tests results)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Jubb MT, Evand JJ. An Investigation of the Utility of the Addenbrooke's Cognitive Examination III in the Early Detection of Dementia in Memory Clinic Patients Aged over 75 Years. Dement Geriatr Cogn Disord 2015; 40:222–232.	
Study type	Prospective cohort
Country	UK
Setting	Leeds and York Partnership NHS Foundation Trust Memory Service
Inclusion criteria	Patients presenting to the Leeds and York Partnership NHS Foundation Trust Memory Service for investigation of a memory or other cognitive problem between March 2013 and July 2014. Included is a) aged between 75 and 85 years inclusive, (b) not currently on treatment (cognitive enhancers), (c) able to consent to participate, (d) not overly distressed by the clinical assessment process, and (e) had not completed the ACE-III for clinical assessment.
Exclusion criteria	There was evidence of causes of significant cognitive impairment other than degenerative or vascular pathology (e.g. closed head injury, epilepsy, alcoholism, acutely psychotic, severely depressed or anxious) or they were unable to complete the ACE-III. Participants with mild to moderate mood disorders were eligible for inclusion.

Jubb MT, Evand JJ. An Investigation of the Utility of the Addenbrooke's Cognitive Examination III in the Early Detection of Dementia in Memory Clinic Patients Aged over 75 Years. Dement Geriatr Cogn Disord 2015; 40:222–232.							
Sex	61.0% male						
Age	Mean age 80.0 years (2.7)						
Presentation	Memory or other cognitive problems						
Reference standard	Dementia was diagnosed based on DSM-IV; AD according to NINCDS-ADRDA; NINCDS-AIREN for VaD; Peterson criteria for MCI.						
Dementia versus no dementia							
Index Test: Addenbrooke's Cognitive Examination-III, ACE- III (<88) Addenbrooke's Cognitive ExaminationIII, ACE- III (<88)							
Results	**True positives:**	25	**False negatives:**	1	**False positives:**	17	**True negatives:** 17
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Serious (Study population was confined to >75 years)						
Index Test: Addenbrooke's Cognitive Examination-III, ACE- III (<84) Addenbrooke's Cognitive ExaminationIII, ACE- III (<84)							
Results	**True positives:**	24	**False negatives:**	2	**False positives:**	13	**True negatives:** 20
Additional comments							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Serious (Optimised threshold used for analysis.)						
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low	
Overall	Serious (Study population was confined to >75 years)						

Jubb MT, Evand JJ. An Investigation of the Utility of the Addenbrooke's Cognitive Examination III in the Early Detection of Dementia in Memory Clinic Patients Aged over 75 Years. Dement Geriatr Cogn Disord 2015; 40:222–232.							
indirectness							
Index Test: Addenbrooke's Cognitive Examination-III, ACE- III (<81) Addenbrooke's Cognitive ExaminationIII, ACE- III (<81)							
Results	**True positives:**	21	**False negatives:**	5	**False positives:**	10	**True negatives:**	23
Additional comments							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (Study population was confined to >75 years)						
Index Test: Addenbrooke's Cognitive Examination-III, ACE- III (<82) Addenbrooke's Cognitive ExaminationIII, ACE- III (<82)							
Results	**True positives:**	21	**False negatives:**	5	**False positives:**	1	**True negatives:**	32
Additional comments							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Optimised threshold used for analysis.)						
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (Study population was confined to >75 years)						

P.1.11 K

Kaneta T, Nakatsuka M, Nakamura K, Seki T, Yamaguchi S et al. Improved diagnostic accuracy of SPECT through statistical analysis and the detection of hot spots at the primary sensorimotor area for the diagnosis of Alzheimer disease in a community-based study. Clinical Nuclear Medicine 2016; 41: e1-6.								
Study type	Prospective cohort							
Country	Japan							
Setting	Memory clinic at Osaki-Tajiri SKIP Centre							
Inclusion criteria	Patients visiting the clinic with a previous diagnosis of dementia based on DSM-IV, a CDR of 1+ and who received a final diagnosis of dementia subtype; medical treatment for dementia for > 3 months and additional evidence of dementia on the Cognitive Abilities Screening instrument and Wechsler Memory Scale-Revised Neuropsychological Tests.							
Exclusion criteria	Patients with depression according to the Geriatric Depression Scale.							
Sex	23.6% male							
Age	Mean age 81.6 years (SD 5.0)							
Presentation	Dementia with subtype to be determined							
Reference standard	Clinician diagnosis using the following criteria and additional tests: NINCDS-ADRDA for probable AD and AD with cerebrovascular disease; VaD according to NINDS-AIREN; DLB/PDD and FTLD using McKeith (1996, 2006).							
AD (including mixed AD and VaD) versus not AD								
Index Test: 99mTc-ECD SPECT, visual assessment method 99mTc-ECD SPECT was carried out using a triple-headed gamma camera (Prism Irix) with high-resolution fan beam collimators. Visual assessment of images by specialist.								
Results	**True positives:**	16	**False negatives:**	32	**False positives:**	11	**True negatives:**	30
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: 99mTc-ECD SPECT, automated method								

Kaneta T, Nakatsuka M, Nakamura K, Seki T, Yamaguchi S et al. Improved diagnostic accuracy of SPECT through statistical analysis and the detection of hot spots at the primary sensorimotor area for the diagnosis of Alzheimer disease in a community-based study. Clinical Nuclear Medicine 2016; 41: e1-6.								
99mTc-ECD SPECT was carried out using a triple-headed gamma camera (Prism Irix) with high-resolution fan beam collimators. Automated diagnosis based on Easy Z- score imaging system with a cut-off value for discriminating between healthy controls and patients with early AD of 14.2%.								
Results	**True positives:**	19	**False negatives:**	29	**False positives:**	7	**True negatives:**	34
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: 99mTc-ECD SPECT, automated and visual method 99mTc-ECD SPECT was carried out using a triple-headed gamma camera (Prism Irix) with high-resolution fan beam collimators. Automated diagnosis based on visual assess ment and Easy Z- score imaging system with a cut-off value for discriminating between healthy controls and patients with early AD of 14.2%.								
Results	**True positives:**	20	**False negatives:**	28	**False positives:**	6	**True negatives:**	35
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: 99mTc-ECD SPECT, positive SMG sign								

Kaneta T, Nakatsuka M, Nakamura K, Seki T, Yamaguchi S et al. Improved diagnostic accuracy of SPECT through statistical analysis and the detection of hot spots at the primary sensorimotor area for the diagnosis of Alzheimer disease in a community-based study. Clinical Nuclear Medicine 2016; 41: e1-6.								
99mTc-ECD SPECT was carried out using a triple-headed gamma camera (Prism Irix) with high-resolution fan beam collimators. Diagnosis using positive sensorimotor hotspot sign.								
Results	**True positives:**	28	**False negatives:**	20	**False positives:**	10	**True negatives:**	31
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Serious (The SMH was defined based on the data and it was unclear whether the index test results were interpreted without knowledge of the results of the reference standard or whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: 99mTc-ECD SPECT, positive SMG sign and visual assessment 99mTc-ECD SPECT was carried out using a triple-headed gamma camera (Prism Irix) with high-resolution fan beam collimators. Diagnosis using positive sensorimotor hotspot sign and visual assessment.								
Results	**True positives:**	31	**False negatives:**	17	**False positives:**	15	**True negatives:**	26
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Serious (The SMH was defined based on the data and it was unclear whether the index test results were interpreted without knowledge of the results of the reference standard or whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall	Not serious							

Kaneta T, Nakatsuka M, Nakamura K, Seki T, Yamaguchi S et al. Improved diagnostic accuracy of SPECT through statistical analysis and the detection of hot spots at the primary sensorimotor area for the diagnosis of Alzheimer disease in a community-based study. Clinical Nuclear Medicine 2016; 41: e1-6.								
indirectness								
Index Test: 99mTc-ECD SPECT, all information method 99mTc-ECD SPECT was carried out using a triple-headed gamma camera (Prism Irix) with high-resolution fan beam collimators. Diagnosis using positive sensorimotor hotspot sign and the automated results from the Easy Z- score imaging system (with a cut-off value for discriminating between healthy controls and patients with early AD of 14.2%).								
Results	**True positives:**	34	**False negatives:**	14	**False positives:**	13	**True negatives:**	28
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Serious (The SMH was defined based on the data and it was unclear whether the index test results were interpreted without knowledge of the results of the reference standard or whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Kemp PM, Clyde K, Holmes C. Impact of 123I-FP-CIT (DaTSCAN) SPECT on the diagnosis and management of patients with dementia with Lewy bodies: a retrospective study. Nucl Med Commun 2011;32: 298-302.	
Study type	Retrospective cohort
Country	UK
Setting	Department of Nuclear Medicine, Southampton University Hospitals Trust
Inclusion criteria	Referred to the unit for imaging with suspected DLB by a specialist in old age psychiatry working at a memory clinic
Exclusion criteria	None stated
Sex	51.0% male
Age	Mean age 79.0 years (SD7.3)

Kemp PM, Clyde K, Holmes C. Impact of 123I-FP-CIT (DaTSCAN) SPECT on the diagnosis and management of patients with dementia with Lewy bodies: a retrospective study. Nucl Med Commun 2011;32: 298-302.								
Presentation	Clinical suspicion of DLB							
Reference standard	Clinician diagnosis - not supported by any specific set of diagnostic criteria, but using the results of the imaging							
DLB vs no-DLB								
Index Test: 123I-FP-CIT SPECT MEDISO Nucline X-Ring/4R SPECT camera dedicated for brain imaging with low-energy high-resolution collimators. 128 projections acquired with a photopeak window at 159keV and 6% upper and lower scatter windows								
Results	**True positives:**	18	**False negatives:**	2	**False positives:**	2	**True negatives:**	58
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	High	**Flow and timing:**	Low
Overall risk of bias	Serious (Index test used as part of the reference standard)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Kenney K, Brechtel C, Takahashi H, Kurohara K, Anderson P, Gibbs CJ Jr. An enzyme-linked immunosorbent assay to quantify 14-3-3 proteins in the cerebrospinal fluid of suspected Creutzfeldt-Jakob disease patients. Ann Neurol 2000; 48: 395–398.	
Study type	Prospective cohort
Country	USA
Setting	Not stated
Inclusion criteria	People referred for diagnosis with suspected CJD
Exclusion criteria	Not stated
Sex	Not stated
Age	Not stated
Presentation	Rapidly progressive dementia leading to suspected CJD
Reference standard	Criteria for CJD based on Kretzschmar (1996)

Kenney K, Brechtel C, Takahashi H, Kurohara K, Anderson P, Gibbs CJ Jr. An enzyme-linked immunosorbent assay to quantify 14-3-3 proteins in the cerebrospinal fluid of suspected Creutzfeldt-Jakob disease patients. Ann Neurol 2000; 48: 395–398.							
CJD (definite and probable) versus not CJD							
Index Test: CSF 14-3-3 ELISA CSF 14-3-3 protein detected by ELISA with 8.3ng/ml cut off							
Results	**True positives:**	56	**False negatives:**	7	**False positives:**	2	**True negatives:** 82
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:** Low
Overall risk of bias	Serious (The test threshold was not pre-specified and it was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
CJD (definite) versus not CJD							
Index Test: CSF 14-3-3 ELISA CSF 14-3-3 protein detected by ELISA with 8.3ng/ml cut off							
Results	**True positives:**	38	**False negatives:**	3	**False positives:**	2	**True negatives:** 82
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:** High
Overall risk of bias	Very serious (Subgroup analysis with >10% population excluded, the test threshold was not pre-specified and it was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
CJD (definite and probable) versus not CJD							

Kenney K, Brechtel C, Takahashi H, Kurohara K, Anderson P, Gibbs CJ Jr. An enzyme-linked immunosorbent assay to quantify 14-3-3 proteins in the cerebrospinal fluid of suspected Creutzfeldt-Jakob disease patients. Ann Neurol 2000; 48: 395–398.								
Index Test: CSF 14-3-3 immunoblotting CSF 14-3-3 protein detected by immunoblotting								
Results	**True positives:**	59	**False negatives:**	4	**False positives:**	2	**True negatives:**	82
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
CJD (definite) versus not CJD								
Index Test: CSF 14-3-3 immunoblotting CSF 14-3-3 protein detected by immunoblotting								
Results	**True positives:**	39	**False negatives:**	2	**False positives:**	2	**True negatives:**	82
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with >10% population excluded and it was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Kerklaan BJ, van Berckel BNM, Herholz K, Dols A, van der Flier WM et al. The added value of 18-Fluorodeoxyglucose-positron Emission tomography in the diagnosis of the behavioural variant of Frontotemporal Dementia.

Kerklaan BJ, van Berckel BNM, Herholz K, Dols A, van der Flier WM et al. The added value of 18-Fluorodeoxyglucose-positron Emission tomography in the diagnosis of the behavioural variant of Frontotemporal Dementia.								
Study type	Retrospective cohort							
Country	The Netherlands							
Setting	VU Medical centre Alzheimer's Centre							
Inclusion criteria	Clinical suspicion of bvFTD; no MRI abnormalities characteristic of a neurodegenerative disorder; 2 years of clinical follow up after the scan.							
Exclusion criteria	None							
Sex	81.0% male							
Age	Mean age 65.0 (SD 8.1)							
Presentation	Suspected bvFTD							
Reference standard	FTD diagnosed according to Neary (1998) plus functional decline at 2 years.							
bvFTD/fd+ versus not bvFTD/fd+								
Index Test: FDG-PET 18f-FDG -PET. EC80 EXACT HR+ scanner. Imaging was interpreted as positive (FTD pattern), normal or deviant otherwise (non-FTD pattern).								
Results	**True positives:**	7	**False negatives:**	8	**False positives:**	3	**True negatives:**	34
Additional comments	bvFTD/fd+ refers to bvFTD with cognitive decline							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Kiesman M, Canson J-B, Godot J, Vogel T, Schweiger L, Chayer S, Kalthenbach G. The Movement disorders Society criteria for the diagnosis of Parkinson's disease dementia: their usefulness and limitations in elderly patients. J. Neurol 2013; 260: 2569-2579.	
Study type	Prospective cohort

Kiesman M, Canson J-B, Godot J, Vogel T, Schweiger L, Chayer S, Kalthenbach G. The Movement disorders Society criteria for the diagnosis of Parkinson's disease dementia: their usefulness and limitations in elderly patients. J. Neurol 2013; 260: 2569-2579.								
Country	France							
Setting	Strasbourg geriatric centre							
Inclusion criteria	≥ 65 years old; PD diagnosed with the UK PDS Brain bank criteria; stable motor function; CDR. 0.5 and MMSE> 16.							
Exclusion criteria	Dementia due to a cause other than PD; delirium < 3 months before study inclusion; severe depressive syndrome; previous major stroke, anticholinergic treatment and unable to consent.							
Sex	40.0% male							
Age	Mean age 80.5 years (SD 4.9)							
Presentation	Suspected PDD							
Reference standard	Clinician diagnosis							
PDD versus not PDD								
Index Test: Movement disorders criteria for PDD (≤120) Movement disorders criteria for PDD, cut-off ≤ 120								
Results	**True positives:**	25	**False negatives:**	6	**False positives:**	0	**True negatives:**	9
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Test threshold was not pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Movement disorders criteria for PDD (≤123) Movement disorders criteria for PDD, cut -off ≤ 123								
Results	**True positives:**	29	**False negatives:**	2	**False positives:**	2	**True negatives:**	7
Additional comments								
Risk of bias	**Patient**	Low	**Index test:**	High	**Reference**	Low	**Flow and**	Low

Kiesman M, Canson J-B, Godot J, Vogel T, Schweiger L, Chayer S, Kalthenbach G. The Movement disorders Society criteria for the diagnosis of Parkinson's disease dementia: their usefulness and limitations in elderly patients. J. Neurol 2013; 260: 2569-2579.								
	selection:				**standard:**		**timing:**	
Overall risk of bias	Serious (Test threshold was not pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Movement disorders criteria for PDD (≤132) Movement disorders criteria for PDD, Cut-off ≤ 132								
Results	**True positives:**	31	**False negatives:**	0	**False positives:**	5	**True negatives:**	4
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Test threshold was not pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: FCSRT-IR 3- FR (≤22) The Grober and Buschke's 3 and cued selective reminding test with immediate recall (French version) 3 Free recalls. Cut-off≤ 22								
Results	**True positives:**	26	**False negatives:**	5	**False positives:**	2	**True negatives:**	7
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Test threshold was not pre-specified.)							
Indirectness	**Patient**	Low	**Index test:**	Low	**Reference**	Low		

Kiesman M, Canson J-B, Godot J, Vogel T, Schweiger L, Chayer S, Kalthenbach G. The Movement disorders Society criteria for the diagnosis of Parkinson's disease dementia: their usefulness and limitations in elderly patients. J. Neurol 2013; 260: 2569-2579.								
	selection:				**standard:**			
Overall indirectness	Not serious							
Index Test: Rey-Osterrieth complex figure test, ROCF (≤21) The Rey-Osterrieth complex figure test, cut-off ≤ 21								
Results	**True positives:**	28	**False negatives:**	3	**False positives:**	2	**True negatives:**	7
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Test threshold was not pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Knafelc R, Lo Giudice D, Harrigan S, Cook R, Flicker L, Mackinnon A, et al. The combination of cognitive testing and an informant questionnaire in screening for dementia. Age and Ageing 2003; 32: 541–7.	
Study type	Prospective cohort
Country	Australia
Setting	Memory clinic
Inclusion criteria	Patients attending memory clinic with an informant.
Exclusion criteria	Patients lacking an informant to complete the IQCODE for them. Patients who were unable to speak English.
Sex	37.2% male
Age	Mean age 74.4 years (SD 8.8)
Presentation	Memory problems.
Reference standard	Clinician diagnosis based on DSM-III-R criteria

Knafelc R, Lo Giudice D, Harrigan S, Cook R, Flicker L, Mackinnon A, et al. The combination of cognitive testing and an informant questionnaire in screening for dementia. Age and Ageing 2003; 32: 541–7.								
Dementia versus no dementia								
Index Test: Informant Questionnaire on Cognitive Decline ,IQCODE (16 item, >3.5) IQCODE (16 item) 3.6 threshold for study								
Results	**True positives:**	215	**False negatives:**	14	**False positives:**	50	**True negatives:**	44
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Unclear
Overall risk of bias	Serious (Unclear whether all patients were included in the analysis; unclear interval between index and reference tests; lack of a pre-specified threshold.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<24) MMSE carried out as part of the CAMDEX test, cut-off< 24.								
Results	**True positives:**	192	**False negatives:**	37	**False positives:**	25	**True negatives:**	69
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Unclear
Overall risk of bias	Serious (Unclear whether all patients were included in the analysis; unclear interval between index and reference tests; lack of a pre-specified threshold.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Knapsgog A-B, Engedal K, Braekhus A. Performance of cerebrospinal fluid biomarkers in Alzheimer disease in a memory clinic in Norway. Alzheimer disease and associate disorders 2016: 1: 8-14.

Knapsgog A-B, Engedal K, Braekhus A. Performance of cerebrospinal fluid biomarkers in Alzheimer disease in a memory clinic in Norway. Alzheimer disease and associate disorders 2016: 1: 8-14.							
Study type	Retrospective cohort						
Country	Norway						
Setting	Oslo University Hospital						
Inclusion criteria	Patients undergoing lumbar puncture for the study of amyloid beta and tau.						
Exclusion criteria	None						
Sex	53.7% male						
Age	Mean age 61 (SD 6.4)						
Presentation	Suspected dementia						
Reference standard	ICD-10 for dementia						
AD versus not AD							
Index Test: Amyloid Beta 1-42 Amyloid Beta 1-42 INNOTEST ELISA, cut-off < 550 pg/ml.							
Results	**True positives:**	59	**False negatives:**	79	**False positives:**	12	**True negatives:** 55
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: Total Tau Total-tau, INNOTEST ELISA with cut-offs > 300 pg/ml for people under 50, > 450 pg/ml for people 50-69, > 500 pg/ml for 70 or older							
Results	**True positives:**	90	**False negatives:**	48	**False positives:**	15	**True negatives:** 52
Additional comments							

Knapsgog A-B, Engedal K, Braekhus A. Performance of cerebrospinal fluid biomarkers in Alzheimer disease in a memory clinic in Norway. Alzheimer disease and associate disorders 2016: 1: 8-14.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: p-tau 181 p-tau, INNOTEST ELISA, cut-off > 80 pg/ml							
Results	**True positives:**	65	**False negatives:**	73	**False positives:**	7	**True negatives:** 60
Additional comments							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						

Koikkalainena J, Rhodius-Meesterb H, Tolonena A, Barkhofc F, Tijmsb B, Lemstrab AW, Tongd T, Guerrerod R, Schuhd A, Ledigd C, Rueckertd D, Soininene H, Remese AM et al. Differential diagnosis of neurodegenerative diseases using structural MRI data. NeuroImage: Clinical, 2016; 11: 435–449.	
Study type	Prospective cohort
Country	The Netherlands
Setting	Alzheimer Centre of the VU University Medical Centre.
Inclusion criteria	Patients referred to the centre for analysis of their cognitive complaints (and subsequently enrolled in the Amsterdam Dementia Cohort). Patients were included if MRI and MMSE results were available

Koikkalainena J, Rhodius-Meesterb H, Tolonena A, Barkhofc F, Tijmsb B, Lemstrab AW, Tongd T, Guerrerod R, Schuhd A, Ledigd C, Rueckertd D, Soininene H, Remese AM et al. Differential diagnosis of neurodegenerative diseases using structural MRI data. NeuroImage: Clinical, 2016; 11: 435–449.								
Exclusion criteria	Not stated							
Sex	66.0% male							
Age	Mean age 64.0 years (8.0)							
Presentation	Cognitive complaints							
Reference standard	Patients were diagnosed with probable AD using the criteria of the National Institute for Neurological and Communicative Diseases Alzheimer's Disease and Related Disorders Association; all patients also met the core clinical criteria of the National Institute on Aging-Alzheimer's Association guidelines for AD (McKhann et al., 1984; McKhann et al., 2011). FTD was diagnosed using the Neary criteria; patients also met the core criteria from Rasckovsky (Neary et al., 1998; Rascovsky et al., 2011). VaD was diagnosed using the National Institute of Neurological Disorders and Stroke and Association Internationale pour la Recherché et l'Enseignement en Neurosciences criteria (Román et al., 1993), and DLB using the McKeith criteria (McKeith et al., 1996; McKeith et al., 2005)							
AD versus non-AD								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes.								
Results	**True positives:**	65	**False negatives:**	158	**False positives:**	45	**True negatives:**	236
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low
Results	**True positives:**	65	**False negatives:**	Overall risk of bias	**Not serious**	37	**True negatives:**	126
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Indirectness	**Patient selection:**	Low	**Index test:**	Low

Koikkalainena J, Rhodius-Meesterb H, Tolonena A, Barkhofc F, Tijmsb B, Lemstrab AW, Tongd T, Guerrerod R, Schuhd A, Ledigd C, Rueckertd D, Soininene H, Remese AM et al. Differential diagnosis of neurodegenerative diseases using structural MRI data. NeuroImage: Clinical, 2016; 11: 435–449.								
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	AD versus non-AD dementias	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus FTD								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes.								
Results	**True positives:**	65	**False negatives:**	158	**False positives:**	21	**True negatives:**	71
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus DLB								

Koikkalainena J, Rhodius-Meesterb H, Tolonena A, Barkhofc F, Tijmsb B, Lemstrab AW, Tongd T, Guerrerod R, Schuhd A, Ledigd C, Rueckertd D, Soininene H, Remese AM et al. Differential diagnosis of neurodegenerative diseases using structural MRI data. NeuroImage: Clinical, 2016; 11: 435–449.								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes.								
Results	**True positives:**	65	**False negatives:**	158	**False positives:**	13	**True negatives:**	34
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus VaD								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes.								
Results	**True positives:**	65	**False negatives:**	158	**False positives:**	3	**True negatives:**	21
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		

Koikkalainena J, Rhodius-Meesterb H, Tolonena A, Barkhofc F, Tijmsb B, Lemstrab AW, Tongd T, Guerrerod R, Schuhd A, Ledigd C, Rueckertd D, Soininene H, Remese AM et al. Differential diagnosis of neurodegenerative diseases using structural MRI data. NeuroImage: Clinical, 2016; 11: 435–449.								
Overall indirectness	Not serious							
FTD versus non-FTD								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes.								
Results	**True positives:**	46	**False negatives:**	46	**False positives:**	66	**True negatives:**	346
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
FTD versus non-FTD dementias								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes.								
Results	**True positives:**	46	**False negatives:**	46	**False positives:**	66	**True negatives:**	228
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient**	Low	**Index test:**	Low	**Reference**	Low		

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	selection:				**standard:**			
Overall indirectness	Not serious							
FTD versus AD								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes.								
Results	**True positives:**	46	**False negatives:**	46	**False positives:**	62	**True negatives:**	161
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
FTD versus DLB								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes.								
Results	**True positives:**	46	**False negatives:**	46	**False positives:**	3	**True negatives:**	44
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible							

Koikkalainena J, Rhodius-Meesterb H, Tolonena A, Barkhofc F, Tijmsb B, Lemstrab AW, Tongd T, Guerrerod R, Schuhd A, Ledigd C, Rueckertd D, Soininene H, Remese AM et al. Differential diagnosis of neurodegenerative diseases using structural MRI data. NeuroImage: Clinical, 2016; 11: 435–449.								
	patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
FTD versus VaD								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes.								
Results	**True positives:**	46	**False negatives:**	46	**False positives:**	1	**True negatives:**	23
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
DLB versus non-DLB								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes.								
Results	**True positives:**	20	**False negatives:**	27	**False positives:**	108	**True negatives:**	349

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Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
DLB versus non-DLB dementias								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes.								
Results	**True positives:**	20	**False negatives:**	27	**False positives:**	80	**True negatives:**	259
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
DLB versus AD								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes.								
Results	**True positives:**	20	**False**	27	**False positives:**	64	**True negatives:**	159

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			negatives:					
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
DLB versus FTD								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes.								
Results	**True positives:**	20	**False negatives:**	27	**False positives:**	13	**True negatives:**	79
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
DLB versus VaD								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence.								

Koikkalainena J, Rhodius-Meesterb H, Tolonena A, Barkhofc F, Tijmsb B, Lemstrab AW, Tongd T, Guerrerod R, Schuhd A, Ledigd C, Rueckertd D, Soininene H, Remese AM et al. Differential diagnosis of neurodegenerative diseases using structural MRI data. NeuroImage: Clinical, 2016; 11: 435–449.								
Imaging data were assessed visually for atrophy and vascular changes.								
Results	**True positives:**	20	**False negatives:**	27	**False positives:**	3	**True negatives:**	21
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
VaD versus non-VaD dementias								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes.								
Results	**True positives:**	17	**False negatives:**	7	**False positives:**	18	**True negatives:**	462
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence.								

Koikkalainena J, Rhodius-Meesterb H, Tolonena A, Barkhofc F, Tijmsb B, Lemstrab AW, Tongd T, Guerrerod R, Schuhd A, Ledigd C, Rueckertd D, Soininene H, Remese AM et al. Differential diagnosis of neurodegenerative diseases using structural MRI data. NeuroImage: Clinical, 2016; 11: 435–449.								
Imaging data were assessed visually for atrophy and vascular changes.								
Results	**True positives:**	17	**False negatives:**	7	**False positives:**	13	**True negatives:**	349
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
VaD versus AD								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes.								
Results	**True positives:**	17	**False negatives:**	7	**False positives:**	7	**True negatives:**	216
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		

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Overall indirectness	Not serious							
VaD versus FTD								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes.								
Results	**True positives:**	17	**False negatives:**	7	**False positives:**	4	**True negatives:**	88
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
VaD versus DLB								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes.								
Results	**True positives:**	17	**False negatives:**	7	**False positives:**	2	**True negatives:**	45
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the							

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	reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus non-AD								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed using an automatic image quantification method.								
Results	**True positives:**	164	**False negatives:**	59	**False positives:**	47	**True negatives:**	234
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus non-AD dementias								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed using an automatic image quantification method.								
Results	**True positives:**	164	**False negatives:**	59	**False positives:**	37	**True negatives:**	126
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							

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Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus FTD								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed using an automatic image quantification method.								
Results	**True positives:**	164	**False negatives:**	59	**False positives:**	19	**True negatives:**	73
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus DLB								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed using an automatic image quantification method.								
Results	**True positives:**	164	**False negatives:**	59	**False positives:**	18	**True negatives:**	29
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the							

Koikkalainena J, Rhodius-Meesterb H, Tolonena A, Barkhofc F, Tijmsb B, Lemstrab AW, Tongd T, Guerrerod R, Schuhd A, Ledigd C, Rueckertd D, Soininene H, Remese AM et al. Differential diagnosis of neurodegenerative diseases using structural MRI data. NeuroImage: Clinical, 2016; 11: 435–449.								
	reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus VaD								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed using an automatic image quantification method.								
Results	**True positives:**	164	**False negatives:**	59	**False positives:**	0	**True negatives:**	24
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
FTD versus non-FTD								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed using an automatic image quantification method.								
Results	**True positives:**	57	**False negatives:**	35	**False positives:**	20	**True negatives:**	392
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Not serious							

Koikkalainena J, Rhodius-Meesterb H, Tolonena A, Barkhofc F, Tijmsb B, Lemstrab AW, Tongd T, Guerrerod R, Schuhd A, Ledigd C, Rueckertd D, Soininene H, Remese AM et al. Differential diagnosis of neurodegenerative diseases using structural MRI data. NeuroImage: Clinical, 2016; 11: 435–449.								
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
FTD versus non-FTD dementias								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed using an automatic image quantification method.								
Results	**True positives:**	57	**False negatives:**	35	**False positives:**	18	**True negatives:**	276
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
FTD versus AD								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed using an automatic image quantification method.								
Results	**True positives:**	57	**False negatives:**	35	**False positives:**	14	**True negatives:**	209
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the							

Koikkalainena J, Rhodius-Meesterb H, Tolonena A, Barkhofc F, Tijmsb B, Lemstrab AW, Tongd T, Guerrerod R, Schuhd A, Ledigd C, Rueckertd D, Soininene H, Remese AM et al. Differential diagnosis of neurodegenerative diseases using structural MRI data. NeuroImage: Clinical, 2016; 11: 435–449.								
	reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
FTD versus DLB								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed using an automatic image quantification method.								
Results	**True positives:**	57	**False negatives:**	35	**False positives:**	4	**True negatives:**	43
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
FTD versus VaD								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed using an automatic image quantification method.								
Results	**True positives:**	57	**False negatives:**	35	**False positives:**	0	**True negatives:**	24
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible							

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	patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
DLB versus non-DLB								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed using an automatic image quantification method.								
Results	**True positives:**	15	**False negatives:**	32	**False positives:**	27	**True negatives:**	430
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
DLB versus non-DLB dementias								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed using an automatic image quantification method.								
Results	**True positives:**	15	**False negatives:**	32	**False positives:**	18	**True negatives:**	321
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the							

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	reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
DLB versus AD								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed using an automatic image quantification method.								
Results	**True positives:**	15	**False negatives:**	32	**False positives:**	12	**True negatives:**	211
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
DLB versus FTD								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed using an automatic image quantification method.								
Results	**True positives:**	15	**False negatives:**	32	**False positives:**	5	**True negatives:**	87
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible							

Koikkalainena J, Rhodius-Meesterb H, Tolonena A, Barkhofc F, Tijmsb B, Lemstrab AW, Tongd T, Guerrerod R, Schuhd A, Ledigd C, Rueckertd D, Soininene H, Remese AM et al. Differential diagnosis of neurodegenerative diseases using structural MRI data. NeuroImage: Clinical, 2016; 11: 435–449.								
	patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
DLB versus VaD								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed using an automatic image quantification method.								
Results	**True positives:**	15	**False negatives:**	32	**False positives:**	1	**True negatives:**	23
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
VaD versus non-VaD								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed using an automatic image quantification method.								
Results	**True positives:**	23	**False negatives:**	1	**False positives:**	26	**True negatives:**	454
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low

Koikkalainena J, Rhodius-Meesterb H, Tolonena A, Barkhofc F, Tijmsb B, Lemstrab AW, Tongd T, Guerrerod R, Schuhd A, Ledigd C, Rueckertd D, Soininene H, Remese AM et al. Differential diagnosis of neurodegenerative diseases using structural MRI data. NeuroImage: Clinical, 2016; 11: 435–449.								
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
VaD versus non-VaD dementias								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed using an automatic image quantification method.								
Results	**True positives:**	23	**False negatives:**	1	**False positives:**	26	**True negatives:**	336
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
VaD versus AD								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed using an automatic image quantification method.								
Results	**True positives:**	23	**False negatives:**	1	**False positives:**	19	**True negatives:**	204
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible							

Koikkalainena J, Rhodius-Meesterb H, Tolonena A, Barkhofc F, Tijmsb B, Lemstrab AW, Tongd T, Guerrerod R, Schuhd A, Ledigd C, Rueckertd D, Soininene H, Remese AM et al. Differential diagnosis of neurodegenerative diseases using structural MRI data. NeuroImage: Clinical, 2016; 11: 435–449.								
	patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
VaD versus FTD								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed using an automatic image quantification method.								
Results	**True positives:**	23	**False negatives:**	1	**False positives:**	5	**True negatives:**	87
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
VaD versus DLB								
Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed using an automatic image quantification method.								
Results	**True positives:**	23	**False negatives:**	1	**False positives:**	2	**True negatives:**	45
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High

Koikkalainena J, Rhodius-Meesterb H, Tolonena A, Barkhofc F, Tijmsb B, Lemstrab AW, Tongd T, Guerrerod R, Schuhd A, Ledigd C, Rueckertd D, Soininene H, Remese AM et al. Differential diagnosis of neurodegenerative diseases using structural MRI data. NeuroImage: Clinical, 2016; 11: 435–449.								
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Kukull WA, Larson EB, Teri L, Bowen J, McCormick W, Pfanschmidt ML. The mini mental state examination score and the clinical diagnosis of dementia. J Clin Epidemiol 1994; 47: 1061-1067.								
Study type	Prospective Cohort							
Country	USA							
Setting	Not stated							
Inclusion criteria	People with suspected dementia who had medical insurance cover with a particular health maintenance organisation. Identified by primary care, neurology and other speciality clinics.							
Exclusion criteria	Previous diagnosis of dementia							
Sex	45.9% male							
Age	Mean age 71.6 years (SD 8.8)							
Presentation	Suspected dementia							
Reference standard	DSM-IIIR criteria was used to diagnose dementia.							
Dementia versus no dementia								
Index Test: MMSE (<25) MMSE, 25								
Results	**True positives:**	56	**False negatives:**	24	**False positives:**	7	**True negatives:**	46
Additional comments	The data for cut offs above 25 was not extracted as these values are not commonly used.							
Risk of bias	**Patient**	Low	**Index test:**	High	**Reference**	Low	**Flow and**	Low

Koikkalainena J, Rhodius-Meesterb H, Tolonena A, Barkhofc F, Tijmsb B, Lemstrab AW, Tongd T, Guerrerod R, Schuhd A, Ledigd C, Rueckertd D, Soininene H, Remese AM et al. Differential diagnosis of neurodegenerative diseases using structural MRI data. NeuroImage: Clinical, 2016; 11: 435–449.								
	selection:				**standard:**		**timing:**	
Overall risk of bias	Serious (It is unclear whether the index test results were interpreted without knowledge of the results of the reference standard; multiple pre-specified cut-offs were used to determine the optimal cut-off; the index test result was known during the reference standard diagnosis.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<24) MMSE, 24								
Results	**True positives:**	50	**False negatives:**	30	**False positives:**	2	**True negatives:**	51
Additional comments	The data for cut offs above 25 was not extracted as these values are not commonly used.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It is unclear whether the index test results were interpreted without knowledge of the results of the reference standard; multiple pre-specified cut offs were used to determine the optimal cut off; the index test result was known during the reference standard diagnosis.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<23) MMSE, 23								
Results	**True positives:**	45	**False negatives:**	35	**False positives:**	0	**True negatives:**	53
Additional comments	The data for cut offs above 25 was not extracted as these values are not commonly used.							

Koikkalainena J, Rhodius-Meesterb H, Tolonena A, Barkhofc F, Tijmsb B, Lemstrab AW, Tongd T, Guerrerod R, Schuhd A, Ledigd C, Rueckertd D, Soininene H, Remese AM et al. Differential diagnosis of neurodegenerative diseases using structural MRI data. NeuroImage: Clinical, 2016; 11: 435–449.								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It is unclear whether the index test results were interpreted without knowledge of the results of the reference standard; multiple pre-specified cut offs were used to determine the optimal cut off; the index test result was known during the reference standard diagnosis.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<22) MMSE, 22								
Results	**True positives:**	45	**False negatives:**	35	**False positives:**	0	**True negatives:**	53
Additional comments	The data for cut offs above 25 was not extracted as these values are not commonly used.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It is unclear whether the index test results were interpreted without knowledge of the results of the reference standard; multiple pre-specified cut offs were used to determine the optimal cut off; the index test result was known during the reference standard diagnosis.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

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Larner AJ. Addenbrooke's Cognitive Examination (ACE) for the diagnosis and differential diagnosis of dementia. Clinical Neurology and Neurosurgery 2007; 109 : 491–494	
Study type	Prospective cohort

Larner AJ. Addenbrooke's Cognitive Examination (ACE) for the diagnosis and differential diagnosis of dementia. Clinical Neurology and Neurosurgery 2007; 109 : 491–494							
Country	UK						
Setting	Cognitive function clinic						
Inclusion criteria	Consecutive new referrals to the memory clinic						
Exclusion criteria	No exclusion criteria						
Sex	52.0% male						
Age	Not stated.						
Presentation	Suspected dementia						
Reference standard	Dementia was diagnosed using DSM-IV criteria.						
Dementia versus no dementia							
Index Test: Addenbrooke's Cognitive Examination, ACE (<88) Addenbrooke's Cognitive Examination (ACE) <88/100							
Results	**True positives:**	140	**False negatives:**	0	**False positives:**	83	**True negatives:** 62
Additional comments	The data on using VLOM ratios to differentiate between dementia subtypes was not extracted here as this test would not be used in practice for this purpose.						
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: Addenbrooke's Cognitive Examination, ACE (<83) Addenbrooke's Cognitive Examination (ACE) <83/100							
Results	**True positives:**	134	**False negatives:**	6	**False positives:**	54	**True negatives:** 91
Additional comments	The data on using VLOM ratios to differentiate between dementia subtypes was not extracted here as this test would not be used in practice for this purpose.						

Larner AJ. Addenbrooke's Cognitive Examination (ACE) for the diagnosis and differential diagnosis of dementia. Clinical Neurology and Neurosurgery 2007; 109 : 491–494								
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Addenbrooke's Cognitive Examination, ACE (<75) Addenbrooke's Cognitive Examination (ACE) <75/100								
Results	**True positives:**	119	**False negatives:**	21	**False positives:**	25	**True negatives:**	120
Additional comments	The data on using VLOM ratios to differentiate between dementia subtypes was not extracted here as this test would not be used in practice for this purpose.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Larner AJ. AD8 Informant questionnaire: pragmatice diagnostic test accuracy study. Journal of Geriatr. Psychiatry, 2015; 28: 198-202.	
Study type	Prospective cohort
Country	UK
Setting	Cognitive function clinic at a regional neuroscience centre
Inclusion criteria	New referrals to the clinic over a 12-month period, who had not previously been diagnosed with dementia and were accompanied by a reliable informant who was fluent in English and not < 10 years old.
Exclusion criteria	Not stated
Sex	50.0% male

Larner AJ. AD8 Informant questionnaire: pragmatice diagnostic test accuracy study. Journal of Geriatr. Psychiatry, 2015; 28: 198-202.								
Age	Median age 64.4 years (range 16-92)							
Presentation	Cognitive complaints							
Reference standard	Dementia diagnosed according to DSM-IV criteria.							
Dementia versus not dementia								
Index Test: AD8 (≥2) AD8, ≥ 2/8 defined as cognitive impairment								
Results	**True positives:**	67	**False negatives:**	2	**False positives:**	127	**True negatives:**	16
Additional comments	Data for 6CIT could not be analysed as it was presented for cognitive impairment (dementia plus MCI) versus no CI.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<25) MMSE, ≤24/30								
Results	**True positives:**	21	**False negatives:**	7	**False positives:**	30	**True negatives:**	67
Additional comments	Data for 6CIT could not be analysed as it was presented for cognitive impairment (dementia plus MCI) versus no CI.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall	Not serious							

Larner AJ. AD8 Informant questionnaire: pragmatice diagnostic test accuracy study. Journal of Geriatr. Psychiatry, 2015; 28: 198-202.	
indirectness	

Larner AJ. MACE versus MoCA: equivalence or superiority? Pragmatic diagnostic test accuracy study. Int. Psych. Geriatr. 2017; 29: 931-7.							
Study type	Prospective cohort						
Country	UK						
Setting	Cognitive functional clinic at a regional neuroscience centre						
Inclusion criteria	New patient referrals from a cognitive function clinic.						
Exclusion criteria	Pre-existing diagnosis of dementia						
Sex	65.0% male						
Age	Median 69 years (range 31-89 years)						
Presentation	Not specified.						
Reference standard	DSM-IV diagnosis of dementia						
Dementia versus no dementia (including MCI and SMC)							
Index Test: Mini-ACE (<26) Mini-ACE, ≤ 25/30							
Results	**True positives:**	42	**False negatives:**	1	**False positives:**	141	**True negatives:** 76
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Dementia versus no dementia MCI and SMC							
Index Test: Montreal Cognitive Assessment, MoCA (<26) MoCA (<26)							
Results	**True positives:**	43	**False**	0	**False positives:**	150	**True negatives:** 67

Larner AJ. MACE versus MoCA: equivalence or superiority? Pragmatic diagnostic test accuracy study. Int. Psych. Geriatr. 2017; 29: 931-7.								
			negatives:					
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Lattanzio F, Abu-Rumelleh S, Franceschini A, Kal H, Amore G et al. Prion‐specific and surrogate CSF biomarkers in Creutzfeldt‐Jakob disease: diagnostic accuracy in relation to molecular subtypes and analysis of neuropathological correlates of p‐tau and Aβ42 levels. Acta Neuropathol 2017; 133: 559–578.	
Study type	Retrospective cohort
Country	Italy
Setting	Laboratory of Neuropathology (NP-Lab) of the Institute of Neurological Sciences of Bologna (ISNB) (major reference laboratory for prion disease in Italy).
Inclusion criteria	Samples from suspected CJD cases submitted for diagnostic purposes between January 2003 and June 2016, to the Laboratory of Neuropathology.
Exclusion criteria	None stated
Sex	Not stated
Age	Not stated
Presentation	Suspected CJD
Reference standard	Diagnosis of CJD was carried out using the updated WHO criteria (Zerr, 2009), with the exclusion of CSF biomarker data for the classification of “possible” and “probable” CJD. Definite CJD cases were classified based on post-mortem examination, but also included genetic cases lacking neuropathology data.
CJD (definite, probable, possible and genetic) versus not CJD	
Index Test: Real-time quaking-induced prion conversion, RT-QuIC. Real-time quaking-induced prion conversion (RT-QuIC). The fluorescence intensity of ThT-PrPSc aggregates, expressed as relative fluorescence units (rfu), was taken every 45 min using 450 ± 10 nm (excitation) and 480 ± 10 nm (emission) wavelengths, with a bottom read. A CSF sample was considered prion positive if the mean of at least two out four sample replicates gave a fluorescence signal higher than the threshold cut-off value of 7000 rfu. This	

Lattanzio F, Abu-Rumelleh S, Franceschini A, Kal H, Amore G et al. Prion-specific and surrogate CSF biomarkers in Creutzfeldt-Jakob disease: diagnostic accuracy in relation to molecular subtypes and analysis of neuropathological correlates of p-tau and Aβ42 levels. Acta Neuropathol 2017; 133: 559–578.								
threshold represents the mean rfu values of negative samples plus at least five standard deviations. Samples were considered negative if none of the replicates surpassed the chosen cut-off. In case only one replicate went over the threshold, the test was considered ambiguous/ unclear and repeated.								
Results	**True positives:**	289	**False negatives:**	63	**False positives:**	2	**True negatives:**	346
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
CJD (definite) versus not CJD (definite)								
Index Test: Real-time quaking-induced prion conversion, RT-QuIC. Real-time quaking-induced prion conversion (RT-QuIC). The fluorescence intensity of ThT-PrPSc aggregates, expressed as relative fluorescence units (rfu), was taken every 45 min using 450 ± 10 nm (excitation) and 480 ± 10 nm (emission) wavelengths, with a bottom read. A CSF sample was considered prion positive if the mean of at least two out four sample replicates gave a fluorescence signal higher than the threshold cut-off value of 7000 rfu. This threshold represents the mean rfu values of negative samples plus at least five standard deviations. Samples were considered negative if none of the replicates surpassed the chosen cut-off. In case only one replicate went over the threshold, the test was considered ambiguous/ unclear and repeated.								
Results	**True positives:**	190	**False negatives:**	35	**False positives:**	1	**True negatives:**	162
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
CJD (definite, probable, possible and genetic) versus not CJD								
Index Test: CSF 14-3-3 immunoblotting								

Lattanzio F, Abu-Rumelleh S, Franceschini A, Kal H, Amore G et al. Prion-specific and surrogate CSF biomarkers in Creutzfeldt-Jakob disease: diagnostic accuracy in relation to molecular subtypes and analysis of neuropathological correlates of p-tau and Aβ42 levels. Acta Neuropathol 2017; 133: 559–578.								
14-3-4 detected by immunoblotting. The immunoreactivity signals were rated as negative, ambiguous or positive, on the basis of the optical densitometric (OD) comparison with the weakly positive control.								
Results	**True positives:**	298	**False negatives:**	61	**False positives:**	118	**True negatives:**	585
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
CJD (definite) versus not CJD (definite)								
Index Test: CSF 14-3-3 immunoblotting 14-3-4 detected by immunoblotting. The immunoreactivity signals were rated as negative, ambiguous or positive, on the basis of the optical densitometric (OD) comparison with the weakly positive control.								
Results	**True positives:**	194	**False negatives:**	39	**False positives:**	79	**True negatives:**	133
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
CJD (definite, probable, possible and genetic) versus not CJD								
Index Test: Total Tau Total-tau, > 1250pm/ml. INNOTEST ELISA.								
Results	**True positives:**	321	**False**	38	**False positives:**	84	**True negatives:**	619

Lattanzio F, Abu-Rumelleh S, Franceschini A, Kal H, Amore G et al. Prion-specific and surrogate CSF biomarkers in Creutzfeldt-Jakob disease: diagnostic accuracy in relation to molecular subtypes and analysis of neuropathological correlates of p-tau and Aβ42 levels. Acta Neuropathol 2017; 133: 559–578.								
			negatives:					
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (An optimised threshold was used for the assay.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
CJD (definite) versus not CJD (definite)								
Index Test: Total Tau Total-tau, > 1250pm/ml. INNOTEST ELISA.								
Results	**True positives:**	207	**False negatives:**	26	**False positives:**	54	**True negatives:**	158
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (An optimised threshold was used for the assay.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Launes J, Sulkava R, Erkinjuntti T, Nikkinen P, Lindroth L, Liewendahl K, et al. 99Tcm-HMPAO SPECT in suspected dementia. Nuclear Medicine Communications 1991;12: 757–65.	
Study type	Prospective cohort
Country	Finland
Setting	University hospital out-patient memory disorder clinic
Inclusion criteria	Patients with suspected dementia admitted to the outpatient memory disorder clinic
Exclusion criteria	Not stated

Launes J, Sulkava R, Erkinjuntti T, Nikkinen P, Lindroth L, Liewendahl K, et al. 99Tcm-HMPAO SPECT in suspected dementia. Nuclear Medicine Communications 1991;12: 757–65.							
Sex	38.8% male						
Age	mean age 64.2 years (SD 8.7)						
Presentation	Suspected dementia						
Reference standard	Neary 1998 criteria (FTD), NINCDS-ADRDA (AD), DSM-III-R (VaD)						
AD versus non-AD							
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT; threshold: not pre-specified; visual interpretation, using magenta scale: bilateral anterior CBF abnormality or bilateral anterior plus unilateral posterior CBF abnormality (SPECT indicative of FTLD). Visual interpretation with image analysis; single- headed camera used to take images. SPECT FTD pattern indicative of FTD: bilateral anterior brain hypoperfusion.							
Results	**True positives:**	23	**False negatives:**	13	**False positives:**	17	**True negatives:** 107
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
AD versus VaD							
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT; threshold pre-specified at 25% for lower threshold value; rCBF patterns on the SPECT scans were interpreted visually and without knowledge of the clinical diagnosis. BUT single head camera used - less accurate and not in clinical use today. Image analysis was not performed. AD pattern used to determine positive results.							
Results	**True positives:**	23	**False negatives:**	13	**False positives:**	5	**True negatives:** 28
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** High
Overall risk of bias	Serious (Subgroup analysis used with >10% study population excluded.)						

Launes J, Sulkava R, Erkinjuntti T, Nikkinen P, Lindroth L, Liewendahl K, et al. 99Tcm-HMPAO SPECT in suspected dementia. Nuclear Medicine Communications 1991;12: 757–65.								
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus FTD								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT; threshold pre-specified at 25% for lower threshold value; rCBF patterns on the SPECT scans were interpreted visually and without knowledge of the clinical diagnosis. BUT single head camera used - less accurate and not in clinical use today. Image analysis was not performed. AD pattern used to determine positive results.								
Results	**True positives:**	23	**False negatives:**	13	**False positives:**	1	**True negatives:**	4
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis used with >10% study population excluded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
VaD versus non-VaD								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT; threshold pre-specified at 25% for lower threshold value; rCBF patterns on the SPECT scans were interpreted visually and without knowledge of the clinical diagnosis. BUT single head camera used - less accurate and not in clinical use today. Image analysis was not performed. VaD pattern used to determine positive results.								
Results	**True positives:**	25	**False negatives:**	8	**False positives:**	60	**True negatives:**	67
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		

Launes J, Sulkava R, Erkinjuntti T, Nikkinen P, Lindroth L, Liewendahl K, et al. 99Tcm-HMPAO SPECT in suspected dementia. Nuclear Medicine Communications 1991;12: 757–65.								
Overall indirectness	Not serious							
VaD versus AD								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT; threshold pre-specified at 25% for lower threshold value; rCBF patterns on the SPECT scans were interpreted visually and without knowledge of the clinical diagnosis. BUT single head camera used - less accurate and not in clinical use today. Image analysis was not performed. VaD pattern used to determine positive results.								
Results	**True positives:**	25	**False negatives:**	8	**False positives:**	10	**True negatives:**	26
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis used with >10% study population excluded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
VaD versus FTD								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT; threshold pre-specified at 25% for lower threshold value; rCBF patterns on the SPECT scans were interpreted visually and without knowledge of the clinical diagnosis. BUT single head camera used - less accurate and not in clinical use today. Image analysis was not performed. VaD pattern used to determine positive results.								
Results	**True positives:**	25	**False negatives:**	8	**False positives:**	2	**True negatives:**	3
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis used with >10% study population excluded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Launes J, Sulkava R, Erkinjuntti T, Nikkinen P, Lindroth L, Liewendahl K, et al. 99Tcm-HMPAO SPECT in suspected dementia. Nuclear Medicine Communications 1991;12: 757–65.								
FTD versus non-FTD								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT; Threshold: pre-specified at 25% for lower threshold value; rCBF patterns on the SPECT scans were interpreted visually and without knowledge of the clinical diagnosis. BUT single head camera used - less accurate and not in clinical use today. Image analysis was not performed. FTD pattern used to determine positive results.								
Results	**True positives:**	2	**False negatives:**	3	**False positives:**	8	**True negatives:**	147
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
FTD versus AD								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT; threshold pre-specified at 25% for lower threshold value; rCBF patterns on the SPECT scans were interpreted visually and without knowledge of the clinical diagnosis. BUT single head camera used - less accurate and not in clinical use today. Image analysis was not performed. FTD pattern used to determine positive results.								
Results	**True positives:**	2	**False negatives:**	3	**False positives:**	1	**True negatives:**	35
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis used with >10% study population excluded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
FTD versus VaD								
Index Test: 99mTc-HMPAO SPECT								

Launes J, Sulkava R, Erkinjuntti T, Nikkinen P, Lindroth L, Liewendahl K, et al. 99Tcm-HMPAO SPECT in suspected dementia. Nuclear Medicine Communications 1991;12: 757–65.								
99mTc-HMPAO SPECT; threshold pre-specified at 25% for lower threshold value; rCBF patterns on the SPECT scans were interpreted visually and without knowledge of the clinical diagnosis. BUT single head camera used - less accurate and not in clinical use today. Image analysis was not performed. FTD pattern used to determine positive results.								
Results	**True positives:**	2	**False negatives:**	3	**False positives:**	2	**True negatives:**	31
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis used with >10% study population excluded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Leitao MJ, Baldeiras I, Almeida MR, Ribeiro MH, Santos AC, Ribeiro M, Tomas J et al. Sporadic Creutzfeldt-Jakob disease diagnostic accuracy is improved by a new CSF ELISA 14-3-3γ assay. Neuroscience 2016; 322: 398-407.								
Study type	Retrospective cohort							
Country	Portugal							
Setting	Neurochemistry laboratory at University Hospital, Coimbra							
Inclusion criteria	Clinical suspicion of sporadic CJD							
Exclusion criteria	None stated							
Sex	88.3% male							
Age	Mean age 64.6 (SD 12.1)							
Presentation	Suspected CJD							
Reference standard	Neuropathology							
CJD versus not CJD								
Index Test: CSF 14-3-3 ELISA 14-3--3, Circulex 14-3-3γ ELISA. Cut-off >14552 arbitrary units/ml								
Results	**True positives:**	70	**False**	2	**False positives:**	4	**True negatives:**	69

Leitao MJ, Baldeiras I, Almeida MR, Ribeiro MH, Santos AC, Ribeiro M, Tomas J et al. Sporadic Creutzfeldt-Jakob disease diagnostic accuracy is improved by a new CSF ELISA 14-3-3γ assay. Neuroscience 2016; 322: 398-407.								
			negatives:					
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether: a consecutive or random sample of patients was enrolled; the study avoided inappropriate exclusions; test thresholds were pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Total Tau Total tau, INNOTEST ELISA, cut-off > 1035 pg/ml								
Results	**True positives:**	70	**False negatives:**	2	**False positives:**	5	**True negatives:**	66
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether: a consecutive or random sample of patients was enrolled; the study avoided inappropriate exclusions; test thresholds were pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: p-tau/total tau ratio of p-tau/t-tau, INNOTEST ELISA, cut-off < 45.56								
Results	**True positives:**	70	**False negatives:**	2	**False positives:**	9	**True negatives:**	64
Additional comments								
Risk of bias	**Patient**	Unclear	**Index test:**	Unclear	**Reference**	Low	**Flow and**	Low

Leitao MJ, Baldeiras I, Almeida MR, Ribeiro MH, Santos AC, Ribeiro M, Tomas J et al. Sporadic Creutzfeldt-Jakob disease diagnostic accuracy is improved by a new CSF ELISA 14-3-3γ assay. Neuroscience 2016; 322: 398-407.								
	selection:				**standard:**		**timing:**	
Overall risk of bias	Serious (It was unclear whether: a consecutive or random sample of patients was enrolled; the study avoided inappropriate exclusions; test thresholds were pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Lemstra AW, van Meegen MT, Vreyling JP, Meijerink PH, Jansen GH, Bulk S, Baas F, van Gool WA. 14-3-3 testing in diagnosing Creutzfeldt-Jakob disease: A prospective study in 112 patients.Neurology 2000; 55: 514-6								
Study type	Prospective cohort							
Country	Netherlands							
Setting	The only specialist laboratory facility used to test for 14-3-3 in CSF in Netherlands.							
Inclusion criteria	Samples from patients with suspected CJD that were sent to the laboratory for testing.							
Exclusion criteria	Not stated							
Sex	Not stated							
Age	Not stated							
Presentation	Rapidly progressive dementia leading to suspected CJD							
Reference standard	Diagnosis based on criteria using information from referring physicians, with pathology confirmation of CJD in 25/33 CJD positive cases. The criteria used are not specified.							
CJD versus not CJD								
Index Test: CSF 14-3-3 immunoblotting Detection of presence of 14-3-3 protein in CSF by immunoblotting, threshold of detection not stated.								
Results	**True positives:**	32	**False negatives:**	1	**False positives:**	10	**True negatives:**	67
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Serious (Unclear whether the reference and index tests were carried out blind to each other; it is unclear whether the index test (as carried out) was able to detect 14-3-3 protein at an appropriate threshold level.)							

Lemstra AW, van Meegen MT, Vreyling JP, Meijerink PH, Jansen GH, Bulk S, Baas F, van Gool WA. 14-3-3 testing in diagnosing Creutzfeldt-Jakob disease: A prospective study in 112 patients.Neurology 2000; 55: 514-6						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low
Overall indirectness	Not serious					

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Maddalena A, Papassotiropoulos A, Muller-Tillmanns B, et al. Biochemical diagnosis of Alzheimer disease by measuring the cerebrospinal fluid ratio of phosphorylated tau protein to beta-amyloid peptide(42). Arch Neurol 2003; 60: 1202–6.								
Study type	Prospective cohort							
Country	Switzerland							
Setting	Memory disorders unit							
Inclusion criteria	Outpatients at a memory disorders unit who were referred for diagnostic workup.							
Exclusion criteria	Not stated							
Sex	54.0% male							
Age	Mean age 68.4 years (SD9.4)							
Presentation	Suspected dementia							
Reference standard	Diagnosis according to NINCDS-ADRDA for AD; The Lund and Manchester groups criteria for FTD; McKeith criteria for DLB; NINDS-AIREN for VaD.							
AD versus non-AD dementia								
Index Test: Amyloid Beta 1-42 Amyloid Beta 1-42, INNOTEST Beta Amyloid ELISA, cut off 0.49mg/ml								
Results	**True positives:**	40	**False negatives:**	11	**False positives:**	9	**True negatives:**	21
Additional comments	We excluded healthy controls as they did not have suspected dementia at baseline. We were unable to compare dementia versus no dementia as the authors used different cut offs within the same test for different analyses and we cannot obtain a 2x2 table of the complete data set as a result.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low

Maddalena A, Papassotiropoulos A, Muller-Tillmanns B, et al. Biochemical diagnosis of Alzheimer disease by measuring the cerebrospinal fluid ratio of phosphorylated tau protein to beta-amyloid peptide(42). Arch Neurol 2003; 60: 1202–6.								
Overall risk of bias	Serious (It was unclear whether inappropriate exclusions had been made; an optimised threshold was used for each test and within each test for different analyses; it was unclear whether the index and reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: p-tau 181 p-tau, INNOTEST p-tau 181 ELISA, cut off 35pg/ml								
Results	**True positives:**	37	**False negatives:**	14	**False positives:**	11	**True negatives:**	19
Additional comments	We excluded healthy controls as they did not have suspected dementia at baseline. We were unable to compare dementia versus no dementia as the authors used different cut offs within the same test for different analyses and we cannot obtain a 2x2 table of the complete data set as a result.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether inappropriate exclusions had been made; an optimised threshold was used for each test and within each test for different analyses; it was unclear whether the index and reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: p-tau/Amyloid Beta 1-42 p-tau/Amyloid Beta 1-42, cut off 83								
Results	**True positives:**	41	**False negatives:**	10	**False positives:**	8	**True negatives:**	22
Additional comments	We excluded healthy controls as they did not have suspected dementia at baseline. We were unable to compare dementia versus no dementia as the authors used different cut offs within the same test for different analyses and we cannot obtain a 2x2 table of the complete data set as a result.							

Maddalena A, Papassotiropoulos A, Muller-Tillmanns B, et al. Biochemical diagnosis of Alzheimer disease by measuring the cerebrospinal fluid ratio of phosphorylated tau protein to beta-amyloid peptide(42). Arch Neurol 2003; 60: 1202–6.								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether inappropriate exclusions had been made; an optimised threshold was used for each test and within each test for different analyses; it was unclear whether the index and reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus no dementia								
Index Test: Amyloid Beta 1-42 Amyloid Beta 1-42, INNOTEST Beta Amyloid ELISA, cut off 0.58ng/ml								
Results	**True positives:**	43	**False negatives:**	8	**False positives:**	3	**True negatives:**	16
Additional comments	We excluded healthy controls as they did not have suspected dementia at baseline. We were unable to compare dementia versus no dementia as the authors used different cut offs within the same test for different analyses and we cannot obtain a 2x2 table of the complete data set as a result.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether inappropriate exclusions had been made; an optimised threshold was used for each test and within each test for different analyses; it was unclear whether the index and reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: p-tau 181 p-tau, INNOTEST p-tau 181 ELISA, cut off 39pg/ml								
Results	**True positives:**	34	**False negatives:**	17	**False positives:**	7	**True negatives:**	12

Maddalena A, Papassotiropoulos A, Muller-Tillmanns B, et al. Biochemical diagnosis of Alzheimer disease by measuring the cerebrospinal fluid ratio of phosphorylated tau protein to beta-amyloid peptide(42). Arch Neurol 2003; 60: 1202–6.								
Additional comments	We excluded healthy controls as they did not have suspected dementia at baseline. We were unable to compare dementia versus no dementia as the authors used different cut offs within the same test for different analyses and we cannot obtain a 2x2 table of the complete data set as a result.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether inappropriate exclusions had been made; an optimised threshold was used for each test and within each test for different analyses; it was unclear whether the index and reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: p-tau/Amyloid Beta 1-42 p-tau/Amyloid Beta 1-42, cut off 84								
Results	**True positives:**	41	**False negatives:**	10	**False positives:**	2	**True negatives:**	17
Additional comments	We excluded healthy controls as they did not have suspected dementia at baseline. We were unable to compare dementia versus no dementia as the authors used different cut offs within the same test for different analyses and we cannot obtain a 2x2 table of the complete data set as a result.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether inappropriate exclusions had been made; an optimised threshold was used for each test and within each test for different analyses; it was unclear whether the index and reference tests were interpreted independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Malhotra C, Chan A, Matcher D, Seow D, Chuo A, Do YK. Diagnostic Performance of Short Portable Mental Status Questionnaire for Screening Dementia Among Patients Attending Cognitive Assessment Clinics in Singapore. Ann Acad Med Singapore 2013; 42: 315-9.								
Study type	Prospective cohort							
Country	Singapore							
Setting	Cognitive assessment clinics at Singapore General Hospital, Changi General Hospital and Tan Tock Seng Hospital							
Inclusion criteria	Patients attending cognitive assessment clinics.							
Exclusion criteria	None stated							
Sex	30.7% male							
Age	Ages ranged from 60-94 years							
Presentation	Suspected dementia							
Reference standard	Clinician diagnosis -criteria not stated							
Dementia versus no dementia (including MCI)								
Index Test: Short Portable Mental Status Questionnaire, SPMSQ (≥5) Short Portable Mental Status Questionnaire (SPMSQ), cut-off ≥ 5, in English or Chinese								
Results	**True positives:**	80	**False negatives:**	23	**False positives:**	6	**True negatives:**	18
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Yes	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether the study avoided inappropriate exclusions and optimised test cut-offs were used for different population groups.)							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (60% participants had < 6 years education)							
Index Test: Short Portable Mental Status Questionnaire, SPMSQ (≥6) Short Portable Mental Status Questionnaire (SPMSQ), cut-off ≥ 6, in English or Chinese								
Results	**True positives:**	74	**False negatives:**	29	**False positives:**	14	**True negatives:**	10

Malhotra C, Chan A, Matcher D, Seow D, Chuo A, Do YK. Diagnostic Performance of Short Portable Mental Status Questionnaire for Screening Dementia Among Patients Attending Cognitive Assessment Clinics in Singapore. Ann Acad Med Singapore 2013; 42: 315-9.								
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Yes	**Flow and timing:**	High
Overall risk of bias	Very serious (It was unclear whether the study avoided inappropriate exclusions; optimised test cut-offs were used for different population group and a subgroup analysis was used which excluded 40% study population.)							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (Participants had < 6 years education)							
Index Test: Short Portable Mental Status Questionnaire, SPMSQ (≥4) Short Portable Mental Status Questionnaire (SPMSQ), cut-off ≥ 4, in English or Chinese								
Results	**True positives:**	81	**False negatives:**	22	**False positives:**	6	**True negatives:**	18
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Yes	**Flow and timing:**	High
Overall risk of bias	Very serious (It was unclear whether the study avoided inappropriate exclusions; optimised test cut-offs were used for different population group and a subgroup analysis was used which excluded 60% study population.)							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious (Participants had ≥ 6 years education)							

Manabe Y, Inui Y, Toyama H and Kosaka K. 123I-metaiodobenzylguanidine myocardial scintigraphy with early images alone is useful for the differential diagnosis of dementia with Lewy bodies. Psychiatry Research: Neuroimaging, 2017; 261: 75–79.	
Study type	Prospective cohort
Country	Japan

Manabe Y, Inui Y, Toyama H and Kosaka K. 123I-metaiodobenzylguanidine myocardial scintigraphy with early images alone is useful for the differential diagnosis of dementia with Lewy bodies. Psychiatry Research: Neuroimaging, 2017; 261: 75–79.								
Setting	Hospital radiology unit							
Inclusion criteria	Clinical diagnosis of suspected DLB aiming at its differential diagnosis with a completed mini mental state examination score. Information regarding: the age and sex of the patient; the presence/absence of complications of diabetes and their severity; presence/absence of complications of heart disease; presence/ absence of history of depression and oral administration of antidepressants; presence/absence of parkinsonism; presence/absence of visual hallucinations; and the presence/absence of cognitive fluctuations.							
Exclusion criteria	Patients who had received tricyclic or tetracyclic antidepressants within 6 months prior to examination, patients with serious heart disease such as heart failure with an ejection fraction below 60%, and patients with severe diabetes requiring insulin treatment were excluded.							
Sex	47.7% male							
Age	Mean age 78.3 years (SD 7.2)							
Presentation	Suspected DLB							
Reference standard	DLB was diagnosed according to the Consensus Criteria for the Clinical Diagnosis of Probable and Possible DLB (McKeith, 2005).							
DLB versus not DLB								
Index Test: 123I-MIBG cardiac scintigraphy 123I-MIBG cardiac scintigraphy, H/M ratio = 2.27 for early images. Imaging was performed using a Symbia T16 SPECT/CT system (Siemens AG) equipped with an LMEGP collimator. They carried out a 4-min static acquisition 15 min after intravenous injection of 111 MBq MIBG in the right arm, followed by a 20-min SPECT acquisition if uptake was observed. MIBG imaging scans were read and interpreted centrally by a radiologist and a neurologist. In addition, semi-quantitative evaluation of the H/M ratio was performed. The H/M ratio and washout ratio were calculated using the Standardized Method for Automatic Region of Interest (ROI) setting in MIBG (smart MIBG) software. According to the method reported previously, each H/M ratio was corrected to that of the standard ME collimator condition.								
Results	**True positives:**	53	**False negatives:**	26	**False positives:**	9	**True negatives:**	23
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Serious (Optimised test cut-offs were calculated and it was unclear whether the reference standard was interpreted without knowledge of the results of the index test or the index test was interpreted without knowledge of the results of the reference test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		

Manabe Y, Inui Y, Toyama H and Kosaka K. 123I-metaiodobenzylguanidine myocardial scintigraphy with early images alone is useful for the differential diagnosis of dementia with Lewy bodies. Psychiatry Research: Neuroimaging, 2017; 261: 75–79.								
Overall indirectness	Not serious							
Index Test: 123I-MIBG cardiac scintigraphy 123I-MIBG cardiac scintigraphy, H/M ratio = 2.23 for delayed images. Imaging was performed using a Symbia T16 SPECT/CT system (Siemens AG) equipped with an LMEGP collimator. They carried out a 4-min static acquisition 15 min after intravenous injection of 111 MBq MIBG in the right arm, followed by a 20-min SPECT acquisition if uptake was observed. MIBG imaging scans were read and interpreted centrally by a radiologist and a neurologist. In addition, semi-quantitative evaluation of the H/M ratio was performed. The H/M ratio and washout ratio were calculated using the Standardized Method for Automatic Region of Interest (ROI) setting in MIBG (smart MIBG) software. According to the method reported previously, each H/M ratio was corrected to that of the standard ME collimator condition.								
Results	**True positives:**	74	**False negatives:**	5	**False positives:**	1	**True negatives:**	31
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Serious (Optimised test cut-offs were calculated and it was unclear whether the reference standard was interpreted without knowledge of the results of the index test or the index test was interpreted without knowledge of the results of the reference test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Masterman DL, Mendez MF, Fairbanks LA, Cummings JL. Sensitivity, specificity, and positive predictive value of technetium 99-HMPAO SPECT in discriminating Alzheimer's disease from other dementias. J Geriatr Psychiatry Neurol 1997; 10: 15–21.	
Study type	Prospective cohort
Country	USA
Setting	UCLA Geriatric Behavioural Neurology Clinic
Inclusion criteria	People self-presenting with memory complaints or referred to clinic by physicians. Of these people 159/306 had a clinical history of memory difficulties and at least mild abnormalities following detailed cognitive and behavioural testing and were referred for SPECT as part of their initial work up.

Masterman DL, Mendez MF, Fairbanks LA, Cummings JL. Sensitivity, specificity, and positive predictive value of technetium 99-HMPAO SPECT in discriminating Alzheimer's disease from other dementias. J Geriatr Psychiatry Neurol 1997; 10: 15–21.								
Exclusion criteria	Not stated							
Sex	40.0% male							
Age	Mean age 74.9 years (SD 7.9)							
Presentation	Memory complaints							
Reference standard	Clinician diagnosis of probable, possible or AD unlikely based on NINCDS-ADRDA for AD and other diagnoses made using all available information.							
probable AD versus AD unlikely								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT scanning 2 hrs after injection. First acquisitions completed in 10 minutes, acquiring in 30 mins 12 parallel transaxial images extending 14.4cm above the orbitomeatal line. Transaxial, saggital and coronal images displayed with a colour scale. Scans were independently reviewed by 2 neuroimaging specialists. Analysis only included high resolution images n=139/159).								
Results	**True positives:**	38	**False negatives:**	13	**False positives:**	14	**True negatives:**	17
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% study population excluded)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
probable and possible AD versus AD unlikely								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT scanning 2 hrs after injection. First acquisitions completed in 10 minutes, acquiring in 30 mins 12 parallel transaxial images extending 14.4cm above the orbitomeatal line. Transaxial, saggital and coronal images displayed with a colour scale. Scans were independently reviewed by 2 neuroimaging specialists. Analysis only included high resolution images n=139/159).								
Results	**True positives:**	37	**False negatives:**	20	**False positives:**	14	**True negatives:**	17
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low

Masterman DL, Mendez MF, Fairbanks LA, Cummings JL. Sensitivity, specificity, and positive predictive value of technetium 99-HMPAO SPECT in discriminating Alzheimer's disease from other dementias. J Geriatr Psychiatry Neurol 1997; 10: 15–21.								
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
possible AD versus AD unlikely								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT scanning 2 hrs after injection. First acquisitions completed in 10 minutes, acquiring in 30 mins 12 parallel transaxial images extending 14.4cm above the orbitomeatal line. Transaxial, saggital and coronal images displayed with a colour scale. Scans were independently reviewed by 2 neuroimaging specialists. Analysis only included high resolution images n=139/159).								
Results	**True positives:**	75	**False negatives:**	33	**False positives:**	14	**True negatives:**	17
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis where >10% study population excluded)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Mathuranath PS, Nestor PJ, Berrios GE, Rakowicz W and Hodges JR. A biref cognitive test battery to differentiate Alzheimer's disease and frontotemporal dementia. Neurology 2000; 55: 1613-1620.	
Study type	Prospective cohort
Country	UK
Setting	Cambridge memory clinic
Inclusion criteria	New patients attending the memory clinic between June 1996 and October 1998 who met the following criteria: follow up of at least 12 months; able to complete the full assessment; and CDR and neuropsychological tests completed within 90 days of ACE.
Exclusion criteria	Evidence of two or more pathologies, either of which could independently be the main cause of dementia; major depression by the DSM-IV or other psychiatric illness; causes of cognitive impairment other than vascular or degenerative pathology (eg. head injuries, alcoholism).

Mathuranath PS, Nestor PJ, Berrios GE, Rakowicz W and Hodges JR. A biref cognitive test battery to differentiate Alzheimer's disease and frontotemporal dementia. Neurology 2000; 55: 1613-1620.							
Sex	57.6% male						
Age	Mean age 66.1 years (SD 8.6)						
Presentation	Suspected dementia						
Reference standard	Dementia was diagnosed according to the DSM-IV.						
Dementia versus no dementia							
Index Test: Addenbrooke's Cognitive Examination, ACE (<88) Addenbrooke's Cognitive Exam (ACE), cut-off 88							
Results	**True positives:**	107	**False negatives:**	8	**False positives:**	7	**True negatives:** 17
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Serious (Optimised test-threshold used and it was unclear whether the index test results were interpreted without knowledge of the results of the reference standard.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: Addenbrooke's Cognitive Examination, ACE (<83) Addenbrooke's Cognitive Exam (ACE), cut-off 83.							
Results	**True positives:**	94	**False negatives:**	21	**False positives:**	1	**True negatives:** 23
Additional comments							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Serious (Optimised test-threshold used and it was unclear whether the index test results were interpreted without knowledge of the results of the reference standard.)						
Indirectness	**Patient**	Low	**Index test:**	Low	**Reference**	Low	

Mathuranath PS, Nestor PJ, Berrios GE, Rakowicz W and Hodges JR. A biref cognitive test battery to differentiate Alzheimer's disease and frontotemporal dementia. Neurology 2000; 55: 1613-1620.								
	selection:				**standard:**			
Overall indirectness	Not serious							
Index Test: MMSE (<27) MMSE, cut-off 27.								
Results	**True positives:**	85	**False negatives:**	30	**False positives:**	1	**True negatives:**	23
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Optimised test-threshold used and it was unclear whether the index test results were interpreted without knowledge of the results of the reference standard.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<24) MMSE, conventional cut-off 24.								
Results	**True positives:**	60	**False negatives:**	55	**False positives:**	1	**True negatives:**	23
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Mayeux R, Saunders A, Shea S, Mirra S, Evans D, Roses AD, Hyman BT et al. Utility of the Apolipoprotein E genotype in the diagnosis of Alzheimer's disease. NEJM 1998; 338: 506-511.								
Study type	Retrospective cohort							
Country	USA							
Setting	Twenty-six Alzheimer's disease centres across USA.							
Inclusion criteria	People referred to 26 Alzheimer's disease centres for the evaluation of dementia.							
Exclusion criteria	Not stated							
Sex	49.0% male							
Age	Mean age 72.0 years (SD10.0) at diagnosis, 77.0 years (SD 10.0) at death.							
Presentation	Dementia requiring evaluation.							
Reference standard	At most centres the diagnoses were based on the standardized neuropathological criteria from the Consortium to Establish a Registry for Alzheimer's Disease (CERAD). Some centres used the Khachaturian criteria for the diagnosis of Alzheimer's disease, which are similar to the CERAD criteria. If neither were used, centre investigators specified how the post-mortem diagnosis was made.							
AD dementia versus non-AD dementia								
Index Test: Apo E (≥1 allele) Apo E, ≥ 1 allele as determined by PCR using DNA from tissue or blood samples; if this was not available frozen tissue was assayed.								
Results	**True positives:**	1142	**False negatives:**	628	**False positives:**	133	**True negatives:**	285
Additional comments	Data on the diagnostic test accuracy of the initial clinical diagnosis was not compared to the pathological diagnosis as more than one clinical criteria was used across the 26 study sites.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

McMurdo ME, Grant DJ, Kennedy NS, Gilchrist J,Findlay D, McLennan JM. The value of HMPAO SPECT scanning in the diagnosis of early Alzheimer's disease in patients attending a memory clinic. Nucl Med Commun 1994; 15: 405-409.								
Study type	Prospective cohort							
Country	UK							
Setting	Memory clinic, Dundee.							
Inclusion criteria	Referrals from general practitioners of patients over 55 years old with progressive memory difficulties of recent onset.							
Exclusion criteria	Patients with advanced dementia who would be unable to give consent or co-operate with scanning were excluded.							
Sex	40.9% male							
Age	Mean age 69 years (range 59-84)							
Presentation	People with progressive memory difficulties of recent onset							
Reference standard	Clinician diagnosis of AD according to the NINCDS-ADRDA criteria.							
AD versus non-AD								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT imaging was carried out using a single-headed camera with a high-resolution parallel-hole collimator. Sixty-four 35s views were collected using a 128x128 matrix, around an elliptical orbit off 360 degrees. Images were reconstructed and classified into one of four SPECT patterns: normal; AD pattern; ischemic pattern (VaD); abnormal other. Here the data is analysed for the AD pattern.								
Results	**True positives:**	15	**False negatives:**	11	**False positives:**	1	**True negatives:**	17
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus VaD								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT imaging was carried out using a single-headed camera with a high-resolution parallel-hole collimator. Sixty-four 35s views were collected using a 128x128 matrix, around an elliptical orbit off 360 degrees. Images were reconstructed and classified into one of four SPECT patterns: normal; AD pattern; ischemic pattern (VaD); abnormal other. Here the data is analysed for the AD pattern.								

McMurdo ME, Grant DJ, Kennedy NS, Gilchrist J,Findlay D, McLennan JM. The value of HMPAO SPECT scanning in the diagnosis of early Alzheimer's disease in patients attending a memory clinic. Nucl Med Commun 1994; 15: 405-409.								
Results	**True positives:**	15	**False negatives:**	11	**False positives:**	0	**True negatives:**	2
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis used with >10% study population discarded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
VaD versus non-VaD								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT imaging was carried out using a single-headed camera with a high-resolution parallel-hole collimator. Sixty-four 35s views were collected using a 128x128 matrix, around an elliptical orbit off 360 degrees. Images were reconstructed and classified into one of four SPECT patterns: normal; AD pattern; ischemic pattern (VaD); abnormal other. Here the data is analysed for the AD pattern.								
Results	**True positives:**	2	**False negatives:**	0	**False positives:**	10	**True negatives:**	32
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
VaD versus AD								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT imaging was carried out using a single-headed camera with a high-resolution parallel-hole collimator. Sixty-four 35s views were collected using a 128x128 matrix, around an elliptical orbit off 360 degrees. Images were reconstructed and classified into one of four SPECT patterns: normal; AD pattern; ischemic pattern (VaD); abnormal other. Here the data is analysed for the AD pattern.								
Results	**True positives:**	2	**False negatives:**	0	**False positives:**	4	**True negatives:**	22

McMurdo ME, Grant DJ, Kennedy NS, Gilchrist J,Findlay D, McLennan JM. The value of HMPAO SPECT scanning in the diagnosis of early Alzheimer's disease in patients attending a memory clinic. Nucl Med Commun 1994; 15: 405-409.								
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis used with >10% study population discarded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Mendez MF, Shapira JS, McMurtray A, Licht E, Miller BL. Accuracy of the clinical evaluation of Frontotemporal dementia. Arch Neurol 2007; 64: 830-835.								
Study type	Retrospective cohort							
Country	USA							
Setting	Neurology clinic at UCLA.							
Inclusion criteria	People with suspected FTD referred to the clinic for diagnosis.							
Exclusion criteria	Patients with language-predominant variants (PA or semantic dementia) and frontotemporal lobar degeneration.							
Sex	43.3% male							
Age	Mean age 63.4 years (SD 7.5)							
Presentation	Suspected FTD							
Reference standard	Clinician diagnosis after 2 years follow up.							
FTD versus not FTD								
Index Test: FTD consensus criteria FTD consensus criteria (Neary, 1998)								
Results	**True positives:**	23	**False negatives:**	40	**False positives:**	0	**True negatives:**	71
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							

Mendez MF, Shapira JS, McMurtray A, Licht E, Miller BL. Accuracy of the clinical evaluation of Frontotemporal dementia. Arch Neurol 2007; 64: 830-835.								
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MRI MRI. Details of machines used not stated, as existing scans were re-analysed by the researchers.								
Results	**True positives:**	40	**False negatives:**	23	**False positives:**	21	**True negatives:**	50
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: SPECT/PET SPECT/PET. Details of machines used not stated, some patients had SPECT and others PET results which were re-analysed by the researchers. Results rated for atrophy, hypometabolism or hypoperfusion on a 4 point scale.								
Results	**True positives:**	57	**False negatives:**	6	**False positives:**	18	**True negatives:**	53
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall	Not serious							

Mendez MF, Shapira JS, McMurtray A, Licht E, Miller BL. Accuracy of the clinical evaluation of Frontotemporal dementia. Arch Neurol 2007; 64: 830-835.	
indirectness	

Milian M, Leiherr AM, Straten G, Muller S, Leyhe T, Eschweiler GW. The Mini-Cog versus the Mini-Mental State Examination and the Clock Drawing Test in daily clinical practice: screening value in a German Memory Clinic. International Psychogeriatrics 2012; 24: 766-74							
Study type	Retrospective Cohort						
Country	Germany						
Setting	Memory clinic of the Department of Psychiatry and Psychotherapy at the University Hospital of Tubingen.						
Inclusion criteria	People admitted to the memory clinic between 2004 and 2009.						
Exclusion criteria	Not stated						
Sex	38.6% male						
Age	Mean age 74.8 years (SD 8.1)						
Presentation	Suspected dementia						
Reference standard	Diagnosis of dementia based on the DSM-IV criteria and the NINCDS-ADRDA criteria for AD.						
Dementia versus no dementia							
Index Test: Mini-Cog (Scanlan and Borson algorithm) Mini-Cog, Scanlan and Borson algorithm							
Results	**True positives:**	380	**False negatives:**	58	**False positives:**	0	**True negatives:** 64
Additional comments	Diagnostic test accuracy data was not extracted for detecting AD or non-AD dementia because it is unclear which comparator groups were used for the analysis and no raw data is presented.						
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:** Low
Overall risk of bias	Serious (Unclear whether inappropriate exclusions were avoided; whether the patients were a random or consecutive sample and whether the reference standard result was interpreted without knowledge of the results of the index test.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						

Milian M, Leiherr AM, Straten G, Muller S, Leyhe T, Eschweiler GW. The Mini-Cog versus the Mini-Mental State Examination and the Clock Drawing Test in daily clinical practice: screening value in a German Memory Clinic. International Psychogeriatrics 2012; 24: 766-74								
Index Test: Clock Drawing Test, CDT, Shulman scoring method (>2) Clock Drawing Test, CDT, cut-off >2, modified version of Shulman and Gold (1 perfect, 6 no reasonable representation of a clock)								
Results	**True positives:**	342	**False negatives:**	96	**False positives:**	2	**True negatives:**	62
Additional comments	Diagnostic test accuracy data was not extracted for detecting AD or non-AD dementia because it is unclear which comparator groups were used for the analysis and no raw data is presented.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Serious (Unclear whether inappropriate exclusions were avoided; whether the patients were a random or consecutive sample and whether the reference standard result was interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<25) MMSE, ≤ 24								
Results	**True positives:**	318	**False negatives:**	120	**False positives:**	0	**True negatives:**	64
Additional comments	Diagnostic test accuracy data was not extracted for detecting AD or non-AD dementia because it is unclear which comparator groups were used for the analysis and no raw data is presented.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Serious (Unclear whether inappropriate exclusions were avoided; whether the patients were a random or consecutive sample and whether the reference standard result was interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<26) MMSE, ≤ 25								

Milian M, Leiherr AM, Straten G, Muller S, Leyhe T, Eschweiler GW. The Mini-Cog versus the Mini-Mental State Examination and the Clock Drawing Test in daily clinical practice: screening value in a German Memory Clinic. International Psychogeriatrics 2012; 24: 766-74								
Results	**True positives:**	347	**False negatives:**	91	**False positives:**	0	**True negatives:**	64
Additional comments	Diagnostic test accuracy data was not extracted for detecting AD or non-AD dementia because it is unclear which comparator groups were used for the analysis and no raw data is presented.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Serious (Unclear whether inappropriate exclusions were avoided; whether the patients were a random or consecutive sample and whether the reference standard result was interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Mormont E, Jamart J, Robaye L. Validity of the Five -word testfor the evaluation of verbal episodic memory and dementia in a memory clinic setting. Journal of Geriatr Psych and Neurol 2012; 25: 78-84.	
Study type	Prospective cohort
Country	Belgium
Setting	Memory clinic
Inclusion criteria	French speaking participants at their first visit to the memory clinic.
Exclusion criteria	MMSE < 16, inadequate ability to understand and speak French, severe visual disturbance making reading impossible, refusal to complete neuropsychological examination.
Sex	41.5% male
Age	Mean age 70.0 (SD 9.4)
Presentation	Suspected dementia
Reference standard	Clinician diagnosis of dementia according to DSM-IV.
Dementia versus SMC (MCI excluded)	
Index Test: MMSE (<28) MMSE, ≤ 27	

Mormont E, Jamart J, Robaye L. Validity of the Five -word testfor the evaluation of verbal episodic memory and dementia in a memory clinic setting. Journal of Geriatr Psych and Neurol 2012; 25: 78-84.							
Results	**True positives:**	89	**False negatives:**	7	**False positives:**	11	**True negatives:** 38
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:** High
Overall risk of bias	Very serious (Exclusion of >35% population at analysis and use of optimised test thresholds.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: Free recall score of 5- word test, ≤ 6 for all dementia Free recall score of 5- word test, ≤ 6 for all dementia							
Results	**True positives:**	75	**False negatives:**	21	**False positives:**	5	**True negatives:** 44
Additional comments							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:** High
Overall risk of bias	Very serious (Exclusion of >35% population at analysis and use of optimised test thresholds.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: Total recall score of 5-word test, ≤ 9 Total recall score of 5-word test, ≤ 10							
Results	**True positives:**	78	**False negatives:**	18	**False positives:**	5	**True negatives:** 44
Additional comments							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:** High

Mormont E, Jamart J, Robaye L. Validity of the Five -word testfor the evaluation of verbal episodic memory and dementia in a memory clinic setting. Journal of Geriatr Psych and Neurol 2012; 25: 78-84.								
Overall risk of bias	Very serious (Exclusion of >35% population at analysis and use of optimised test thresholds.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Total weighted score of 5-word test, ≤ 15 Total weighted score of 5-word test, ≤ 16								
Results	**True positives:**	72	**False negatives:**	24	**False positives:**	2	**True negatives:**	47
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Exclusion of >35% population at analysis and use of optimised test thresholds.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus SMC (MCI excluded)								
Index Test: MMSE (<28) MMSE, ≤ 28								
Results	**True positives:**	60	**False negatives:**	1	**False positives:**	11	**True negatives:**	38
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Exclusion of >35% population at analysis and use of optimised test thresholds.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall	Not serious							

Mormont E, Jamart J, Robaye L. Validity of the Five -word testfor the evaluation of verbal episodic memory and dementia in a memory clinic setting. Journal of Geriatr Psych and Neurol 2012; 25: 78-84.							
indirectness							
Index Test: Free recall score of 5- word test, ≤ 5 for AD Free recall score of 5- word test, ≤ 5 for AD							
Results	**True positives:**	50	**False negatives:**	11	**False positives:**	0	**True negatives:** 49
Additional comments							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:** High
Overall risk of bias	Very serious (Exclusion of >35% population at analysis and use of optimised test thresholds.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: Total recall score of 5-word test, ≤ 9 Total recall score of 5-word test, ≤ 10							
Results	**True positives:**	56	**False negatives:**	5	**False positives:**	5	**True negatives:** 44
Additional comments							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:** High
Overall risk of bias	Very serious (Exclusion of >35% population at analysis and use of optimised test thresholds.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: Total weighted score of 5-word test, ≤ 15 Total weighted score of 5-word test, ≤ 16							

Mormont E, Jamart J, Robaye L. Validity of the Five -word testfor the evaluation of verbal episodic memory and dementia in a memory clinic setting. Journal of Geriatr Psych and Neurol 2012; 25: 78-84.								
Results	**True positives:**	55	**False negatives:**	6	**False positives:**	2	**True negatives:**	47
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Exclusion of >35% population at analysis and use of optimised test thresholds.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Motara H, Olusoga T, Russell G, Jamieson S, Ahmed S, Brindle N, Pillai A et al. Clinical impact and diagnostic accuracy of 2-[18F]- fluoro-2-deoxy-D-glucose positron-emission tomography/computed tomography (PET/CT) brain imaging in patients with cognitive impairment: a tertiary centre experience in the UK. Clinical Radiology, 2017; 72: 63-73.	
Study type	Retrospective cohort
Country	UK
Setting	Nuclear Medicine, Leeds Teaching Hospitals NHS Trust,
Inclusion criteria	Patients who had undergone brain FDG PET/CT for the evaluation of cognitive impairment, following a negative brain CT or MRI, and where no specific diagnosis was possible after an expert assessment by a clinician experienced in managing patients with cognitive impairment and dementia. Cognitive impairment was defined clinically for the purposes of this clinicoradiological pathway as an identifiable decline in memory, language, thinking, and/or judgement interfering with activities of daily living.
Exclusion criteria	There were 22 exclusions, i.e., patients who had brain PET/CT imaging performed for other indications, such as epilepsy or tumour assessment. Details of all 22 are not presented.
Sex	53.0% male
Age	Mean age 64.9 years (SD 10.5)
Presentation	Suspected dementia, clinically ambiguous dementia, early onset dementia, inconclusive neuropsychological assessment or diagnostic difficulties
Reference standard	Criteria/tests used not stated

Motara H, Olusoga T, Russell G, Jamieson S, Ahmed S, Brindle N, Pillai A et al. Clinical impact and diagnostic accuracy of 2-[18F]- fluoro-2-deoxy-D-glucose positron-emission tomography/computed tomography (PET/CT) brain imaging in patients with cognitive impairment: a tertiary centre experience in the UK. Clinical Radiology, 2017; 72: 63-73.								
AD versus not AD								
Index Test: FDG-PET/CT 18F FDG-PET examinations were performed on a GE Discovery 690 PET/CT system. Image reconstruction parameters were as follows: time-of-flight algorithm (Vue Point FX, GE Healthcare), with iterative reconstruction involving 24 subsets, two iterations, and a 3.2 mm spatial filter. The CT component of the study was carried out using the following parameters: 125 kV, 250 mAs, and 3.75 mm section thickness. The clinical reportwas generated following visual PET data review in transaxial, sagittal, and coronal planes with and without PET/CT image fusion on a GE Advantage Workstation. Standard and accepted reporting criteria were applied in terms of well- ecognised patterns of regional hypometabolism to distinguish between the various causes of cognitive impairment.								
Results	**True positives:**	40	**False negatives:**	6	**False positives:**	2	**True negatives:**	50
Additional comments	TP, TN etc. were calculated from the sensitivity and specificity values plus CI given in the paper.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Serious (There were 22 unstated reasons for exclusion; it was unclear whether a random or consecutive sample of patients was enrolled; whether the reference standard was likely to correctly classify the target condition or if it was interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (There were 22 unstated reasons for exclusion)							

Mulder C, Verway NA, van der Flier WM, Bouwman FH, Kok A, van Elk EJ, Scheltens P, Blankenstein MA. Amyloid- (1– 42), Total Tau, and Phosphorylated Tau as Cerebrospinal Fluid Biomarkers for the Diagnosis of Alzheimer Disease. Clinical Chemistry 2010; 56: 248-253.	
Study type	Prospective cohort
Country	Netherlands
Setting	Alzheimer Centre of the VU University Medical Centre.
Inclusion criteria	People referred to the Alzheimer Centre

Mulder C, Verway NA, van der Flier WM, Bouwman FH, Kok A, van Elk EJ, Scheltens P, Blankenstein MA. Amyloid- (1– 42), Total Tau, and Phosphorylated Tau as Cerebrospinal Fluid Biomarkers for the Diagnosis of Alzheimer Disease. Clinical Chemistry 2010; 56: 248-253.								
Exclusion criteria	Not stated							
Sex	50.4% male							
Age	Mean age 64.9 years (SD 9.5)							
Presentation	Suspected dementia							
Reference standard	Probable AD was diagnosed according to NINCDS-ADRDA criteria; patients with all normal test results were considered to have subjective memory complaints and used as controls.							
Probable AD versus not AD								
Index Test: Amyloid Beta 1-42 CSF Beta Amyloid 42, 550ng/ml								
Results	**True positives:**	211	**False negatives:**	37	**False positives:**	22	**True negatives:**	109
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It is unclear whether participants were consecutively or randomly recruited; the test cut offs were not pre-specified but selected to obtain 85% sensitivity; the timing between the reference and index tests is unclear and it is unclear whether the index test was interpreted independently of the reference test results)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Total Tau Tau, 375ng/ml								
Results	**True positives:**	211	**False negatives:**	37	**False positives:**	29	**True negatives:**	102
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low

Mulder C, Verway NA, van der Flier WM, Bouwman FH, Kok A, van Elk EJ, Scheltens P, Blankenstein MA. Amyloid- (1– 42), Total Tau, and Phosphorylated Tau as Cerebrospinal Fluid Biomarkers for the Diagnosis of Alzheimer Disease. Clinical Chemistry 2010; 56: 248-253.								
Overall risk of bias	Very Serious (It is unclear whether participants were consecutively or randomly recruited; the test cut offs were not pre-specified but selected to obtain 85% sensitivity; the timing between the reference and index tests is unclear and it is unclear whether the index test was interpreted independently of the reference test results)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: p-tau 181 p-Tau, 52ng/ml								
Results	**True positives:**	211	**False negatives:**	37	**False positives:**	42	**True negatives:**	89
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Very Serious (It is unclear whether participants were consecutively or randomly recruited; the test cut offs were not pre-specified but selected to obtain 85% sensitivity; the timing between the reference and index tests is unclear and it is unclear whether the index test was interpreted independently of the reference test results)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

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Nielsen TR, Andersen BB, Gottrup H, et al. Validation of the RUDAS for multicultural screening in Danish memory clinics. Dement Geriatr Cogn Disord 2013; 36: 354-62.	
Study type	Prospective cohort
Country	Denmark
Setting	Memory clinics at Copenhagen University Hospital Roskilde, Aarhus University Hospital and Copenhagen University Hospital.

Nielsen TR, Andersen BB, Gottrup H, et al. Validation of the RUDAS for multicultural screening in Danish memory clinics. Dement Geriatr Cogn Disord 2013; 36: 354-62.							
Inclusion criteria	People referred to the memory clinics for the evaluation of possible dementia. After March 2012 selective inclusion of immigrants with suspected dementia occurred.						
Exclusion criteria	After a March 2012 people from a non-immigrant background with suspected dementia were excluded.						
Sex	52.6% male						
Age	Dementia median age 77 years (Q1-Q3= 71.5-81); non-dementia 61 years (50.5-70).						
Presentation	Suspected dementia						
Reference standard	Dementia diagnosed according to the DSM-IV-TR criteria; patients with MCI included in the non-dementia group.						
Dementia versus no dementia							
Index Test: Rowland Universal Dementia Assessment Scale, RUDAS (<22) RUDAS (Rowland Universal Dementia Assessment Scale), <22/30							
Results	**True positives:**	35	**False negatives:**	37	**False positives:**	6	**True negatives:** 59
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Very serious (The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; a variety of test thresholds are reported.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: Rowland Universal Dementia Assessment Scale, RUDAS (<23) RUDAS (Rowland Universal Dementia Assessment Scale), <23/30							
Results	**True positives:**	46	**False negatives:**	26	**False positives:**	11	**True negatives:** 54
Additional comments							
Risk of bias	**Patient**	High	**Index test:**	High	**Reference**	Low	**Flow and** Low

Nielsen TR, Andersen BB, Gottrup H, et al. Validation of the RUDAS for multicultural screening in Danish memory clinics. Dement Geriatr Cogn Disord 2013; 36: 354-62.								
	selection:				**standard:**		**timing:**	
Overall risk of bias	Very serious (The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; a variety of test thresholds are reported.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Rowland Universal Dementia Assessment Scale, RUDAS (<24) RUDAS (Rowland Universal Dementia Assessment Scale), <24/30								
Results	**True positives:**	50	**False negatives:**	22	**False positives:**	13	**True negatives:**	52
Additional comments								
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Very serious (The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; a variety of test thresholds are reported.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Rowland Universal Dementia Assessment Scale, RUDAS (<25) RUDAS (Rowland Universal Dementia Assessment Scale), <25/30								
Results	**True positives:**	55	**False negatives:**	17	**False positives:**	22	**True negatives:**	43
Additional comments								
Risk of bias	**Patient**	High	**Index test:**	High	**Reference**	Low	**Flow and**	Low

Nielsen TR, Andersen BB, Gottrup H, et al. Validation of the RUDAS for multicultural screening in Danish memory clinics. Dement Geriatr Cogn Disord 2013; 36: 354-62.								
	selection:				**standard:**		**timing:**	
Overall risk of bias	Very serious (The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; ; a variety of test thresholds are reported.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Rowland Universal Dementia Assessment Scale, RUDAS (<26) RUDAS (Rowland Universal Dementia Assessment Scale), <26/30								
Results	**True positives:**	59	**False negatives:**	13	**False positives:**	23	**True negatives:**	42
Additional comments								
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Very serious (The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; ; a variety of test thresholds are reported.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<23) MMSE, <23/30								
Results	**True positives:**	38	**False negatives:**	33	**False positives:**	8	**True negatives:**	52
Additional comments	6 participants lacked MMSE data and so were excluded from the analysis by the authors							
Risk of bias	**Patient**	High	**Index test:**	High	**Reference**	Low	**Flow and**	Low

Nielsen TR, Andersen BB, Gottrup H, et al. Validation of the RUDAS for multicultural screening in Danish memory clinics. Dement Geriatr Cogn Disord 2013; 36: 354-62.								
	selection:				**standard:**		**timing:**	
Overall risk of bias	Very serious (The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; the test threshold was not pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<24) MMSE, <24/30								
Results	**True positives:**	46	**False negatives:**	25	**False positives:**	8	**True negatives:**	52
Additional comments	6 participants lacked MMSE data and so were excluded from the analysis by the authors							
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Very serious (The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; the test threshold was not pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<25) MMSE, <25/30								
Results	**True positives:**	54	**False negatives:**	17	**False positives:**	10	**True negatives:**	50
Additional comments	6 participants lacked MMSE data and so were excluded from the analysis by the authors							
Risk of bias	**Patient**	High	**Index test:**	High	**Reference**	Low	**Flow and**	Low

Nielsen TR, Andersen BB, Gottrup H, et al. Validation of the RUDAS for multicultural screening in Danish memory clinics. Dement Geriatr Cogn Disord 2013; 36: 354-62.								
	selection:				**standard:**		**timing:**	
Overall risk of bias	Very serious (The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; the test threshold was not pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<26) MMSE, <26/30								
Results	**True positives:**	54	**False negatives:**	17	**False positives:**	16	**True negatives:**	44
Additional comments	6 participants lacked MMSE data and so were excluded from the analysis by the authors							
Risk of bias	**Patient selection:**	High	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Very serious (The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; the test threshold was not pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<27) MMSE, <27/30								
Results	**True positives:**	63	**False negatives:**	8	**False positives:**	22	**True negatives:**	38
Additional comments	6 participants lacked MMSE data and so were excluded from the analysis by the authors							
Risk of bias	**Patient**	High	**Index test:**	High	**Reference**	Low	**Flow and**	Low

Nielsen TR, Andersen BB, Gottrup H, et al. Validation of the RUDAS for multicultural screening in Danish memory clinics. Dement Geriatr Cogn Disord 2013; 36: 354-62.								
	selection:				**standard:**		**timing:**	
Overall risk of bias	Very serious (The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; the test threshold was not pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

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O'Brien JT, Metcalfe S, Swann A, et al. Medial temporal lobe width on CT scanning in Alzheimer's disease: comparison with vascular dementia, depression and dementia with Lewy bodies. Dement Geriatr Cogn Disord. 2000;11: 114-118.						
Study type	Prospective Cohort					
Country	UK					
Setting	Old age psychiatry service					
Inclusion criteria	People referred to the clinic for diagnostic investigation of dementia or depression.					
Exclusion criteria	People with uncertain diagnoses or cases where a standard (not angled) CT scan was carried out.					
Sex	42.2% male					
Age	Mean age 79.2 years (SD 7.0)					
Presentation	Suspected dementia or depression					
Reference standard	AD was diagnosed using the NINCDS-ADRDA criteria; VaD using NINDS-AIREN; DLB using the consensus criteria (McKeith) and depression using DSM-IV.					
Dementia versus no dementia						
Index Test: CT CT scans were carried out using an IGE CT 9800 head scanner. Angled scans 5mm through the temporal lobes were acquired approximately 20-25 degrees C caudal to the orbito-meatal line. The medium width of the medial temporal line (MTL) was measured from hard copies using callipers, through the section that corresponded most closely to that passing through the mid-point of the temporal lobes. The medium width of the MTL on either side of the anterior and posterior margins of the brain stem was chosen for analysis. Cut off < 11.5mm.						
Results	**True positives:**	56	**False**	47	**False positives:**	3	**True negatives:**	10

O'Brien JT, Metcalfe S, Swann A, et al. Medial temporal lobe width on CT scanning in Alzheimer's disease: comparison with vascular dementia, depression and dementia with Lewy bodies. Dement Geriatr Cogn Disord. 2000;11: 114-118.								
			negatives:					
Additional comments	Subgroup analysis was not carried out for DLB as the numbers of patients was very small (n=9)							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus VaD								
Index Test: CT CT scans were carried out using an IGE CT 9800 head scanner. Angled scans 5mm through the temporal lobes were acquired approximately 20-25 degrees C caudal to the orbito-meatal line. The medium width of the medial temporal line (MTL) was measured from hard copies using callipers, through the section that corresponded most closely to that passing through the mid-point of the temporal lobes. The medium width of the MTL on either side of the anterior and posterior margins of the brain stem was chosen for analysis. Cut off < 11.5mm.								
Results	**True positives:**	35	**False negatives:**	34	**False positives:**	17	**True negatives:**	8
Additional comments	Subgroup analysis was not carried out for DLB as the numbers of patients was very small (n=9)							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with >10% population excluded)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus other dementias								
Index Test: CT CT scans were carried out using an IGE CT 9800 head scanner. Angled scans 5mm through the temporal lobes were acquired approximately 20-25								

O'Brien JT, Metcalfe S, Swann A, et al. Medial temporal lobe width on CT scanning in Alzheimer's disease: comparison with vascular dementia, depression and dementia with Lewy bodies. Dement Geriatr Cogn Disord. 2000;11: 114-118.								
degrees C caudal to the orbito-meatal line. The medium width of the medial temporal line (MTL) was measured from hard copies using callipers, through the section that corresponded most closely to that passing through the mid-point of the temporal lobes. The medium width of the MTL on either side of the anterior and posterior margins of the brain stem was chosen for analysis. Cut off < 11.5mm.								
Results	**True positives:**	35	**False negatives:**	34	**False positives:**	21	**True negatives:**	13
Additional comments	Subgroup analysis was not carried out for DLB as the numbers of patients was very small (n=9)							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with >10% population excluded)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
O'Brien JT, McKeith IG, Walker Z, Tatsch K, Booij J et al. Diagnostic accuracy of 123I-FP-CIT SPECT in possible dementia with Lewy bodies. The British Journal of Psychiatry 2009; 194: 34-39.								
Study type	Prospective cohort							
Country	UK							
Setting	Not stated							
Inclusion criteria	People aged 55-90 years with a DSM-IV diagnosis of dementia and possible dementia with Lewy bodies ; an MMSE score of 10 or more.							
Exclusion criteria	People with dementia who developed parkinsonism more than 1 year before the onset of dementia, who were deemed to have Parkinson's disease with dementia; people with structural imaging findings indicative of infarction in the region of the basal ganglia, including the internal capsule. Use of medication known or suspected to interact with striatal binding of 123I-FP-CIT was not permitted.							
Sex	Not stated							
Age	Age range 55-90 years (mean age not stated)							
Presentation	possible DLB							
Reference standard	Clinician diagnosis after 12 months follow-up using NINCDS-ADRDA for AD, NINDS-AIREN for VaD, DLB consensus criteria for DLB.							

O'Brien JT, Metcalfe S, Swann A, et al. Medial temporal lobe width on CT scanning in Alzheimer's disease: comparison with vascular dementia, depression and dementia with Lewy bodies. Dement Geriatr Cogn Disord. 2000;11: 114-118.								
DLB versus non-DLB								
Index Test: 123I-FP-CIT SPECT 123I-FP-CIT SPECT, taken at baseline with SPECT images acquired using a two- or three-headed camera. Visaul assessment of scans using a 4-point scale (0, normal uptake; 1, unilateral putamen loss; 2, bilateral putamen loss; 3, virtually absent uptake); only the dichotomous division of normal (0) v. abnormal (1–3) images were used for analysis.								
Results	**True positives:**	12	**False negatives:**	7	**False positives:**	0	**True negatives:**	7
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Ossenkoppele R, Prins ND, Pijnenburg YA, Lemstra AW, van der Flier WM, Adriaanse SF, Windhorst AD, Handels RL, Wolfs CA, Aalten P, Verhey FR, Verbeek MM, van Buchem MA, Hoekstra OS, Lammertsma AA, Scheltens P, van Berckel BN: Impact of molecular imaging on the diagnostic process in a memory clinic. Alzheimers Dement 2013; 9: 414–421.	
Study type	Prospective cohort
Country	The Netherlands
Setting	Outpatient memory clinic of the VU University Medical Centre.
Inclusion criteria	Cohort one was taken from people enrolled in the Centre for Translational Molecular Medicine (CTMM) Leiden Alzheimer Research Netherlands (LeARN) project to evaluate the cost-effectiveness of ancillary investigations in a memory clinic setting. Participants had a Mini-Mental State Examination (MMSE) score of 20 and a maximum clinical dementia rating (CDR) of 1, without major neurologic and psychiatric disorders, recent vascular events, and excessive substance abuse. Cohort two was recruited from cases where there was a substantial uncertainty about the diagnosis after the standard diagnostic work-up.
Exclusion criteria	Not stated
Sex	64.9% male
Age	62.4 years (7.4)

Ossenkoppele R, Prins ND, Pijnenburg YA, Lemstra AW, van der Flier WM, Adriaanse SF, Windhorst AD, Handels RL, Wolfs CA, Aalten P, Verhey FR, Verbeek MM, van Buchem MA, Hoekstra OS, Lammertsma AA, Scheltens P, van Berckel BN: Impact of molecular imaging on the diagnostic process in a memory clinic. **Alzheimers Dement 2013; 9: 414–421.**								
Presentation	Suspected dementia or ambiguous diagnosis following a dementia work-up.							
Reference standard	AD diagnosed using the NINCDS-ARDRA criteria; supranuclear palsy using NINDS-SPS workshop criteria; FTD using the criteria in Neary (1998); MCI according to the Peterson criteria (2001); Corticobasal degeneration according to Riley (2000).							
AD versus non-AD								
Index Test: FDG-PET 185 MBq of 18F-FDG was administered. Patients underwent a 10-minute transmission scan followed by a 15-minute emission scan using an ECAT Exact HR1 scanner (Siemens/CTI, Knoxville, TN). Parametric SUVr images were extracted from the interval between 45 and 60 minutes after injection. Scans were analysed using the PMOD Alzheimer's discrimination (PALZ) tool.T1-weighted MRI (3T Signa HDxt; General Electric, Milwaukee, WI) scans were used for coregistration and segmentation. [18F]FDG PET scans were interpreted as either normal or deviant and suggestive for AD (posterior cingulate and parietotemporal hypometabolism), FTD (frontotemporal metabolic impairment), DLB (occipital hypometabolism with relatively intact posterior cingulate gyrus), or dementia other (PSP: mesenchepalon, prefrontal, caudate nucleus, and thalamus hypometabolism; CBD: asymmetric hypometabolism with involvement of the basal ganglia).								
Results	**True positives:**	38	**False negatives:**	27	**False positives:**	27	**True negatives:**	61
Additional comments	The study population consisted of 2 groups that could not be separated during the analysis. The data for [11C] Pittsburgh compound B ([11C] PIB) imaging was not extracted as this test is only used for research in the UK.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the index test was interpreted with knowledge of the reference diagnosis.)							
Indirectness	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.)							
AD versus non-AD dementias								
Index Test: FDG-PET 185 MBq of 18F-FDG was administered. Patients underwent a 10-minute transmission scan followed by a 15-minute emission scan using an ECAT Exact								

Ossenkoppele R, Prins ND, Pijnenburg YA, Lemstra AW, van der Flier WM, Adriaanse SF, Windhorst AD, Handels RL, Wolfs CA, Aalten P, Verhey FR, Verbeek MM, van Buchem MA, Hoekstra OS, Lammertsma AA, Scheltens P, van Berckel BN: Impact of molecular imaging on the diagnostic process in a memory clinic. **Alzheimers Dement 2013; 9: 414–421.**								
HR1 scanner (Siemens/CTI, Knoxville, TN). Parametric SUVr images were extracted from the interval between 45 and 60 minutes after injection. Scans were analysed using the PMOD Alzheimer's discrimination (PALZ) tool.T1-weighted MRI (3T Signa HDxt; General Electric, Milwaukee, WI) scans were used for coregistration and segmentation. [18F]FDG PET scans were interpreted as either normal or deviant and suggestive for AD (posterior cingulate and parietotemporal hypometabolism), FTD (frontotemporal metabolic impairment), DLB (occipital hypometabolism with relatively intact posterior cingulate gyrus), or dementia other (PSP: mesenchepalon, prefrontal, caudate nucleus, and thalamus hypometabolism; CBD: asymmetric hypometabolism with involvement of the basal ganglia).								
Results	**True positives:**	38	**False negatives:**	27	**False positives:**	11	**True negatives:**	22
Additional comments	The study population consisted of 2 groups that could not be separated during the analysis. The data for [11C] Pittsburgh compound B ([11C] PIB) imaging was not extracted as this test is only used for research in the UK.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the index test was interpreted with knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.)							
Indirectness	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.)							
AD versus FTD								
Index Test: FDG-PET 185 MBq of 18F-FDG was administered. Patients underwent a 10-minute transmission scan followed by a 15-minute emission scan using an ECAT Exact HR1 scanner (Siemens/CTI, Knoxville, TN). Parametric SUVr images were extracted from the interval between 45 and 60 minutes after injection. Scans were analysed using the PMOD Alzheimer's discrimination (PALZ) tool.T1-weighted MRI (3T Signa HDxt; General Electric, Milwaukee, WI) scans were used for coregistration and segmentation. [18F]FDG PET scans were interpreted as either normal or deviant and suggestive for AD (posterior cingulate and parietotemporal hypometabolism), FTD (frontotemporal metabolic impairment), DLB (occipital hypometabolism with relatively intact posterior cingulate gyrus), or dementia other (PSP: mesenchepalon, prefrontal, caudate nucleus, and thalamus hypometabolism; CBD: asymmetric hypometabolism with involvement of the basal ganglia).								

Ossenkoppele R, Prins ND, Pijnenburg YA, Lemstra AW, van der Flier WM, Adriaanse SF, Windhorst AD, Handels RL, Wolfs CA, Aalten P, Verhey FR, Verbeek MM, van Buchem MA, Hoekstra OS, Lammertsma AA, Scheltens P, van Berckel BN: Impact of molecular imaging on the diagnostic process in a memory clinic. **Alzheimers Dement 2013; 9: 414–421.**								
Results	**True positives:**	38	**False negatives:**	27	**False positives:**	4	**True negatives:**	14
Additional comments	The study population consisted of 2 groups that could not be separated during the analysis. The data for [11C] Pittsburgh compound B ([11C] PIB) imaging was not extracted as this test is only used for research in the UK.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the index test was interpreted with knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.)							
Indirectness	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.)							
AD versus DLB								
Index Test: FDG-PET 185 MBq of 18F-FDG was administered. Patients underwent a 10-minute transmission scan followed by a 15-minute emission scan using an ECAT Exact HR1 scanner (Siemens/CTI, Knoxville, TN). Parametric SUVr images were extracted from the interval between 45 and 60 minutes after injection. Scans were analysed using the PMOD Alzheimer's discrimination (PALZ) tool.T1-weighted MRI (3T Signa HDxt; General Electric, Milwaukee, WI) scans were used for coregistration and segmentation. [18F]FDG PET scans were interpreted as either normal or deviant and suggestive for AD (posterior cingulate and parietotemporal hypometabolism), FTD (frontotemporal metabolic impairment), DLB (occipital hypometabolism with relatively intact posterior cingulate gyrus), or dementia other (PSP: mesenchepalon, prefrontal, caudate nucleus, and thalamus hypometabolism; CBD: asymmetric hypometabolism with involvement of the basal ganglia).								
Results	**True positives:**	38	**False negatives:**	27	**False positives:**	4	**True negatives:**	1
Additional comments	The study population consisted of 2 groups that could not be separated during the analysis. The data for [11C] Pittsburgh compound B ([11C] PIB) imaging was not extracted as this test is only used for research in the UK.							
Risk of bias	**Patient**	Unclear	**Index test:**	High	**Reference**	Low	**Flow and**	High

Ossenkoppele R, Prins ND, Pijnenburg YA, Lemstra AW, van der Flier WM, Adriaanse SF, Windhorst AD, Handels RL, Wolfs CA, Aalten P, Verhey FR, Verbeek MM, van Buchem MA, Hoekstra OS, Lammertsma AA, Scheltens P, van Berckel BN: Impact of molecular imaging on the diagnostic process in a memory clinic. **Alzheimers Dement 2013; 9: 414–421.**								
	selection:				**standard:**		**timing:**	
Overall risk of bias	Very serious (It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the index test was interpreted with knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.)							
Indirectness	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.)							
FTD versus non- FTD								
Index Test: FDG-PET 185 MBq of 18F-FDG was administered. Patients underwent a 10-minute transmission scan followed by a 15-minute emission scan using an ECAT Exact HR1 scanner (Siemens/CTI, Knoxville, TN). Parametric SUVr images were extracted from the interval between 45 and 60 minutes after injection. Scans were analysed using the PMOD Alzheimer's discrimination (PALZ) tool.T1-weighted MRI (3T Signa HDxt; General Electric, Milwaukee, WI) scans were used for coregistration and segmentation. [18F]FDG PET scans were interpreted as either normal or deviant and suggestive for AD (posterior cingulate and parietotemporal hypometabolism), FTD (frontotemporal metabolic impairment), DLB (occipital hypometabolism with relatively intact posterior cingulate gyrus), or dementia other (PSP: mesenchepalon, prefrontal, caudate nucleus, and thalamus hypometabolism; CBD: asymmetric hypometabolism with involvement of the basal ganglia).								
Results	**True positives:**	6	**False negatives:**	12	**False positives:**	12	**True negatives:**	123
Additional comments	The study population consisted of 2 groups that could not be separated during the analysis. The data for [11C] Pittsburgh compound B ([11C] PIB) imaging was not extracted as this test is only used for research in the UK.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the index test was interpreted with knowledge of the reference diagnosis.)							
Indirectness	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low		
Overall	Serious (It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.)							

Ossenkoppele R, Prins ND, Pijnenburg YA, Lemstra AW, van der Flier WM, Adriaanse SF, Windhorst AD, Handels RL, Wolfs CA, Aalten P, Verhey FR, Verbeek MM, van Buchem MA, Hoekstra OS, Lammertsma AA, Scheltens P, van Berckel BN: Impact of molecular imaging on the diagnostic process in a memory clinic. **Alzheimers Dement 2013; 9: 414–421.**								
indirectness								
FTD versus non- FTD dementias								
Index Test: FDG-PET 185 MBq of 18F-FDG was administered. Patients underwent a 10-minute transmission scan followed by a 15-minute emission scan using an ECAT Exact HR1 scanner (Siemens/CTI, Knoxville, TN). Parametric SUVr images were extracted from the interval between 45 and 60 minutes after injection. Scans were analysed using the PMOD Alzheimer's discrimination (PALZ) tool.T1-weighted MRI (3T Signa HDxt; General Electric, Milwaukee, WI) scans were used for coregistration and segmentation. [18F]FDG PET scans were interpreted as either normal or deviant and suggestive for AD (posterior cingulate and parietotemporal hypometabolism), FTD (frontotemporal metabolic impairment), DLB (occipital hypometabolism with relatively intact posterior cingulate gyrus), or dementia other (PSP: mesenchepalon, prefrontal, caudate nucleus, and thalamus hypometabolism; CBD: asymmetric hypometabolism with involvement of the basal ganglia).								
Results	**True positives:**	6	**False negatives:**	12	**False positives:**	10	**True negatives:**	70
Additional comments	The study population consisted of 2 groups that could not be separated during the analysis. The data for [11C] Pittsburgh compound B ([11C] PIB) imaging was not extracted as this test is only used for research in the UK.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the index test was interpreted with knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.)							
Indirectness	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.)							
FTD versus DLB								
Index Test: FDG-PET 185 MBq of 18F-FDG was administered. Patients underwent a 10-minute transmission scan followed by a 15-minute emission scan using an ECAT Exact HR1 scanner (Siemens/CTI, Knoxville, TN). Parametric SUVr images were extracted from the interval between 45 and 60 minutes after injection. Scans were analysed using the PMOD Alzheimer's discrimination (PALZ) tool.T1-weighted MRI (3T Signa HDxt; General Electric, Milwaukee, WI) scans were								

Ossenkoppele R, Prins ND, Pijnenburg YA, Lemstra AW, van der Flier WM, Adriaanse SF, Windhorst AD, Handels RL, Wolfs CA, Aalten P, Verhey FR, Verbeek MM, van Buchem MA, Hoekstra OS, Lammertsma AA, Scheltens P, van Berckel BN: Impact of molecular imaging on the diagnostic process in a memory clinic. **Alzheimers Dement 2013; 9: 414–421.**								
used for coregistration and segmentation. [18F]FDG PET scans were interpreted as either normal or deviant and suggestive for AD (posterior cingulate and parietotemporal hypometabolism), FTD (frontotemporal metabolic impairment), DLB (occipital hypometabolism with relatively intact posterior cingulate gyrus), or dementia other (PSP: mesenchepalon, prefrontal, caudate nucleus, and thalamus hypometabolism; CBD: asymmetric hypometabolism with involvement of the basal ganglia).								
Results	**True positives:**	6	**False negatives:**	12	**False positives:**	0	**True negatives:**	5
Additional comments	The study population consisted of 2 groups that could not be separated during the analysis. The data for [11C] Pittsburgh compound B ([11C] PIB) imaging was not extracted as this test is only used for research in the UK.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the index test was interpreted with knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.)							
Indirectness	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.)							
DLB versus non-DLB								
Index Test: FDG-PET 185 MBq of 18F-FDG was administered. Patients underwent a 10-minute transmission scan followed by a 15-minute emission scan using an ECAT Exact HR1 scanner (Siemens/CTI, Knoxville, TN). Parametric SUVr images were extracted from the interval between 45 and 60 minutes after injection. Scans were analysed using the PMOD Alzheimer's discrimination (PALZ) tool.T1-weighted MRI (3T Signa HDxt; General Electric, Milwaukee, WI) scans were used for coregistration and segmentation. [18F]FDG PET scans were interpreted as either normal or deviant and suggestive for AD (posterior cingulate and parietotemporal hypometabolism), FTD (frontotemporal metabolic impairment), DLB (occipital hypometabolism with relatively intact posterior cingulate gyrus), or dementia other (PSP: mesenchepalon, prefrontal, caudate nucleus, and thalamus hypometabolism; CBD: asymmetric hypometabolism with involvement of the basal ganglia).								
Results	**True positives:**	1	**False negatives:**	4	**False positives:**	6	**True negatives:**	142

Ossenkoppele R, Prins ND, Pijnenburg YA, Lemstra AW, van der Flier WM, Adriaanse SF, Windhorst AD, Handels RL, Wolfs CA, Aalten P, Verhey FR, Verbeek MM, van Buchem MA, Hoekstra OS, Lammertsma AA, Scheltens P, van Berckel BN: Impact of molecular imaging on the diagnostic process in a memory clinic. **Alzheimers Dement 2013; 9: 414–421.**								
Additional comments	The study population consisted of 2 groups that could not be separated during the analysis. The data for [11C] Pittsburgh compound B ([11C] PIB) imaging was not extracted as this test is only used for research in the UK.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the index test was interpreted with knowledge of the reference diagnosis.)							
Indirectness	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.)							
DLB versus non-DLB dementias								
Index Test: FDG-PET 185 MBq of 18F-FDG was administered. Patients underwent a 10-minute transmission scan followed by a 15-minute emission scan using an ECAT Exact HR1 scanner (Siemens/CTI, Knoxville, TN). Parametric SUVr images were extracted from the interval between 45 and 60 minutes after injection. Scans were analysed using the PMOD Alzheimer's discrimination (PALZ) tool.T1-weighted MRI (3T Signa HDxt; General Electric, Milwaukee, WI) scans were used for coregistration and segmentation. [18F]FDG PET scans were interpreted as either normal or deviant and suggestive for AD (posterior cingulate and parietotemporal hypometabolism), FTD (frontotemporal metabolic impairment), DLB (occipital hypometabolism with relatively intact posterior cingulate gyrus), or dementia other (PSP: mesenchepalon, prefrontal, caudate nucleus, and thalamus hypometabolism; CBD: asymmetric hypometabolism with involvement of the basal ganglia).								
Results	**True positives:**	1	**False negatives:**	4	**False positives:**	5	**True negatives:**	88
Additional comments	The study population consisted of 2 groups that could not be separated during the analysis. The data for [11C] Pittsburgh compound B ([11C] PIB) imaging was not extracted as this test is only used for research in the UK.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the index test was interpreted with knowledge of the reference diagnosis; a subgroup analysis was used where							

Ossenkoppele R, Prins ND, Pijnenburg YA, Lemstra AW, van der Flier WM, Adriaanse SF, Windhorst AD, Handels RL, Wolfs CA, Aalten P, Verhey FR, Verbeek MM, van Buchem MA, Hoekstra OS, Lammertsma AA, Scheltens P, van Berckel BN: Impact of molecular imaging on the diagnostic process in a memory clinic. Alzheimers Dement 2013; 9: 414–421.						
	>10% study population was excluded.)					
Indirectness	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low
Overall indirectness	Serious (It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.)					

P.1.16 P

Panegyres PK, Rogers JM, McCarthy M, Campbell A, Wu JS. Fluorodeoxyglucose-Positron Emission Tomography in the differential diagnosis of early-onset dementia: a prospective, community-based study. BMC Neurology 2009; 9: 41-49.	
Study type	Prospective cohort
Country	Australia
Setting	Young onset dementia clinic
Inclusion criteria	Individuals referred to a young onset dementia clinic (<65 years old) for specialist neurologic investigation of suspected dementia over the years from 1998 to 2006.
Exclusion criteria	Not stated
Sex	53.9% male
Age	Mean age of symptom onset was 60.0 years (SD 4.2)
Presentation	suspected dementia
Reference standard	A diagnosis of Dementia was made using the DSM-IV manual; FTD was diagnosed according to Neary (1998); AD according to the NINCDS-ADRDA criteria; DLB according to McKeith (1996); VaD according to NINDS-AIREN.
AD versus non-AD	
Index Test: FDG-PET 18F FDG-PET was imaged using an Allegro GSO PET scanner. Brain images were attenuation corrected using the 137Cs attenuation source build into the Allegro camera system. Scatter and random correction was performed as part of the RAMLA-3D reconstruction algorithm as provided by the camera manufacturer, Phillips. The FDG PET images were displayed using the Siemens "cool" colour scale. Maximum cortical activity was extracted using the three-dimensional stereotactic surface projection (3D-SSP) method and the data sets were normalized to the average cerebral count for each patient. The 3D-SSP images were compared individually with age appropriate and modality appropriate normal databases generated in the PET centre. A statistically significant threshold, controlling for multiple pixel comparisons and shape of the stochastic process on 3D-SSP format, of $Z = 4.53$ ($p < 0.05$) was used.	

Panegyres PK, Rogers JM, McCarthy M, Campbell A, Wu JS. Fluorodeoxyglucose-Positron Emission Tomography in the differential diagnosis of early-onset dementia: a prospective, community-based study. BMC Neurology 2009; 9: 41-49.								
The severity of the reductions in each of the lobes was evaluated using volumes of interest analysis. Depending on the pattern of cerebral metabolism, each case was classified as either: normal; possible AD; possible FTLD; possible LBD; possible PPA or possible depression.								
Results	**True positives:**	38	**False negatives:**	11	**False positives:**	10	**True negatives:**	43
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (The study only recruited people with early onset dementia (<65 years old).)							
FTD versus not FTD								
Index Test: FDG-PET 18F FDG-PET was imaged using an Allegro GSO PET scanner. Brain images were attenuation corrected using the 137Cs attenuation source build into the Allegro camera system. Scatter and random correction was performed as part of the RAMLA-3D reconstruction algorithm as provided by the camera manufacturer, Phillips. The FDG PET images were displayed using the Siemens "cool" colour scale. Maximum cortical activity was extracted using the three-dimensional stereotactic surface projection (3D-SSP) method and the data sets were normalized to the average cerebral count for each patient. The 3D-SSP images were compared individually with age appropriate and modality appropriate normal databases generated in the PET centre. A statistically significant threshold, controlling for multiple pixel comparisons and shape of the stochastic process on 3D-SSP format, of Z = 4.53 ($p < 0.05$) was used. The severity of the reductions in each of the lobes was evaluated using volumes of interest analysis. Depending on the pattern of cerebral metabolism, each case was classified as either: normal; possible AD; possible FTLD; possible LBD; possible PPA or possible depression.								
Results	**True positives:**	9	**False negatives:**	8	**False positives:**	4	**True negatives:**	81
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (The study only recruited people with early onset dementia (<65 years old).)							
DLB versus not DLB								

Panegyres PK, Rogers JM, McCarthy M, Campbell A, Wu JS. Fluorodeoxyglucose-Positron Emission Tomography in the differential diagnosis of early-onset dementia: a prospective, community-based study. BMC Neurology 2009; 9: 41-49.								
Index Test: FDG-PET 18F FDG-PET was imaged using an Allegro GSO PET scanner. Brain images were attenuation corrected using the 137Cs attenuation source build into the Allegro camera system. Scatter and random correction was performed as part of the RAMLA-3D reconstruction algorithm as provided by the camera manufacturer, Phillips. The FDG PET images were displayed using the Siemens "cool" colour scale. Maximum cortical activity was extracted using the three-dimensional stereotactic surface projection (3D-SSP) method and the data sets were normalized to the average cerebral count for each patient. The 3D-SSP images were compared individually with age appropriate and modality appropriate normal databases generated in the PET centre. A statistically significant threshold, controlling for multiple pixel comparisons and shape of the stochastic process on 3D-SSP format, of Z = 4.53 ($p < 0.05$) was used. The severity of the reductions in each of the lobes was evaluated using volumes of interest analysis. Depending on the pattern of cerebral metabolism, each case was classified as either: normal; possible AD; possible FTLD; possible LBD; possible PPA or possible depression.								
Results	**True positives:**	5	**False negatives:**	1	**False positives:**	1	**True negatives:**	95
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (The study only recruited people with early onset dementia (<65 years old).)							
PPA versus not PPA								
Index Test: FDG-PET 18F FDG-PET was imaged using an Allegro GSO PET scanner. Brain images were attenuation corrected using the 137Cs attenuation source build into the Allegro camera system. Scatter and random correction was performed as part of the RAMLA-3D reconstruction algorithm as provided by the camera manufacturer, Phillips. The FDG PET images were displayed using the Siemens "cool" colour scale. Maximum cortical activity was extracted using the three-dimensional stereotactic surface projection (3D-SSP) method and the data sets were normalized to the average cerebral count for each patient. The 3D-SSP images were compared individually with age appropriate and modality appropriate normal databases generated in the PET centre. A statistically significant threshold, controlling for multiple pixel comparisons and shape of the stochastic process on 3D-SSP format, of Z = 4.53 ($p < 0.05$) was used. The severity of the reductions in each of the lobes was evaluated using volumes of interest analysis. Depending on the pattern of cerebral metabolism, each case was classified as either: normal; possible AD; possible FTLD; possible LBD; possible PPA or possible depression.								
Results	**True positives:**	3	**False negatives:**	3	**False positives:**	0	**True negatives:**	96
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low

Panegyres PK, Rogers JM, McCarthy M, Campbell A, Wu JS. Fluorodeoxyglucose-Positron Emission Tomography in the differential diagnosis of early-onset dementia: a prospective, community-based study. BMC Neurology 2009; 9: 41-49.						
Overall risk of bias	Not serious					
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low
Overall indirectness	Serious (The study only recruited people with early onset dementia (<65 years old).)					

Postel-Vinay N, Hanon O, Clerson P, Brown JM, menard J et al. Validation of the Test Your Memory (FTYM Test) in a French Memory Clinic Population. The Clinical Neuropsychologist, 2014; 28: 994–1007.							
Study type	Prospective cohort						
Country	France						
Setting	Five secondary referral hospital centres in France						
Inclusion criteria	Consecutive ambulatory patients with memory complaints who visited a memory consultation for the first time between March 2011 and December 2011 were recruited.						
Exclusion criteria	Inability to read or write or understand French, known dementia, and major depressive disorder.						
Sex	32.0% male						
Age	Mean age 76.0 (SD 10.0)						
Presentation	Memory complaints						
Reference standard	A consensus diagnosis of dementia was made according to DSM-IV criteria.						
Dementia versus no dementia							
Index Test: Test Your Memory, TYM (≤39) Test Your Memory (F-TYM Test), French version. Cross-cultural adaptation was needed for the sentence to be copied and this adaptation respected the author's requirements. In the verbal fluency test, names of animals beginning with "S" were replaced by names beginning with "C" as there are more animals whose name starts with "C" than with "S" in French. Cut-off ≤ 39.							
Results	**True positives:**	61	**False negatives:**	7	**False positives:**	40	**True negatives:** 93
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Serious (Optimised cut-off was used; the study was not downgraded for exclusions as <10% population was excluded)						

Postel-Vinay N, Hanon O, Clerson P, Brown JM, menard J et al. Validation of the Test Your Memory (FTYM Test) in a French Memory Clinic Population. The Clinical Neuropsychologist, 2014; 28: 994–1007.								
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<24) MMSE, French language, cut-off 24/30								
Results	**True positives:**	60	**False negatives:**	8	**False positives:**	23	**True negatives:**	110
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Optimised cut-off was used; the study was not downgraded for exclusions as <10% population was excluded)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

P.1.17 R

Read SL, Miller BL, Mena I, Kim R, Itabashi H, Darby A. SPECT in dementia: clinical and pathological correlation. Journal of the American Geriatrics Society 1995;43: 1243–7.	
Study type	Retrospective cohort
Country	USA
Setting	University-based specialist dementia clinic
Inclusion criteria	Memory disorder clinic patients who had with diagnosed dementia, SPECT imaging results and biopsy or pathology data.
Exclusion criteria	Not stated
Sex	63.0% male
Age	Mean age 66.7 years (SD 11.7)
Presentation	Previously diagnosed dementia

Read SL, Miller BL, Mena I, Kim R, Itabashi H, Darby A. SPECT in dementia: clinical and pathological correlation. Journal of the American Geriatrics Society 1995;43: 1243–7.								
Reference standard	Pathology (brain biopsy or post-mortem brain pathology)							
FTD versus non-FTD								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT, threshold pre-specified; four patterns emerged, each corresponding to a distinct pathological entry. Images taken with a single-headed camera.								
Results	**True positives:**	7	**False negatives:**	0	**False positives:**	0	**True negatives:**	20
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
FTD versus AD								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT, threshold pre-specified; four patterns emerged, each corresponding to a distinct pathological entry. Images taken with a single-headed camera.								
Results	**True positives:**	7	**False negatives:**	0	**False positives:**	0	**True negatives:**	13
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis used with >10% study population excluded; unclear whether random or consecutive patient enrolment was used; unclear if inappropriate exclusions avoided.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Rohan Z, Smetakova M, Kukal J, Rusina R, Matej R. Proteinase-activated receptor 2 and disease biomarkers in cerebrospinal fluid in cases with autopsy-confirmed prion diseases and other neurodegenerative diseases. BMC Neurology, 2015; 15: 50- 54.								
Study type	Retrospective cohort							
Country	Czech Republic							
Setting	National Reference Laboratory for Diagnostics of Human Prion Diseases, Thomayer Hospital, Prague							
Inclusion criteria	Patients referred for dementia (including possible/ probable Creutzfeldt-Jakob disease; CJD) with a neuropathologically confirmed diagnosis of neurodegenerative disease and an ante mortem CSF analysis of T-tau, P-tau, Aβ, and protein 14-3-3 were included in the study.							
Exclusion criteria	Not stated							
Sex	45.7% male							
Age	Mean age at death 66.3 years (SD 9.1)							
Presentation	Suspected dementia, including possible/probable CJD)							
Reference standard	A definite diagnosis of CJD was confirmed through neuropathological examination and western blot detection of the proteinase K resistant form of prion protein. In positive cases, the prion protein gene (PRNP) was analysed for codon 129 polymorphisms and disease-associated mutations.							
CJD versus not CJD								
Index Test: Total Tau Total tau analysed using INNOTEST hTAU Ag ELISA.> 1200pg/ml as positive for CJD.								
Results	**True positives:**	28	**False negatives:**	8	**False positives:**	7	**True negatives:**	16
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether: a consecutive or random sample of patients was enrolled; the index test results were interpreted without knowledge of the results of the reference standard; a pre-specified cut-off was used for the index tests; the reference standard results were interpreted without knowledge of the index test results.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: CSF 14-3-3 immunoblotting 14-3-3 analysed using immunoblotting. Weakly positive and positive samples taken as indicative of CJD.								

Rohan Z, Smetakova M, Kukal J, Rusina R, Matej R. Proteinase-activated receptor 2 and disease biomarkers in cerebrospinal fluid in cases with autopsy-confirmed prion diseases and other neurodegenerative diseases. BMC Neurology, 2015; 15: 50- 54.								
Results	**True positives:**	32	**False negatives:**	4	**False positives:**	5	**True negatives:**	18
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether: a consecutive or random sample of patients was enrolled; the index test results were interpreted without knowledge of the results of the reference standard; a pre-specified cut-off was used for the index tests; the reference standard results were interpreted without knowledge of the index test results.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Rollin-Silliare A, Bombois S, Deramecourt V, Steinert- Emptaz A, Salleron J, Morvan J, et al. Contribution of single photon emission computed tomography to the differential diagnosis of dementia in a memory clinic.Journal of Alzheimer's Disease 2012; 30: 833–45.	
Study type	Retrospective cohort
Country	France
Setting	Lille/Bailleul Memory Clinic
Inclusion criteria	Clinic patients from 1989-2008 who had (i) a clinical diagnosis of dementia disorder, (ii) SPECT imaging data, and (iii) a definite diagnosis ascertained by neuropathological or genetic evidence.
Exclusion criteria	Not stated
Sex	Not stated
Age	Mean age 67.3 years (SD 8.9)
Presentation	Dementia clinic patients with diagnosis of degenerative or vascular dementia.
Reference standard	Post-mortem diagnosis with pathological diagnosis for FTLD established by the Cairns (2007) criteria, AD by the Ball (1997) criteria, DLB using McKeih (2005) and VaD according to the International Society of Neuropathology (Kalaria, 2004 and Ince, 2005).

Rollin-Silliare A, Bombois S, Deramecourt V, Steinert- Emptaz A, Salleron J, Morvan J, et al. Contribution of single photon emission computed tomography to the differential diagnosis of dementia in a memory clinic.Journal of Alzheimer's Disease 2012; 30: 833–45.								
AD versus non-AD								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT. SPECT imaging data were normalised and represented by fixation values according to a coloured scale for immediate ranking: a value of less than 80% was considered to be significant (Steinling 1988). This cut-off was initially determined to obtain a specificity of 100% and a specificity of 60% for AD diagnosis (Steinling 1989). Threshold pre-specified; visual interpretation of images taken using a multiple- headed camera.								
Results	**True positives:**	13	**False negatives:**	10	**False positives:**	2	**True negatives:**	23
Additional comments	Data was presented for SPECT alone versus final neuropathological diagnosis and for SPECT with clincal data versus neuropathology in the paper. Our analysis uses the SPECT alone results.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
FTD versus non-FTD								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT. SPECT imaging data were normalised and represented by fixation values according to a coloured scale for immediate ranking: a value of less than 80% was considered to be significant (Steinling 1988). This cut-off was initially determined to obtain a specificity of 100% and a specificity of 60% for AD diagnosis (Steinling 1989). Threshold pre-specified; visual interpretation of images taken using a multiple- headed camera.								
Results	**True positives:**	9	**False negatives:**	3	**False positives:**	1	**True negatives:**	35
Additional comments	Data was presented for SPECT alone versus final neuropathological diagnosis and for SPECT with clincal data versus neuropathology in the paper. Our analysis uses the SPECT alone results.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		

Rollin-Silliare A, Bombois S, Deramecourt V, Steinert- Emptaz A, Salleron J, Morvan J, et al. Contribution of single photon emission computed tomography to the differential diagnosis of dementia in a memory clinic.Journal of Alzheimer's Disease 2012; 30: 833–45.							
Overall indirectness	Not serious						
FTD versus AD							
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT. SPECT imaging data were normalised and represented by fixation values according to a coloured scale for immediate ranking: a value of less than 80% was considered to be significant (Steinling 1988). This cut-off was initially determined to obtain a specificity of 100% and a specificity of 60% for AD diagnosis (Steinling 1989). Threshold pre-specified; visual interpretation of images taken using a multiple- headed camera.							
Results	**True positives:**	9	**False negatives:**	3	**False positives:**	0	**True negatives:** 23
Additional comments	Data was presented for SPECT alone versus final neuropathological diagnosis and for SPECT with clincal data versus neuropathology in the paper. Our analysis uses the SPECT alone results.						
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** High
Overall risk of bias	Serious (Subgroup analysis where >10% study population excluded)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						

P.1.18 S

Sager MA, Hermann BP, LaRue A and Woodard JL. Screening for dementia in community-based memory clinics. Wisconsin Medical Journal, 2006; 105: 25–29.	
Study type	Prospective cohort
Country	USA
Setting	Memory diagnostic clinic
Inclusion criteria	People attending a network of memory clinics for memory complaints, ≥ 50 years.
Exclusion criteria	Not stated
Sex	33.3% male
Age	Mean age 78.9 years (SD 7.3)

Sager MA, Hermann BP, LaRue A and Woodard JL. Screening for dementia in community-based memory clinics. Wisconsin Medical Journal, 2006; 105: 25–29.								
Presentation	Suspected dementia							
Reference standard	DSM-IV with Clinical Dementia Rating, neuropsychological tests and research diagnostic criteria for MCI, DLB and FTD.							
Dementia versus non-dementia (including MCI)								
Index Test: Clock Drawing Test, CDT, scoring method unclear (<8) Clock Drawing Test, CDT <8 out of 10 (free- hand- draw own circle)								
Results	**True positives:**	187	**False negatives:**	74	**False positives:**	18	**True negatives:**	85
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<24) MMSE <24								
Results	**True positives:**	157	**False negatives:**	104	**False positives:**	1	**True negatives:**	102
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Verbal category fluency (animal naming), VF (<14)								

Sager MA, Hermann BP, LaRue A and Woodard JL. Screening for dementia in community-based memory clinics. Wisconsin Medical Journal, 2006; 105: 25–29.								
Verbal category fluency, <14. Tests ability to generate as many category names in given time. In this case the category was animals and time duration was 60 secs.								
Results	**True positives:**	222	**False negatives:**	39	**False positives:**	41	**True negatives:**	62
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Sakamoto F, Shiraishi S, Yoshida M, Tomiguchi S, Hirai T, Namimoto T, Hashimoto M, Ikeda M et al.Diagnosis of dementia with Lewy bodies: diagnostic performance of combined 123I-IMP brain perfusion SPECT and 123I-MIBG myocardial scintigraphy. Ann Nucl Med, 2014; 28:203–211.	
Study type	Retrospective cohort
Country	Japan
Setting	Kumamoto University Hospital
Inclusion criteria	Patients with suspected DLB who underwent both 123I-IMP brain perfusion SPECT and 123I-MIBG myocardial scintigraphy studies at Kumamoto University Hospital between January 2007 and December 2012. Patients with well-controlled diabetes or hypertension treated with small doses of ACE inhibitors or beta blockers were included although their 123I-MIBG myocardial scintigraphy findings may have been affected.
Exclusion criteria	Patients with possible DLB were excluded because both DLB and other types of dementia were included in this category. Patients with congestive heart failure or taking antipsychotic drugs (tricyclic antidepressants, reserpine) that would affect the results of 123I-MIBG myocardial scintigraphy were also excluded.
Sex	43.0% male
Age	Mean age 72.5 years (SD 10.4)
Presentation	suspected DLB

Sakamoto F, Shiraishi S, Yoshida M, Tomiguchi S, Hirai T, Namimoto T, Hashimoto M, Ikeda M et al.Diagnosis of dementia with Lewy bodies: diagnostic performance of combined 123I-IMP brain perfusion SPECT and 123I-MIBG myocardial scintigraphy. Ann Nucl Med, 2014; 28:203–211.								
Reference standard	A diagnosis of DLB was made according to McKeith (2006), other criteria are not stated.							
DLB versus not DLB								
Index Test: 123I-IMP SPECT and 123I-MIBG cardiac scintigraphy combined 123I -IMP SPECT imaging was carried out using a two-head gamma camera (Millennium VG, GE) equipped with a low-energy general-purpose collimator. Transaxial images were reconstructed with filtered back projection using a Butterworth filter. The reconstructed 123I-IMP SPECT images were analyzed with Neurostat/(3D-SSP) and data were normalized to the mean global activity. Using the SEE method, the whole brain was divided into segments. The parietal lobe hypoperfusion score used here. 123I-MIBG cardiac scintigraphy. Planar scans were acquired using a two-head gamma camera (Millennium VG, GE) equipped with a medium-energy general-purpose collimator. Using the region of interest (ROI) method, we calculated the early and delayed 123I-MIBG heart-to-mediastinum uptake (H/M) ratios on anterior views of the planar images. An irregular circular ROI was manually drawn on the left ventricle and a square ROI was placed in the upper mediastinum area. The early H/M ratio used for analysis here. The formula for calculating the combined index for estimation group was: - 4:72 - 2:48x early H/M +1:07 x parietal lobe hypoperfusion + 0:10 x age								
Results	**True positives:**	23	**False negatives:**	3	**False positives:**	10	**True negatives:**	64
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether the study avoided inappropriate exclusions or whether the reference standard results were interpreted without knowledge of the results of the index test .)							
Indirectness	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
DLB versus not DLB								
Index Test: 123I-MIBG cardiac scintigraphy 123I-MIBG cardiac scintigraphy. Planar scans were acquired using a two-head gamma camera (Millennium VG, GE) equipped with a medium-energy general-purpose collimator. Using the region of interest (ROI) method, we calculated the early and delayed 123I-MIBG heart-to-mediastinum uptake (H/M) ratios on anterior views of the planar images. An irregular circular ROI was manually drawn on the left ventricle and a square ROI was placed in the upper								

Sakamoto F, Shiraishi S, Yoshida M, Tomiguchi S, Hirai T, Namimoto T, Hashimoto M, Ikeda M et al.Diagnosis of dementia with Lewy bodies: diagnostic performance of combined 123I-IMP brain perfusion SPECT and 123I-MIBG myocardial scintigraphy. Ann Nucl Med, 2014; 28:203–211.								
mediastinum area. The early H/M ratio used for analysis here.								
Results	**True positives:**	22	**False negatives:**	4	**False positives:**	11	**True negatives:**	63
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	High	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether the study avoided inappropriate exclusions or whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: 123I-IMP SPECT 123I -IMP SPECT imaging was carried out using a two-head gamma camera (Millennium VG, GE) equipped with a low-energy general-purpose collimator. Transaxial images were reconstructed with filtered back projection using a Butterworth filter. The reconstructed 123I-IMP SPECT images were analyzed with Neurostat/(3D-SSP) and data were normalized to the mean global activity. Using the SEE method, the whole brain was divided into segments. The parietal lobe hypoperfusion score used here.								
Results	**True positives:**	16	**False negatives:**	10	**False positives:**	19	**True negatives:**	56
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	High	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether the study avoided inappropriate exclusions or whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Sakamoto F, Shiraishi S, Tsuda N, Ogasawa K, Yoshida M, Yuki H, Hashimoto M, Tomiguchi S et al. Diagnosis of demetia with Lewy bodies: can 123I-IMP and 123I-MIBG myocardial scintigraphy yield new core features? Br J Radiol 2017; 90: 20160156.								
Study type	Prospective cohort							
Country	Japan							
Setting	Kumamoto University Hospital.							
Inclusion criteria	People with suspected DLB who had undergone both 123I-IMP brain perfusion SPECT and 123I-MIBG myocardial scintigraphy at Kumamoto University Hospital between January 2008 and March 2014.							
Exclusion criteria	Congestive heart failure, ischaemic heart disease, cardiomyopathy and diabetes, and patients taking antipsychotic drugs that affect the resulst of the MIBG scintigraphy.							
Sex	41.6% male							
Age	Mean age 76.0 years (SD 8.3)							
Presentation	Suspected DLB							
Reference standard	Clinician diagnosis using the Consortium on DLB international Workshop criteria (McKeith, 2006)							
DLB versus not DLB								
Index Test: 123I-MIBG cardiac scintigraphy 123-I MIBG cardiac scintigraphy, early heart-to-mediastatinum (H/M) ratio. Images were acquired with a dual-head gamma camera (Symbia T16), equipped with a medium-energy general purpose collimator. Early and delayed imaging was performed at 15 min and 3 hrs after injection. Cut-off <2.0.								
Results	**True positives:**	76	**False negatives:**	16	**False positives:**	9	**True negatives:**	231
Additional comments	Study also looked at 123-I-IMP SPECT but did not present DTA data for this or for other MIBG variables.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Very serious (Selective reporting of sensitivity and specificity of outcome variables and it was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; whether the reference standard results were interpreted without knowledge of the results of the index test or whether the test cut-off was pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Schroter A, Zerr I, Henkel K et al. Magnetic resonance imaging in the clinical diagnosis of Creutzfeldt–Jakob disease. Arch Neurol 2000; 57: 1751-1757.								
Study type	Retrospective cohort							
Country	Germany							
Setting	Magnetic Resonance/Computed Tomography Institute Hamburg							
Inclusion criteria	All cases reported to the German CJD surveillance unit							
Exclusion criteria	Not stated							
Sex	For the CJD positive group 31.5% male, not stated for CJD negtive group							
Age	Mean age 65.5 years (range 38-86) for the CJD positive group, CJD negative not stated							
Presentation	Rapidly progressive dementia leading to suspected CJD							
Reference standard	92 patients underwent clinician diagnosis according to Kretzschmar (1996); 70 patients were diagnosed using neuropathology according to Will (1993)							
CJD versus non-CJD								
Index Test: MRI MRI scans were made with either 1.0-T or 1.5-T magnetic resonance imagers. The following MRI scans were performed: T1-weighted, T2 weighted, proton density- weighted and fluid attenuation inversion recovery.								
Results	**True positives:**	109	**False negatives:**	53	**False positives:**	4	**True negatives:**	53
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Sikkes SA, Van den Berg MT, Knol DL, De-Lange-de Klerk ES, Scheltens P, Uitdehaag BM, et al. How useful is IQCODE for discriminating between Alzheimer's disease, mild cognitive impairment and subjective memory complaints?. Dementia and Geriatric Cognitive Disorders 2010; 30: 411–6.	
Study type	Prospective cohort

Sikkes SA, Van den Berg MT, Knol DL, De-Lange-de Klerk ES, Scheltens P, Uitdehaag BM, et al. How useful is IQCODE for discriminating between Alzheimer's disease, mild cognitive impairment and subjective memory complaints?. Dementia and Geriatric Cognitive Disorders 2010; 30: 411–6.								
Country	The Netherlands							
Setting	Alzheimer Centre at a University Hospital							
Inclusion criteria	Patients visiting the Alzheimer Centre at the VU University Medical Centre between 2004 and 2007							
Exclusion criteria	Not stated							
Sex	56.4% male							
Age	mean age 68.4 years (SD 8.8)							
Presentation	Suspected dementia							
Reference standard	Petersen criteria for MCI, NINCDS-ADRDA for dementia. All remaining patients were classified as having subjective memory complaints.							
AD versus subjective memory complaints (no dementia group)								
Index Test: Informant Questionnaire on Cognitive Decline, IQCODE (16 item, >3.2) IQCODE (Dutch, 16 item) 3.3 primary threshold								
Results	**True positives:**	173	**False negatives:**	7	**False positives:**	52	**True negatives:**	37
Additional comments	Data for 2x2 table obtained from Harrison et al. (2015) Cochrane Review. Not is an accessible format in original paper.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Very serious (Use of subgroup analysis where >10% study population excluded (MCI group); lack of a pre-specified test threshold; unclear that index and reference tests are interpreted without knowledge of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Informant Questionnaire on Cognitive Decline, IQCODE (16 item, >3.3) IQCODE (Dutch, 16 item) 3.4								
Results	**True positives:**	172	**False negatives:**	8	**False positives:**	47	**True negatives:**	42

Sikkes SA, Van den Berg MT, Knol DL, De-Lange-de Klerk ES, Scheltens P, Uitdehaag BM, et al. How useful is IQCODE for discriminating between Alzheimer's disease, mild cognitive impairment and subjective memory complaints?. Dementia and Geriatric Cognitive Disorders 2010; 30: 411–6.								
Additional comments	Data for 2x2 table obtained from Harrison et al. (2015) Cochrane Review. Not is an accessible format in original paper.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Very serious (Use of subgroup analysis where >10% study population excluded (MCI group); lack of a pre-specified test threshold; unclear that index and reference tests are interpreted without knowledge of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Informant Questionnaire on Cognitive Decline, IQCODE (16 item, >3.4) IQCODE (Dutch, 16 item) 3.5								
Results	**True positives:**	165	**False negatives:**	15	**False positives:**	33	**True negatives:**	56
Additional comments	Data for 2x2 table obtained from Harrison et al. (2015) Cochrane Review. Not is an accessible format in original paper.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Very serious (Use of subgroup analysis where >10% study population excluded (MCI group); lack of a pre-specified test threshold; unclear that index and reference tests are interpreted without knowledge of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Informant Questionnaire on Cognitive Decline, IQCODE (16 item, >3.5) IQCODE (Dutch, 16 item) 3.6								
Results	**True positives:**	161	**False negatives:**	19	**False positives:**	28	**True negatives:**	61
Additional comme	Data for 2x2 table obtained from Harrison et al. (2015) Cochrane Review. Not is an accessible format in original paper.							

Sikkes SA, Van den Berg MT, Knol DL, De-Lange-de Klerk ES, Scheltens P, Uitdehaag BM, et al. How useful is IQCODE for discriminating between Alzheimer's disease, mild cognitive impairment and subjective memory complaints?. Dementia and Geriatric Cognitive Disorders 2010; 30: 411–6.								
nts								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Very serious (Use of subgroup analysis where >10% study population excluded (MCI group); lack of a pre-specified test threshold; unclear that index and reference tests are interpreted without knowledge of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Informant Questionnaire on Cognitive Decline ,IQCODE (16 item, >3.6) IQCODE (Dutch, 16 item) >3.6								
Results	**True positives:**	154	**False negatives:**	26	**False positives:**	23	**True negatives:**	66
Additional comments	Data for 2x2 table obtained from Harrison et al. (2015) Cochrane Review. Not is an accessible format in original paper.							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Very serious (Use of subgroup analysis where >10% study population excluded (MCI group); lack of a pre-specified test threshold; unclear that index and reference tests were interpreted without knowledge of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Silverman DHS, Small GW, Chang CY, Lu CS,Kung De Abarto MA, Chen W,et al. Positron emission tomography in evaluation of dementia; regional brain metabolism and long-term outcome. JAMA. 2001; 286: 2120-7.	
Study type	Prospective cohort
Country	USA and Germany
Setting	Neurology, psychiatry and PET facilities associated with 7 academic centres in USA and 1 in Germany.

Silverman DHS, Small GW, Chang CY, Lu CS,Kung De Abarto MA, Chen W,et al. Positron emission tomography in evaluation of dementia; regional brain metabolism and long-term outcome. JAMA. 2001; 286: 2120-7.							
Inclusion criteria	People presenting with symptoms of dementia at one of the academic centres						
Exclusion criteria	Not stated						
Sex	51.4% male						
Age	Mean age 67.0 years (10.0)						
Presentation	Suspected dementia						
Reference standard	Using the methods and criteria standard to each institution at the time of pathological examination- details not provided.						
Dementia versus no dementia							
Index Test: FDG-PET 18 -FDG- PET was carried out using (prior to October 1996) a Siemens/CTI ECAT 831 or 931 scanner or (beginning October 1996) a higher resolution Siemens ECAT EXACT HR or HR+ scanner.							
Results	**True positives:**	191	**False negatives:**	15	**False positives:**	19	**True negatives:** 59
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
AD versus non-AD							
Index Test: FDG-PET 18 -FDG- PET was carried out using (prior to October 1996) a Siemens/CTI ECAT 831 or 931 scanner or (beginning October 1996) a higher resolution Siemens ECAT EXACT HR or HR+ scanner.							
Results	**True positives:**	91	**False negatives:**	6	**False positives:**	11	**True negatives:** 30
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						

Silverman DHS, Small GW, Chang CY, Lu CS,Kung De Abarto MA, Chen W,et al. Positron emission tomography in evaluation of dementia; regional brain metabolism and long-term outcome. JAMA. 2001; 286: 2120-7.						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low
Overall indirectness	Not serious					

Siritho S, Senanarong V, Nako A, Chotinaiwattarukul W, Jamjumrus P et al. Use of Hachinski Ischemic Score in the memory clinic: Thai experience. J Med Assoc Thia 2006; 89: 1822-1827.							
Study type	Prospective cohort						
Country	Thailand						
Setting	Memory clinic at Siriraj Hospital, Mahidol University.						
Inclusion criteria	People with DSM-IV diagnosed dementia						
Exclusion criteria	Not stated						
Sex	30.3% male						
Age	Mean age 71.2 years (SD 10.2)						
Presentation	Diagnosed dementia, but subtype to be determined.						
Reference standard	Clinician diagnosis using standard tests and neuroimaging as needed.						
VaD and mixed dementia (VaD with AD) versus AD							
Index Test: Hachinski Ischemic Score, HIS (≥5) Hachinski Ischemic Score (HIS), cut-off 5.							
Results	**True positives:**	73	**False negatives:**	12	**False positives:**	35	**True negatives:** 94
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:** High
Overall risk of bias	Very serious (Subgroup analysis excluded >45% study population; optimised test-threshold was used and it was unclear whether the index test results were interpreted without knowledge of the results of the reference standard or whether the reference standard was interpreted without knowledge of the results of the index test.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	

Siritho S, Senanarong V, Nako A, Chotinaiwattarukul W, Jamjumrus P et al. Use of Hachinski Ischemic Score in the memory clinic: Thai experience. J Med Assoc Thia 2006; 89: 1822-1827.	
Overall indirectness	Not serious

Skinner S, Adewale AJ, DeBlock L, Gill MJ, Power C. Neurocognitive screening tools in HIV/AIDS: comparative performance among patients exposed to antiretroviral therapy. HIV Medicine, 2009; 10: 246–252.							
Study type	Prospective cohort						
Country	Canada						
Setting	Northern and Southern Alberta neurology clinics						
Inclusion criteria	HIV+ people undergoing evaluation for neuropsychological deficits as part of a neurological consultation.						
Exclusion criteria	Not stated						
Sex	89.1% male						
Age	Mean age 49.3 years (SD 7.9)						
Presentation	HIV+ with suspected dementia						
Reference standard	American Academy of Neurology algorithm for HIV-1 associated cognitive/motor disorder						
HAND versus other neurological disorder in HIV+ people							
Index Test: HIV dementia scale, HDS (<10) HIV dementia scale (HDS) (<10)							
Results	**True positives:**	6	**False negatives:**	7	**False positives:**	4	**True negatives:** 16
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: HIV dementia scale, HDS (<11)							

Skinner S, Adewale AJ, DeBlock L, Gill MJ, Power C. Neurocognitive screening tools in HIV/AIDS: comparative performance among patients exposed to antiretroviral therapy. HIV Medicine, 2009; 10: 246–252.							
HIV dementia scale (HDS) (<11)							
Results	**True positives:**	8	**False negatives:**	5	**False positives:**	4	**True negatives:** 16
Additional comments							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Serious (Use of an optimised threshold.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: International HIV Dementia scale (IHDS) (<10) International HIV Dementia scale (IHDS) (<10)							
Results	**True positives:**	10	**False negatives:**	3	**False positives:**	7	**True negatives:** 13
Additional comments							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						

Skjerev A, , Nordhus IH, Engedal K, Broekhus A, Nygaard HA, Pallesen S, Haugen PK. Validation of the Seven Minute Screen and Syndrom Kurztest among elderly Norwegian outpatients. International Psychogeriatrics, 2008; 20: 4, 807–814.	
Study type	Prospective cohort

Skjerev A, , Nordhus IH, Engedal K, Broekhus A, Nygaard HA, Pallesen S, Haugen PK. Validation of the Seven Minute Screen and Syndrom Kurztest among elderly Norwegian outpatients. International Psychogeriatrics, 2008; 20: 4, 807–814.								
Country	Norway							
Setting	Ten Norwegian geriatric and psychogeriatric outpatient clinics							
Inclusion criteria	65 years and above; complaints of memory problems or other cognitive problems expressed by the patient, a relative or other informant; an MMSE score of 22–30; and the presence of a relative or other informant who could give background information about the patient.							
Exclusion criteria	Exclusion criteria were causes of cognitive impairment other than degenerative or vascular pathology (e.g. head trauma, severe psychiatric disease, mental retardation, severe somatic condition, reversible causes of dementia), and alcoholism or drug dependency.							
Sex	64.2% male							
Age	Mean age 77.7 years (SD 5.0)							
Presentation	Memory or other cognitive problems							
Reference standard	A consensus diagnosis of dementia was made according to ICD-10 (World Health Organization, 1993). Patients who did not fulfil the criteria for dementia were classified as “no cognitive impairment” or mild cognitive impairment (MCI) using Petersen’s criteria (Petersen, 2003).							
Dementia versus no dementia								
Index Test: Seven Minute Screen (P>0.6) The Seven Minute Screen (7MS) comprises four subtests: Orientation, Memory, Clock drawing and Verbal fluency. In the original study (Solomon et al., 1998), the composite 7MS performance score is expressed as a logistic regression formula based on the four subtests; the same formula was used to calculate 7MS performance in the current sample. A probability level (P) > 0.7 indicates a high probability of dementia characteristic of Alzheimer’s disease (AD). Here using P> 0.6.								
Results	**True positives:**	50	**False negatives:**	19	**False positives:**	9	**True negatives:**	17
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Use of an alternative threshold to the standard one and that was not pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Seven Minute Screen (P>0.7)								

Skjerev A, , Nordhus IH, Engedal K, Broekhus A, Nygaard HA, Pallesen S, Haugen PK. Validation of the Seven Minute Screen and Syndrom Kurztest among elderly Norwegian outpatients. International Psychogeriatrics, 2008; 20: 4, 807–814.							
The Seven Minute Screen (7MS) comprises four subtests: Orientation, Memory, Clock drawing and Verbal fluency. In the original study (Solomon et al., 1998), the composite 7MS performance score is expressed as a logistic regression formula based on the four subtests; the same formula was used to calculate 7MS performance in the current sample. A probability level (P) > 0.7 indicates a high probability of dementia characteristic of Alzheimer's disease (AD).Here using P> 0.7.							
Results	**True positives:**	50	**False negatives:**	19	**False positives:**	8	**True negatives:** 18
Additional comments							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: Seven Minute Screen (P>0.8) The Seven Minute Screen (7MS) comprises four subtests: Orientation, Memory, Clock drawing and Verbal fluency. In the original study (Solomon et al., 1998), the composite 7MS performance score is expressed as a logistic regression formula based on the four subtests; the same formula was used to calculate 7MS performance in the current sample. A probability level (P) > 0.7 indicates a high probability of dementia characteristic of Alzheimer's disease (AD).Here using P> 0.8.							
Results	**True positives:**	49	**False negatives:**	20	**False positives:**	7	**True negatives:** 19
Additional comments							
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Serious (Use of an alternative threshold to the standard one and that was not pre-specified.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						

Skjerev A, , Nordhus IH, Engedal K, Broekhus A, Nygaard HA, Pallesen S, Haugen PK. Validation of the Seven Minute Screen and Syndrom Kurztest among elderly Norwegian outpatients. International Psychogeriatrics, 2008; 20: 4, 807–814.								
Index Test: Syndrom Kurztest (≥7) Syndrom Kurztest consists of nine subtests assessing episodic memory (free and cued recall and recognition) and information processing speed (naming items, reading numbers, ordering numbers, shifting numbers, symbol counting, interference). Here raw scores were adjusted for age. Three SKT scores were calculated according to the manual: a memory subscore that includes the scaled scores for three subtests (I, XIII and IX); an attention subscore that includes the scaled scores for the other subtests; and, finally, a total score that includes all scaled scores. According to the manual, a total SKT score of 9 to 13 indicates “mild organic mental or cognitive disorder, possible dementia,” and higher scores indicate more advanced cognitive impairment. Cut -off ≥ 7.								
Results	**True positives:**	49	**False negatives:**	20	**False positives:**	12	**True negatives:**	14
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Use of an alternative threshold to the standard one and that was not pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Syndrom Kurztest (≥8) Syndrom Kurztest consists of nine subtests assessing episodic memory (free and cued recall and recognition) and information processing speed (naming items, reading numbers, ordering numbers, shifting numbers, symbol counting, interference). Here raw scores were adjusted for age. Three SKT scores were calculated according to the manual: a memory subscore that includes the scaled scores for three subtests (I, XIII and IX); an attention subscore that includes the scaled scores for the other subtests; and, finally, a total score that includes all scaled scores. According to the manual, a total SKT score of 9 to 13 indicates “mild organic mental or cognitive disorder, possible dementia,” and higher scores indicate more advanced cognitive impairment. Cut -off ≥ 8.								
Results	**True positives:**	45	**False negatives:**	24	**False positives:**	9	**True negatives:**	17
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low

Skjerev A, , Nordhus IH, Engedal K, Broekhus A, Nygaard HA, Pallesen S, Haugen PK. Validation of the Seven Minute Screen and Syndrom Kurztest among elderly Norwegian outpatients. International Psychogeriatrics, 2008; 20: 4, 807–814.								
Overall risk of bias	Serious (Use of an alternative threshold to the standard one and that was not pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Syndrom Kurztest (≥9) Syndrom Kurztest consists of nine subtests assessing episodic memory (free and cued recall and recognition) and information processing speed (naming items, reading numbers, ordering numbers, shifting numbers, symbol counting, interference). Here raw scores were adjusted for age. Three SKT scores were calculated according to the manual: a memory subscore that includes the scaled scores for three subtests (I, XIII and IX); an attention subscore that includes the scaled scores for the other subtests; and, finally, a total score that includes all scaled scores. According to the manual, a total SKT score of 9 to 13 indicates “mild organic mental or cognitive disorder, possible dementia,” and higher scores indicate more advanced cognitive impairment. Cut -off ≥ 9.								
Results	**True positives:**	40	**False negatives:**	29	**False positives:**	8	**True negatives:**	18
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Skogseth R, Hortobagyi T, Soennesyn H, Chwiszczuk L et al. Accuracy of clinical diagnosis of Dementia with Lewy Bodies versus neuropathology. Journal of Alzheimer's Disease 2017; 59: 1139-1152.	
Study type	Prospective cohort
Country	Norway
Setting	Specialist outpatient clinic and an old age psychiatry service in Hordland and Rogaland.
Inclusion criteria	New diagnosis of dementia at the study sites between 2005 and 2007, plus patients referred from other Neurology clinics. MMSE ≥

Skogseth R, Hortobagyi T, Soennesyn H, Chwiszczuk L et al. Accuracy of clinical diagnosis of Dementia with Lewy Bodies versus neuropathology. Journal of Alzheimer's Disease 2017; 59: 1139-1152.								
	20 and/or CDR ≤ 1; no acute delirium, terminal illness, major somatic or psychiaric illness with effects on cognition. Between 2007 and 2013 only DLB and PDD patients were included to increase sample size.							
Exclusion criteria	None stated							
Sex	48% male							
Age	Mean age 74.0 years (SD 8.2)							
Presentation	People have previously been diagnosed with dementia							
Reference standard	Histological and neuropathological assessment was carried out in accordance with published guidelines and pathological diagnosis was made according to international consensus criteria for DLB and AD (including Brakk et al 1991 and 2003, Mirra et al 1991, Hyman et al 1997, Alafuzoff et al 2009.)							
DLB and PDD versus other dementias								
Index Test: International Consensus DLB diagnostic criteria (McKeith et al 2005)								
Results	**True positives:**	16	**False negatives:**	4	**False positives:**	4	**True negatives:**	32
Risk of bias	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (After 2007 the study selectivey recruited participants with a DLB or PDD diagnosis to increase the sample size for these groups.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Slaets S, Van Acker F, Versijpt J, Hauth L, Goeman J, Martin J-J, Se Deyn PP and Engelborghs S. Diagnostic value of MIBG cardiac scintigraphy for differential dementia diagnosis. Int J Geriatr Psychiatry 2015; 30: 864–869.	
Study type	Prospective cohort
Country	Belgium
Setting	Memory Clinic, Hospital Network Antwerp (ZNA)
Inclusion criteria	Patients visiting the memory clinic between 2006 and 2013 who were given a diagnosis of clinically ambiguous diagnoses (AD or DLB) at baseline and had either one of the following: (i) clinical follow-up of more than six months after MIBG cardiac scintigraphy

Slaets S, Van Acker F, Versijpt J, Hauth L, Goeman J, Martin J-J, Se Deyn PP and Engelborghs S. Diagnostic value of MIBG cardiac scintigraphy for differential dementia diagnosis. Int J Geriatr Psychiatry 2015; 30: 864–869.								
	or (ii) autopsy confirmation of the clinical diagnosis.							
Exclusion criteria	Not stated, but people were not excluded for concomitant diseases and conditions like diabetes mellitus, arterial hypertension, hyperlipidemia, ischemic heart disease, and heart failure as well as pharmacological treatments at the time of MIBG scanning.							
Sex	61.0% male							
Age	Mean age 76.0 years (SD 8.0)							
Presentation	Clinically ambiguous dementia (DLB or AD)							
Reference standard	Clinical diagnosis of probable AD was made according to the NINCDS-ADRDA; probable DLB was diagnosed according to the criteria of McKeith (2005). In case consenting patients died, autopsy was performed in order to establish a definite dementia diagnosis. For the neuropathological diagnosis of AD, the criteria of Braak (1991, 2006) were applied as described earlier (Le Bastard, 2013).							
DLB versus not-DLB								
Index Test: 123I-MIBG cardiac scintigraphy MIBG cardiac scintigraphy data for 67 patients was acquired with a Philips XCT scanner, whereas for 18 patients, the data was acquired with a Varicam (GE) scanner, both with a low-energy, high-resolution collimator. Both cameras had similar hardware characteristics (LEHR collimator, large field double-head camera) and the same settings of acquisition parameters. MIBG uptake was determined by calculating the heart-to-mediastinum-uptake (H/M) ratio.								
Results	**True positives:**	16	**False negatives:**	0	**False positives:**	1	**True negatives:**	3
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	High	**Flow and timing:**	Low
Overall risk of bias	Serious (The diagnosing physicians were not blind to the index test results.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Streit S, Limacher A, Zeller A, Burge M. Detecting dementia in patients with normal neuropsychological screening by Short Smell Test and Palmo-Mental Reflex Test: an observational study. BMC Geriatrics. 2015; 15:90-95.	
Study type	Retrospective cohort
Country	Switzerland

Streit S, Limacher A, Zeller A, Burge M. Detecting dementia in patients with normal neuropsychological screening by Short Smell Test and Palmo-Mental Reflex Test: an observational study. BMC Geriatrics. 2015; 15:90-95.								
Setting	Memory Clinic of the University Department of Geriatrics in Bern.							
Inclusion criteria	Patients referred to the clinic due between May 2009 and December 2012 due to cognitive dysfunction who also had normal results on the MMSE and CDT tests in the Memory Clinic. Test results were normal if MMSE was ≥27 out of 30 points and CDT ≥6 out of 7 points.							
Exclusion criteria	None applied							
Sex	19.0% male							
Age	Mean age 68.5 years (SD 11.0)							
Presentation	Cognitive complaints							
Reference standard	Dementia was diagnosed according to DSM-IV TR criteria; MCI was diagnosed using criteria set by the International Working Group on Mild Cognitive Impairment (Winblad, 2004).							
Dementia versus no dementia								
Index Test: Short smell test Short smell test (SST). This was considered abnormal if patients closed their eyes and could not identify instant coffee powder in a can when it was held 5–10 cm under their nose.								
Results	**True positives:**	9	**False negatives:**	8	**False positives:**	34	**True negatives:**	103
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Patients had to have cognitive complaints, but normal MMSE and CDT tests at baseline.)							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Serious (Patients had to have cognitive complaints, but score as normal on the MMSE and CDT tests.)							
Index Test: Palmo-Mental Reflex Palmo-Mental Reflex (PMR). Considered positive if brushing the thumb under the thenar (the region of the palm at the base of the thumb) elicited a unilateral chin muscle twitch.								
Results	**True positives:**	7	**False negatives:**	10	**False positives:**	25	**True negatives:**	112

Streit S, Limacher A, Zeller A, Burge M. Detecting dementia in patients with normal neuropsychological screening by Short Smell Test and Palmo-Mental Reflex Test: an observational study. BMC Geriatrics. 2015; 15:90-95.								
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Patients had to have cognitive complaints, but normal MMSE and CDT tests at baseline.)							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Palmo-Mental Reflex and Short smell test, 1 positive Palmo-Mental Reflex (PMR) and Short smell test (SST), 1 positive. PMR considered positive if brushing the thumb under the thenar (the region of the palm at the base of the thumb) elicited a unilateral chin muscle twitch. SST was considered abnormal if patients closed their eyes and could not identify instant coffee powder in a can when it was held 5–10 cm under their nose.								
Results	**True positives:**	12	**False negatives:**	5	**False positives:**	50	**True negatives:**	87
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Patients had to have cognitive complaints, but normal MMSE and CDT tests at baseline.)							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Palmo-Mental Reflex and Short smell test, both positive Palmo-Mental Reflex (PMR) and Short smell test (SST), 1 positive. PMR considered positive if brushing the thumb under the thenar (the region of the palm at the base of the thumb) elicited a unilateral chin muscle twitch. SST was considered abnormal if patients closed their eyes and could not identify instant coffee powder in a can when it was held 5–10 cm under their nose.								
Results	**True positives:**	4	**False negatives:**	13	**False positives:**	9	**True negatives:**	128

Streit S, Limacher A, Zeller A, Burge M. Detecting dementia in patients with normal neuropsychological screening by Short Smell Test and Palmo-Mental Reflex Test: an observational study. BMC Geriatrics. 2015; 15:90-95.								
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (Patients had to have cognitive complaints, but normal MMSE and CDT tests at baseline.)							
Indirectness	**Patient selection:**	High	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Suppa P, Anker U, Spies L, Bopp I, Ruegger-Frey, Klaghofer R, Gocke C, Hampel H et al. Fully Automated Atlas-Based Hippocampal Volumetry for Detection of Alzheimer's Disease in a Memory Clinic Setting. Journal of Alzheimer's Disease, 2015; 44: 183–193.
Study type Retrospective cohort
Country Switzerland
Setting Memory clinic of the StadtspitalWaid in Zurich.
Inclusion criteria Patients were included, when (i) a clinical diagnosis was obtained according to the standard diagnostic procedure of the Stadtspital Waid and was clearly stated in the report and (ii) high-resolution MR imaging had been performed.
Exclusion criteria No further selection criteria were applied. In particular, there was no exclusion criterion with respect to the MR image quality
Sex Not stated
Age Mean age 74.6 years (SD not stated)
Presentation Memory complaints
Reference standard Diagnoses are made in consensus by an interdisciplinary board using established clinical criteria to identify AD (NINCDS-ADRDA), mild cognitive impairment (Petersen criteria, 1999).
AD (probable) versus no AD (including possible AD diagnosis and unclear cases)
Index Test: MRI Hippocampal grey matter volume left, HVL. Cut- off 2.69 ml MRI Hippocampal volume, HVL. MRI was carried out using Siemens Avanto 1.5 T (Siemens Erlangen, Germany) deploying 3D T1-weighted magnetization prepared rapid gradient echo (MPRAGE). MR images were segmented and stereotactically normalized to the Montreal Neurological

Suppa P, Anker U, Spies L, Bopp I, Ruegger-Frey, Klaghofer R, Gocke C, Hampel H et al. Fully Automated Atlas-Based Hippocampal Volumetry for Detection of Alzheimer's Disease in a Memory Clinic Setting. Journal of Alzheimer's Disease, 2015; 44: 183–193.								
Institute (MNI) space using a combined segmentation and registration approach. Hippocampal GM volume (HV) was calculated by multiplying the subject's GM component image with a predefined binary mask from a freely available atlas and then summing over all voxel intensities. Masks for the left and the right hemisphere were used separately yielding two sub-volumes for each brain hemisphere, HVL and HVR, respectively. Total HV was obtained by summing the GM volume within both masks. Cut- off 2.69 ml								
Results	**True positives:**	31	**False negatives:**	13	**False positives:**	16	**True negatives:**	40
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; assay cut-offs were determined using ROC analysis.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MRI Hippocampal grey matter volume right, HVR. Cut off 2.70ml. MRI Hippocampal grey matter volume right, HVR. MRI was carried out using Siemens Avanto 1.5 T (Siemens Erlangen, Germany) deploying 3D T1-weighted magnetization prepared rapid gradient echo (MPRAGE). MR images were segmented and stereotactically normalized to the Montreal Neurological Institute (MNI) space using a combined segmentation and registration approach. Hippocampal GM volume (HV) was calculated by multiplying the subject's GM component image with a predefined binary mask from a freely available atlas and then summing over all voxel intensities. Masks for the left and the right hemisphere were used separately yielding two sub-volumes for each brain hemisphere, HVL and HVR, respectively. Total HV was obtained by summing the GM volume within both masks. Cut off 2.70ml.								
Results	**True positives:**	33	**False negatives:**	11	**False positives:**	13	**True negatives:**	43
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; assay cut-offs were determined using ROC analysis.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		

Suppa P, Anker U, Spies L, Bopp I, Ruegger-Frey, Klaghofer R, Gocke C, Hampel H et al. Fully Automated Atlas-Based Hippocampal Volumetry for Detection of Alzheimer's Disease in a Memory Clinic Setting. Journal of Alzheimer's Disease, 2015; 44: 183–193.								
Overall indirectness	Not serious							
Index Test: MRI Total Hippocampal grey matter volume, Hv. Cut off 4.95ml. MRI Total Hippocampal grey matter volume, Hv. MRI was carried out using Siemens Avanto 1.5 T (Siemens Erlangen, Germany) deploying 3D T1-weighted magnetization prepared rapid gradient echo (MPRAGE). MR images were segmented and stereotactically normalized to the Montreal Neurological Institute (MNI) space using a combined segmentation and registration approach. Hippocampal GM volume (HV) was calculated by multiplying the subject's GM component image with a predefined binary mask from a freely available atlas and then summing over all voxel intensities. Masks for the left and the right hemisphere were used separately yielding two sub-volumes for each brain hemisphere, HVL and HVR, respectively. Total HV was obtained by summing the GM volume within both masks. Cut off 4.95ml.								
Results	**True positives:**	27	**False negatives:**	17	**False positives:**	8	**True negatives:**	48
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; assay cut-offs were determined using ROC analysis.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MRI Hippocampal grey matter volume left/ total grey matter volume (HVL/GMV). Cut-off 4.69 per mille. MRI Hippocampal grey matter volume left/ total grey matter volume, (HVL/GMV). MRI was carried out using Siemens Avanto 1.5 T (Siemens Erlangen, Germany) deploying 3D T1-weighted magnetization prepared rapid gradient echo (MPRAGE). MR images were segmented and stereotactically normalized to the Montreal Neurological Institute (MNI) space using a combined segmentation and registration approach. Hippocampal GM volume (HV) was calculated by multiplying the subject's GM component image with a predefined binary mask from a freely available atlas and then summing over all voxel intensities. Masks for the left and the right hemisphere were used separately yielding two sub-volumes for each brain hemisphere, HVL and HVR, respectively. Total HV was obtained by summing the GM volume within both masks. Cut-off 4.69 per mille								
Results	**True positives:**	35	**False negatives:**	9	**False positives:**	19	**True negatives:**	37
Additional comme								

Suppa P, Anker U, Spies L, Bopp I, Ruegger-Frey, Klaghofer R, Gocke C, Hampel H et al. Fully Automated Atlas-Based Hippocampal Volumetry for Detection of Alzheimer's Disease in a Memory Clinic Setting. Journal of Alzheimer's Disease, 2015; 44: 183–193.								
nts								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; assay cut-offs were determined using ROC analysis.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MRI Hippocampal grey matter volume right/ total grey matter volume (HVR/GMV). Cut-off 4.54 per mille. MRI Hippocampal grey matter volume right/ total grey matter volume (HVR/GMV). MRI was carried out using Siemens Avanto 1.5 T (Siemens Erlangen, Germany) deploying 3D T1-weighted magnetization prepared rapid gradient echo (MPRAGE). MR images were segmented and stereotactically normalized to the Montreal Neurological Institute (MNI) space using a combined segmentation and registration approach. Hippocampal GM volume (HV) was calculated by multiplying the subject's GM component image with a predefined binary mask from a freely available atlas and then summing over all voxel intensities. Masks for the left and the right hemisphere were used separately yielding two sub-volumes for each brain hemisphere, HVL and HVR, respectively. Total HV was obtained by summing the GM volume within both masks. Cut-off 4.54 per mille.								
Results	**True positives:**	35	**False negatives:**	9	**False positives:**	11	**True negatives:**	45
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; assay cut-offs were determined using ROC analysis.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MRI Total hippocampal grey matter volume/total grey matter volume (HV/GMV). Cut-off 8.36 per mille. MRI Total hippocampal grey matter volume/total grey matter volume (HV/GMV). MRI was carried out using Siemens Avanto 1.5 T (Siemens Erlangen, Germany) deploying 3D T1-weighted magnetization prepared rapid gradient echo (MPRAGE). MR images were segmented and stereotactically								

Suppa P, Anker U, Spies L, Bopp I, Ruegger-Frey, Klaghofer R, Gocke C, Hampel H et al. Fully Automated Atlas-Based Hippocampal Volumetry for Detection of Alzheimer's Disease in a Memory Clinic Setting. Journal of Alzheimer's Disease, 2015; 44: 183–193.								
normalized to the Montreal Neurological Institute (MNI) space using a combined segmentation and registration approach. Hippocampal GM volume (HV) was calculated by multiplying the subject's GM component image with a predefined binary mask from a freely available atlas and then summing over all voxel intensities. Masks for the left and the right hemisphere were used separately yielding two sub-volumes for each brain hemisphere, HVL and HVR, respectively. Total HV was obtained by summing the GM volume within both masks. Cut-off 8.36 per mille								
Results	**True positives:**	29	**False negatives:**	15	**False positives:**	7	**True negatives:**	49
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; assay cut-offs were determined using ROC analysis.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

P.1.19 T

Tagliapietra M, Zanusso G, Fiorini M, Bonetto N, Zarantonello G, Zambon A, Ermani M, Monaco S et al. Accuracy of diagnostic criteria for sporadic Creutzfeldt-Jakob Disease among rapidly progressive dementia. Journal of Alzheimer's disease 2013; 1: 231-238.	
Study type	Retrospective cohort
Country	Italy
Setting	Memory clinic
Inclusion criteria	Diagnosis of rapidly progressive dementia (RPD), 12 month follow up after first neurological assessment
Exclusion criteria	Cases of RPD where the aetiology could be easily diagnosed by first line investigations; not possible to make a clinical diagnosis according to established criteria; cognitive decline reported before the first clinical symptom of RPD.
Sex	48.6% male
Age	Mean age 68.7 years (SD 11.2)

Tagliapietra M, Zanusso G, Fiorini M, Bonetto N, Zarantonello G, Zambon A, Ermani M, Monaco S et al. Accuracy of diagnostic criteria for sporadic Creutzfeldt-Jakob Disease among rapidly progressive dementia. Journal of Alzheimer's disease 2013; 1: 231-238.							
Presentation	Suspected CJD due to rapidly progressive dementia						
Reference standard	Clinician diagnosis using European sCJD (EUROCJD) consortium criteria (Zerr, 2009) for probable or possible CJD						
CJD versus not CJD							
Index Test: MRI, DWI MRI DWI and FLAIR images were taken. According to the EUROCJD criteria (Zerr 2009) hyperintensities in both caudate and putamen and /or in two cortical regions, in either DWI or FLAIR images, was suggestive for sCJD.							
Results	**True positives:**	8	**False negatives:**	3	**False positives:**	1	**True negatives:** 19
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
Index Test: MRI MRI DWI and FLAIR images were taken. According to the EUROCJD criteria (Zerr 2009) hyperintensities in both caudate and putamen and /or in two cortical regions, in either DWI or FLAIR images, was suggestive for sCJD.							
Results	**True positives:**	4	**False negatives:**	6	**False positives:**	4	**True negatives:** 16
Additional comments							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:** Low
Overall risk of bias	Not serious						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						

Tagliapietra M, Zanusso G, Fiorini M, Bonetto N, Zarantonello G, Zambon A, Ermani M, Monaco S et al. Accuracy of diagnostic criteria for sporadic Creutzfeldt-Jakob Disease among rapidly progressive dementia. Journal of Alzheimer's disease 2013; 1: 231-238.								
Index Test: EEG EEG. The presence and regional distribution of the following were considered: periodic sharp-wave complexes, epileptic activity, slowing of the rhythms, and response of basic rhythms to opening of eyes.								
Results	**True positives:**	11	**False negatives:**	0	**False positives:**	25	**True negatives:**	1
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: CSF 14-3-3 immunoblotting 14-3-4 detected by immunoblotting.								
Results	**True positives:**	11	**False negatives:**	0	**False positives:**	13	**True negatives:**	10
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Total tau Total tau, measured by ELISA (Bioscource Human Total tau kit), cut-off 1300pg/ml.								

Tagliapietra M, Zanusso G, Fiorini M, Bonetto N, Zarantonello G, Zambon A, Ermani M, Monaco S et al. Accuracy of diagnostic criteria for sporadic Creutzfeldt-Jakob Disease among rapidly progressive dementia. Journal of Alzheimer's disease 2013; 1: 231-238.								
Results	**True positives:**	10	**False negatives:**	1	**False positives:**	4	**True negatives:**	19
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Talbot PR, Lloyd JJ, Snowden JS, Neary D, Testa HJ. A clinical role for 99mTc-HMPAO SPECT in the investigation of dementia? Journal of Neurology, Neurosurgery, and Psychiatry 1998;63:306-13.	
Study type	Prospective cohort
Country	UK
Setting	Cerebral function unit at hospital (memory clinic)
Inclusion criteria	Patients referred to clinic with suspected dementia
Exclusion criteria	Not stated
Sex	46.5% male
Age	Mean age 63.2 years (SD 8.0) (of 5 largest diagnostic groups)
Presentation	Suspected dementia
Reference standard	NINCDS-ADRDA (AD), VaD by Roman (1993) criteria, FTD by Brun (1994) criteria; pathological confirmation of AD was established in eight patients (Mann, 1993).
FTD versus non-FTD	
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT; threshold not pre-specified; visual interpretation, using magenta scale: bilateral anterior CBF abnormality or bilateral anterior plus unilateral posterior CBF abnormality (SPECT indicative of FTLD). Visual interpretation with image analysis; single- headed camera used to take images. SPECT FTD pattern indicative of FTD: bilateral anterior brain hypoperfusion.	

Talbot PR, Lloyd JJ, Snowden JS, Neary D, Testa HJ. A clinical role for 99mTc-HMPAO SPECT in the investigation of dementia? Journal of Neurology, Neurosurgery, and Psychiatry 1998;63:306-13.								
Results	**True positives:**	21	**False negatives:**	37	**False positives:**	21	**True negatives:**	235
Additional comments	Data obtained from Archer et al, (2015) Cochrane review as not presented in a useful format in original paper.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Very serious (Unclear if avoided inappropriate exclusions; unclear whether the reference standard results were interpreted without knowledge of the index test and whether the index test was carried out without knowledge of reference test result; no pre-specified index test threshold; subgroup analysis used as data on 'other' clinical diagnosis group is not reported.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
FTD versus VaD								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT; threshold: not pre-specified; visual interpretation, using magenta scale: bilateral anterior CBF abnormality or bilateral anterior plus unilateral posterior CBF abnormality (SPECT indicative of FTLD). Visual interpretation with image analysis; single- headed camera used to take images. SPECT FTD pattern indicative of FTD: bilateral anterior brain hypoperfusion.								
Results	**True positives:**	37	**False negatives:**	43	**False positives:**	21	**True negatives:**	57
Additional comments	Data obtained from Archer et al, (2015) Cochrane review as not presented in a useful format in original paper.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Very serious (Unclear if avoided inappropriate exclusions; unclear whether the reference standard results were interpreted without knowledge of the index test and whether the index test was carried out without knowledge of reference test result; no pre-specified index test threshold; subgroup analysis used with >10% study population excluded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall	Not serious							

Talbot PR, Lloyd JJ, Snowden JS, Neary D, Testa HJ. A clinical role for 99mTc-HMPAO SPECT in the investigation of dementia? Journal of Neurology, Neurosurgery, and Psychiatry 1998;63:306-13.								
indirectness								
FTD versus AD								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT; threshold: not pre-specified; visual interpretation, using magenta scale: bilateral anterior CBF abnormality or bilateral anterior plus unilateral posterior CBF abnormality (SPECT indicative of FTLD). Visual interpretation with image analysis; single- headed camera used to take images. SPECT FTD pattern indicative of FTD: bilateral anterior brain hypoperfusion.								
Results	**True positives:**	37	**False negatives:**	43	**False positives:**	5	**True negatives:**	127
Additional comments	Data obtained from Archer et al, (2015) Cochrane review as not presented in a useful format in original paper.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Very serious (Unclear if avoided inappropriate exclusions; unclear whether the reference standard results were interpreted without knowledge of the index test and whether the index test was carried out without knowledge of reference test result; no pre-specified index test threshold; subgroup analysis used with >10% study population excluded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Terpening Z, Cordato NJ, Hepner IJ, Lucas SK, Lindley RI. Utility of the Addenbrooke's Coginitive Examination- Revised for the diagnosis of dementua syndromes. Australas J Ageing. 2011; 30: 113-8.	
Study type	Prospective Cohort
Country	Australia
Setting	Cognition clinic
Inclusion criteria	People referred to a cognition clinic
Exclusion criteria	Failure to complete all components of ACE-R.
Sex	58.2% male
Age	Mean age 68.7 years (SD9.9)

Terpening Z, Cordato NJ, Hepner IJ, Lucas SK, Lindley RI. Utility of the Addenbrooke's Coginitive Examination- Revised for the diagnosis of dementua syndromes. Australas J Ageing. 2011; 30: 113-8.								
Presentation	Suspected dementia							
Reference standard	DSM-IV for dementia, NINCDS/ADRDA for AD, NINDS-AIREN for VaD, Neary et al (1998) criteria for FTD, McKeith et al. (1999) consensus criteria for DBL.							
Dementia versus no dementia								
Index Test: Addenbrooke's Cognitive Examination-Revised, ACE-R (<83) Addenbrooke's Cognitive Examination-Revised, ACE-R, 82/100 standard cut off from index paper								
Results	**True positives:**	65	**False negatives:**	17	**False positives:**	8	**True negatives:**	32
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Patients lacking a clinical diagnosis were excluded from the analysis)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not Serious							
Index Test: Addenbrooke's Cognitive Examination-Revised, ACE-R (<85) Addenbrooke's Cognitive Examination-Revised, ACE-R, 84/100, optimal cut off from ROC								
Results	**True positives:**	70	**False negatives:**	12	**False positives:**	8	**True negatives:**	32
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Patients lacking a clinical diagnosis were excluded from the analysis)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not Serious							
Index Test: Addenbrooke's Cognitive Examination-Revised, ACE-R (<89)								

Terpening Z, Cordato NJ, Hepner IJ, Lucas SK, Lindley RI. Utility of the Addenbrooke's Coginitive Examination- Revised for the diagnosis of dementua syndromes. Australas J Ageing. 2011; 30: 113-8.								
Addenbrooke's Cognitive Examination-Revised, ACE-R, 88/100 standard cut off from index paper								
Results	**True positives:**	75	**False negatives:**	7	**False positives:**	13	**True negatives:**	27
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Patients lacking a clinical diagnosis were excluded from the analysis)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not Serious							

Thomas AJ, Attems J, Colloby SJ, O'Brien JT, McKeith I, Walker R et al. Autopsy validation of 123I-FP-CIT dopaminergic neuroimaging for the diagnosis of DLB. Neurology 2017; 88:276–283.	
Study type	Retrospective cohort
Country	UK
Setting	Memory clinics in Newcastle and London
Inclusion criteria	Patients >60 years old (at clinical assessment), had had 123I-FP-CIT imaging in the context of a dementia and were part in the Newcastle Brain Tissue Resource.
Exclusion criteria	People with PD.
Sex	61.8% male
Age	Mean age 76.9 years (SD 7.1)
Presentation	People with a previous diagnosis of dementia
Reference standard	Neuropathologic diagnoses were assigned with the use of accepted international neuropathologic criteria, including neuritic Braak stages, Consortium to Establish a Registry for Alzheimer's Disease (CERAD) scores, and Newcastle- McKeith criteria.
DLB versus non-DLB	
Index Test: 123I-FP-CIT SPECT Newcastle patients were scanned for 30 minutes with a triple-head gamma camera. In London, acquisition used a brain-dedicated StrichmanMedical	

Thomas AJ, Attems J, Colloby SJ, O'Brien JT, McKeith I, Walker R et al. Autopsy validation of 123I-FP-CIT dopaminergic neuroimaging for the diagnosis of DLB. Neurology 2017; 88:276–283.								
Equipment 810 gamma camera. After reconstruction, scans were visually rated at each site by independent raters and a consensus rating of either abnormal (consistent with Lewy body disease [LBD]) or normal was agreed on.								
Results	**True positives:**	24	**False negatives:**	6	**False positives:**	2	**True negatives:**	23
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Toledo JB, Brettschneider J, Grossman M, Arnold SE, Hu, WT, Xie SX, Lee VM-Y, Shaw LM, Trojanowski JQ.								
Study type	Retrospective cohort							
Country	USA							
Setting	Penn Centre for Neurodegenerative Disease Research Integrated Neurodegenerative Disease database							
Inclusion criteria	Autopsy confirmation of a diagnosis of AD, DLB, FTD; available MMSE and CDR scores and CSF biomarker data.							
Exclusion criteria	Not stated							
Sex	Not reported							
Age	Mean age 68.9 years (9.5)							
Presentation	clinically ambiguous dementia							
Reference standard	Autopsy confirmation of previous clinical diagnosis							
AD versus FTD								
Index Test: Amyloid Beta 1-42 and Total Tau Tau and Amyloid beta 1-42 ELISA								
Results	**True positives:**	64	**False negatives:**	7	**False positives:**	5	**True negatives:**	24

Toledo JB, Brettschneider J, Grossman M, Arnold SE, Hu, WT, Xie SX, Lee VM-Y, Shaw LM, Trojanowski JQ.								
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (>10% population excluded from analysis; the index test thresholds used are not stated and it is unclear if they were pre-specified)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Toledo JB, Brettschneider								
Study type	Retrospective cohort							
Country	USA							
Setting	Penn Centre for Neurodegenerative Disease Research Integrated Neurodegenerative Disease database							
Inclusion criteria	Autopsy confirmation of a diagnosis of AD, DLB, FTD; available MMSE and CDR scores and CSF biomarker data.							
Exclusion criteria	Not stated							
Sex	Not reported							
Age	Mean age 68.9 years (9.5)							
Presentation	clinically ambiguous dementia							
Reference standard	Autopsy confirmation of previous clinical diagnosis							
AD versus FTD								
Index Test: p-tau 181 p-tau 181, Luminex								
Results	**True positives:**	71	**False negatives:**	0	**False positives:**	4	**True negatives:**	25
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (>10% population excluded from analysis; the index test thresholds used are not stated and it is unclear if they were pre-specified)							

Toledo JB, Brettschneider						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low
Overall indirectness	Not serious					

G.Treglia, E.Cason, P.Cortelli, A.Gabellini, R.Liguori, A.Bagnato, A.Giordano, G. Fagioli, Iodine-123metaiodobenzylguanidine scintigraphy and iodine-123 ioflupane single photon emission computed tomography in Lewy body diseases: complementary or alternative techniques? J. Neuroimaging 24 (2012) 149–154.								
Study type	Prospective cohort							
Country	Italy							
Setting	Unit of Nuclear Medicine, Maggiore Hospital, Bologna							
Inclusion criteria	Patients who underwent both 123I-MIBG scintigraphy and 123I-FP-CIT SPECT within 2 months for differential diagnosis between DLB and other dementias							
Exclusion criteria	Patients taking drugs interfering with myocardial 123I-MIBG or striatal 123I-FP-CIT uptake; heart diseases, diabetes, previous cardiotoxic therapy, or other diseases which may interfere with myocardial 123I-MIBG uptake; pregnancy and breastfeeding; inability to cooperate with the scintigraphic procedures							
Sex	58.1% male							
Age	Mean age 66.1 years (SD11.4)							
Presentation	Clinically ambiguous dementia (CAD)							
Reference standard	Specific criteria used not stated							
DLB vs non-DLB dementia								
Index Test: 123I-MIBG cardiac scintigraphy 123I-MIBG scintigraphy: after i.v. injection of 111 MBq of 123IMIBG, planar images of the chest in anterior view are obtained twice for 5 minutes, starting at 15 minutes after radiopharmaceutical injection (early image) and then at 240 minutes after radiopharmaceutical injection (delayed image). 123I-MIBG myocardial uptake was determined calculating the heart to mediastinum uptake ratio (H/M) which was compared with a control group.								
Results	**True positives:**	18	**False negatives:**	2	**False positives:**	1	**True negatives:**	10
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Unclear	**Flow and timing:**	Low

G.Treglia, E.Cason, P.Cortelli, A.Gabellini, R.Liguori, A.Bagnato, A.Giordano, G. Fagioli, Iodine-123metaiodobenzylguanidine scintigraphy and iodine-123 ioflupane single photon emission computed tomography in Lewy body diseases: complementary or alternative techniques? J. Neuroimaging 24 (2012) 149–154.								
Overall risk of bias	Not serious (Specific criteria used as the reference standard not reported)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: 123I-FP-CIT SPECT 123I-FP-CIT SPECT: 240 minutes after i.v. injection of 148 MBq of 123I-FP-CIT cerebral SPECT images are obtained. 123I-FPCIT striatal uptake was determined by evaluating the cerebral striatal (caudate and putamen)/posterior striatum binding ratio of 123I-FP-CIT, semi-quantitatively assessed by digital evaluation (using regions of interest) and compared with a control group.								
Results	**True positives:**	18	**False negatives:**	2	**False positives:**	1	**True negatives:**	10
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Not serious (Specific criteria used as the reference standard not reported)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Tripathi M, Tripathi M, Vibha, Gowda N, Bal C, Malhotra A. Tc-99 ethylctsteinate dimer SPECT in the differential diagnosis of dementias. Neurology India, 2010; 58:857-862.	
Study type	Prospective cohort
Country	India
Setting	Dementia diagnostic clinic
Inclusion criteria	All referrals for SPECT perfusion
Exclusion criteria	None stated.

Tripathi M, Tripathi M, Vibha, Gowda N, Bal C, Malhotra A. Tc-99 ethylctsteinate dimer SPECT in the differential diagnosis of dementias. Neurology India, 2010; 58:857-862.							
Sex	68.4% male						
Age	Mean age 63.2 years (9.8)						
Presentation	Clinically ambiguous dementia						
Reference standard	NINS-ADRDA for AD; NINDS-AIREN for VaD, DLB consensus criteria for DLB, Lund- Manchester criteria for DLB.						
AD versus non-AD							
Index Test: 99mTc-ECD SPECT, visual assessment method Tc -99m ECD SPECT. Images were acquired on a dual-head gamma camera (Varicam, Elscint) using a high-resolution low-energy or fan beam collimator. Acquisition parameters were 25 seconds per stop, 128X128 matrix,circular orbit of 180° each head, step, and shoot mode. Data were reconstructed using a Butterworth filter order 10, cut-off 0.5 cycles/pixel. These were corrected for gamma ray attenuation using Chang attenuation coefficient of 0.11/cm. Transaxial, coronal, and sagittal sections were reconstructed with 2 pixel slice thickness. Images were viewed on a monitor. A coloured display (brain-fit or brain-french, Xpertpro/Entegra workstation-GE) was used, ranging from blue as the lowest through magenta and orange to white as the highest. Perfusion was considered abnormal if the area of deficit was below the halfway point of this scale on more than two sections. Standard diagnostic patterns were used.							
Results	**True positives:**	71	**False negatives:**	5	**False positives:**	2	**True negatives:** 39
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:** Unclear
Overall risk of bias	Serious (14% of participants were lost to follow up and did not receive a reference standard; it is unclear whether the index test was interpreted without knowledge of the reference standard.)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
FTD versus non-FTD							
Index Test: 99mTc-ECD SPECT, visual assessment method Tc -99m ECD SPECT. Images were acquired on a dual-head gamma camera (Varicam, Elscint) using a high-resolution low-energy or fan beam collimator. Acquisition parameters were 25 seconds per stop, 128X128 matrix,circular orbit of 180° each head, step, and shoot mode. Data were reconstructed using a Butterworth filter order 10, cut-off 0.5 cycles/pixel. These were corrected for gamma ray attenuation using Chang attenuation coefficient of 0.11/cm. Transaxial, coronal, and sagittal sections were reconstructed with 2 pixel slice thickness. Images were viewed on a monitor. A coloured display (brain-fit or brain-french, Xpertpro/Entegra workstation-GE) was used, ranging from blue as the lowest through magenta and orange to							

Tripathi M, Tripathi M, Vibha, Gowda N, Bal C, Malhotra A. Tc-99 ethylctsteinate dimer SPECT in the differential diagnosis of dementias. Neurology India, 2010; 58:857-862.								
white as the highest. Perfusion was considered abnormal if the area of deficit was below the halfway point of this scale on more than two sections. Standard diagnostic patterns were used.								
Results	**True positives:**	26	**False negatives:**	1	**False positives:**	1	**True negatives:**	89
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Unclear
Overall risk of bias	Serious (14% of participants were lost to follow up and did not receive a reference standard; it is unclear whether the index test was interpreted without knowledge of the reference standard.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Tschampa HJ, Kallenberg K, Urbach H, Meissner B, Nicolay C, Kretzschmar HA, et al. MRI in the diagnosis of sporadic Creutzfeldt-Jakob disease: a study on inter-observer agreement. Brain. 2005; 128: 9-33.								
Study type	Retrospective cohort							
Country	Germany							
Setting	German surveillance programme							
Inclusion criteria	Referred to the German CJD surveillance programme							
Exclusion criteria	Not stated							
Sex	Not stated							
Age	Not stated							
Presentation	Suspected CJD							
Reference standard	60 patients were diagnosed by autopsy using Kretzschmar (1996) and 84 were diagnosed using by clinicians using the WHO criteria.							
CJD versus not CJD (excluding possible CJD)								
Index Test: MRI MRI, typical and non-typical MRI patterns listed in paper. Hyperintense grey matter on MRI.								
Results	**True positives:**	86	**False**	58	**False positives:**	6	**True negatives:**	32

Tschampa HJ, Kallenberg K, Urbach H, Meissner B, Nicolay C, Kretzschmar HA, et al. MRI in the diagnosis of sporadic Creutzfeldt-Jakob disease: a study on inter-observer agreement. Brain. 2005; 128: 9-33.								
			negatives:					
Additional comments	Three independent observers rated the index test data. We have used the median sensitivity and specificity data for the 3 observers.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: EEG EEG, Periodic sharp wave complexes, standard process for surveillance unit.								
Results	**True positives:**	42	**False negatives:**	91	**False positives:**	2	**True negatives:**	30
Additional comments	Three independent observers rated the index test data. We have used the median sensitivity and specificity data for the 3 observers.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: CSF 14-3-3 14-3-3, standard process for surveillance unit								
Results	**True positives:**	128	**False negatives:**	12	**False positives:**	19	**True negatives:**	15
Additional comments	Three independent observers rated the index test data. We have used the median sensitivity and specificity data for the 3 observers.							

Tschampa HJ, Kallenberg K, Urbach H, Meissner B, Nicolay C, Kretzschmar HA, et al. MRI in the diagnosis of sporadic Creutzfeldt-Jakob disease: a study on inter-observer agreement. Brain. 2005; 128: 9-33.								
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

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Van Everbroeck B, Quoilin S, Boons J, Martin JJ, Cras P. A prospective study of CSF markers in 250 patients with possible Creutzfeldt-Jakob disease. J neurol Neurosurg Psychiatry 2003; 74: 1210–4.								
Study type	Retrospective cohort							
Country	Belgium							
Setting	Laboratory of neurobiology, University of Antwerp							
Inclusion criteria	Clinical symptoms compatible with the diagnosis of possible CJD at the time of lumbar puncture							
Exclusion criteria	Not stated							
Sex	Not reported							
Age	Mean age 67.0 years (SD 8.0)							
Presentation	suspected CJD							
Reference standard	Clinical diagnosis according to Weber (2000) with neuropathological confirmation.							
CJD versus not CJD								
Index Test: CSF 14-3-3 immunoblotting 14-3-3, immunoblotting. The blot was scored for the presence or absence of an immunoreactive band at 30 kDa.								
Results	**True positives:**	52	**False negatives:**	0	**False positives:**	15	**True negatives:**	183
Risk of bias	**Patient**	Low	**Index test:**	Low	**Reference**	Low	**Flow and**	Low

Van Everbroeck B, Quoilin S, Boons J, Martin JJ, Cras P. A prospective study of CSF markers in 250 patients with possible Creutzfeldt-Jakob disease. J neurol Neurosurg Psychiatry 2003; 74: 1210–4.								
	selection:				**standard:**		**timing:**	
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: CSF 14-3-3 and Amyloid Beta 1-42 14-3-3, Amyloid Beta 1-42. 14-3-3 was detected by immunoblotting. The blot was scored for the presence or absence of an immunoreactive band at 30 kDa. Amyloid Beta 1-42 was detected using an ELISA with a 400 pg/ml cut-off.								
Results	**True positives:**	52	**False negatives:**	0	**False positives:**	4	**True negatives:**	194
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Total Tau Tau, INNOTEST ELISA, cut-off 1300pg/ml								
Results	**True positives:**	45	**False negatives:**	7	**False positives:**	5	**True negatives:**	193
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							

Van Everbroeck B, Quoilin S, Boons J, Martin JJ, Cras P. A prospective study of CSF markers in 250 patients with possible Creutzfeldt-Jakob disease. J neurol Neurosurg Psychiatry 2003; 74: 1210–4.								
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: Amyloid Beta 1-42 and total tau Tau and Amyloid beta 1-42. Tau was detected using INNOTEST ELISA, cut-off 1300pg/ml; Amyloid Beta 1-42 was detected using an ELISA with a 400 pg/ml cut-off.								
Results	**True positives:**	45	**False negatives:**	7	**False positives:**	4	**True negatives:**	194
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Van Everbroeck B, Dobbeleir I, De Waele M, De Deyn P, Martin JJ, Cras P. Differential diagnosis of 201 possible Creutzfeldt-Jakob disease patients.J Neurol. 2004; 251:298-304.	
Study type	Prospective cohort
Country	Belgium
Setting	Laboratory of neurobiology, University of Antwerp.
Inclusion criteria	Rapidly progressive dementia; WHO criteria for sporadic CJD.
Exclusion criteria	Hereditary prion disease; dementia subtypes other than AD, CJD, VD, DLB.
Sex	53.4% male
Age	Median age 68.0 years (range 31-91)
Presentation	Rapidly progressive dementia leading to suspected CJD

Van Everbroeck B, Dobbeleir I, De Waele M, De Deyn P, Martin JJ, Cras P. Differential diagnosis of 201 possible Creutzfeldt-Jakob disease patients.J Neurol. 2004; 251:298-304.								
Reference standard	Autopsy using the detection of prion proteins by immunocytochemistry for CJD.							
CJD versus not CJD								
Index Test: Total Tau Tau >1300pg/ml, by INNOTEST ELISA								
Results	**True positives:**	45	**False negatives:**	7	**False positives:**	2	**True negatives:**	79
Additional comments	Data for Periodic sharp wave complexes (PSWCs) in EEG and 14-3-3- protein were not analysed as they formed part of the reference diagnosis.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (> 10% population excluded from analysis)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MRI MRI, presence of CJD typical lesions in the basal ganglia and thalamus								
Results	**True positives:**	19	**False negatives:**	33	**False positives:**	2	**True negatives:**	79
Additional comments	Data for Periodic sharp wave complexes (PSWCs) in EEG and 14-3-3- protein were not analysed as they formed part of the reference diagnosis.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (> 10% population excluded from analysis)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Velakoulis D, Lloyd JH. The role of SPECT scanning in a neuropsychiatry unit. Aust N Z J Psychiatry 1998; 32: 511-22.								
Study type	Prospective cohort							
Country	Australia							
Setting	Nuclear medicine department of the Royal Melbourne Hospital							
Inclusion criteria	Patients with suspected cerebral lesions and/or cognitive impairment admitted to a neuropsychiatry unit in a general hopital. This unit acts a tertiary referal centre for patients with a wide spectrum of disorders.							
Exclusion criteria	Not stated							
Sex	Not stated							
Age	mean age 53.6 years (no SD provided)							
Presentation	People with suspected cerebral lesions and/or cognitive impairment							
Reference standard	Neuropsychological testing based on individual patient needs, CT or MRI for all participants and EEG in 32 cases.							
Dementia versus no dementia								
Index Test: 99mTc-HMPAO SPECT (AD pattern) 99mTc-HMPAO SPECT imaging carried out in another specialist department. 72 images of tracer distribution with 24 images per scan with image resolution estimated to be 9mm. Planar data was processed to provide transverse slices in the orbitomeatal line and coronal and sagittal images. Images were interpreted visually. AD pattern used for image analysis here.								
Results	**True positives:**	15	**False negatives:**	18	**False positives:**	3	**True negatives:**	20
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Unclear whether: the index test results were interpreted without knowledge of the results of the reference standard; the index test threshold was pre-specified or the reference standard results interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: 99mTc-HMPAO SPECT (FTD pattern) 99mTc-HMPAO SPECT imaging carried out in another specialist department. 72 images of tracer distribution with 24 images per scan with image								

Velakoulis D, Lloyd JH. The role of SPECT scanning in a neuropsychiatry unit. Aust N Z J Psychiatry 1998; 32: 511-22.								
resolution estimated to be 9mm. Planar data was processed to provide transverse slices in the orbitomeatal line and coronal and sagittal images. Images were interpreted visually. FTD pattern used for image analysis here.								
Results	**True positives:**	6	**False negatives:**	27	**False positives:**	9	**True negatives:**	14
Additional comments								
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (Unclear whether: the index test results were interpreted without knowledge of the results of the reference standard; the index test threshold was pre-specified or the reference standard results interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus FTD								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT imaging carried out in another specialist department. 72 images of tracer distribution with 24 images per scan with image resolution estimated to be 9mm. Planar data was processed to provide transverse slices in the orbitomeatal line and coronal and sagittal images. Images were interpreted visually. AD pattern used for image analysis here.								
Results	**True positives:**	8	**False negatives:**	1	**False positives:**	3	**True negatives:**	6
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Very serious (Subgroup analysis where >10% study population excluded and it was unclear whether: the index test results were interpreted without knowledge of the results of the reference standard; the index test threshold was pre-specified or the reference standard results interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Velakoulis D, Lloyd JH. The role of SPECT scanning in a neuropsychiatry unit. Aust N Z J Psychiatry 1998; 32: 511-22.								
FTD versus AD								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT imaging carried out in another specialist department. 72 images of tracer distribution with 24 images per scan with image resolution estimated to be 9mm. Planar data was processed to provide transverse slices in the orbitomeatal line and coronal and sagittal images. Images were interpreted visually. FTD pattern used for image analysis here.								
Results	**True positives:**	5	**False negatives:**	4	**False positives:**	0	**True negatives:**	9
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Very serious (Subgroup analysis where >10% study population excluded and it was unclear whether: the index test results were interpreted without knowledge of the results of the reference standard; the index test threshold was pre-specified or the reference standard results interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus other dementias								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT imaging carried out in another specialist department. 72 images of tracer distribution with 24 images per scan with image resolution estimated to be 9mm. Planar data was processed to provide transverse slices in the orbitomeatal line and coronal and sagittal images. Images were interpreted visually. AD pattern used for image analysis here.								
Results	**True positives:**	8	**False negatives:**	1	**False positives:**	7	**True negatives:**	17
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Very serious (Subgroup analysis where >10% study population excluded and it was unclear whether: the index test results were interpreted without knowledge of the results of the reference standard; the index test threshold was pre-specified or the reference standard results interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall	Not serious							

Velakoulis D, Lloyd JH. The role of SPECT scanning in a neuropsychiatry unit. Aust N Z J Psychiatry 1998; 32: 511-22.								
indirectness								
FTD versus other dementias								
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT imaging carried out in another specialist department. 72 images of tracer distribution with 24 images per scan with image resolution estimated to be 9mm. Planar data was processed to provide transverse slices in the orbitomeatal line and coronal and sagittal images. Images were interpreted visually. FTD pattern used for image analysis here.								
Results	**True positives:**	5	**False negatives:**	4	**False positives:**	1	**True negatives:**	23
Risk of bias	**Patient selection:**	Low	**Index test:**	Unclear	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Very serious (Subgroup analysis where >10% study population excluded and it was unclear whether: the index test results were interpreted without knowledge of the results of the reference standard; the index test threshold was pre-specified or the reference standard results interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Vijverberg EGB, Dols A, Krudop WA, Peters A, Kerssens CJ, van Berckel BNM, Wattjes MP et al. Diagnostic Accuracy of the Frontotemporal Dementia Consensus Criteria in the Late-Onset Frontal Lobe Syndrome. Dement Geriatr Cogn Disord 2016a; 41: 210–219.	
Study type	Prospective cohort
Country	The Netherlands
Setting	VU medical centre Alzheimer Centre and the Department of Old Age Psychiatry of the GGZInGeest, Amsterdam.
Inclusion criteria	Patients referred to the VU medical centre Alzheimer Centre and the Department of Old Age Psychiatry of the GGZInGeest between April 2011 and June 2013 who had dominant behavioural complaints and a score of≥11 on the Frontal Behavioural Inventory (FBI) or a score of≥10 on the Stereotypy Rating Inventory (SRI).
Exclusion criteria	Criteria included: (1) an already established diagnosis of dementia or a psychiatric disorder that could explain behaviour problems; (2) Mini-Mental State Examination (MMSE) no more than 18; (3) medical history, including traumatic brain injury, mental retardation and drugs or alcohol abuse; (4) lack of a reliable informant; (5) insufficient communicative skills of either patient or the closest informant (language, serious hearing impairment or behavioural disturbances, including threatening or physical aggression); (6) acute onset of behavioural problems; (7) clinically apparent aphasia or semantic

Vijverberg EGB, Dols A, Krudop WA, Peters A, Kerssens CJ, van Berckel BNM, Wattjes MP et al. Diagnostic Accuracy of the Frontotemporal Dementia Consensus Criteria in the Late-Onset Frontal Lobe Syndrome. Dement Geriatr Cogn Disord 2016a; 41: 210–219.								
	dementia, and (8) MRI contraindications.							
Sex	80.0% male							
Age	Mean age 62.0 years (SD 6.9)							
Presentation	suspected bvFTD							
Reference standard	Two years after initial diagnosis neuropsychiatric questionnaires, neuropsychological test battery and MRI of the brain were repeated, and a final multidisciplinary diagnosis was established. Diagnoses were based on the published consensus guidelines for dementia (Gorno-Tempini, 2011, for PPA; NINCDS-ADRDA for AD; NINCDS-AIREN for VaD; McKeith, 2005, for DLB; DSM-IV-TR for dementia), and the psychiatric diagnoses were based on current psychiatric criteria (DSM-IV-TR).							
bvFTD versus not bvFTD								
Index Test: FTDC criteria for possible bvFTD FTDC criteria for possible and probable bvFTD (uses information from the psychiatric and neurological examination, informant-based history, results of the neuropsychological test battery and neuroimaging results). A consensus diagnosis between the neurologist and the psychiatrist was made.								
Results	**True positives:**	23	**False negatives:**	4	**False positives:**	65	**True negatives:**	24
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (19% study population was excluded from analysis and it is unclear whether a consecutive or random group of patients was enrolled or whether the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
bvFTD versus not bvFTD								
Index Test: FTDC criteria for probable bvFTD FTDC criteria for possible and probable bvFTD (uses information from the psychiatric and neurological examination, informant-based history, results of the neuropsychological test battery and neuroimaging results). A consensus diagnosis between the neurologist and the psychiatrist was made.								
Results	**True positives:**	23	**False negatives:**	4	**False positives:**	16	**True negatives:**	73
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	High

Vijverberg EGB, Dols A, Krudop WA, Peters A, Kerssens CJ, van Berckel BNM, Wattjes MP et al. Diagnostic Accuracy of the Frontotemporal Dementia Consensus Criteria in the Late-Onset Frontal Lobe Syndrome. Dement Geriatr Cogn Disord 2016a; 41: 210–219.						
Overall risk of bias	Serious (19% study population was excluded from analysis and it is unclear whether a consecutive or random group of patients was enrolled or whether the reference standard results were interpreted without knowledge of the results of the index test.)					
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low
Overall indirectness	Not serious					

Vijverberg EGB, Wattjes MP, Dols A, Krudop WA, Moller C, Peters A, Kerssens CJ et al. Diagnostic Accuracy of MRI and Additional [18F]FDG-PET for Behavioral Variant Frontotemporal Dementia in Patients with Late Onset Behavioral Changes. Journal of Alzheimer's Disease, 2016b; 53: 1287–1297.								
Study type	Prospective cohort							
Country	The Netherlands							
Setting	VU medical centre Alzheimer Centre and the Department of Old Age Psychiatry of the GGZInGeest, Amsterdam.							
Inclusion criteria	Patients referred to the VU medical centre Alzheimer Centre and the Department of Old Age Psychiatry of the GGZInGeest between April 2011 and June 2013 who had dominant behavioural complaints and a score of≥11 on the Frontal Behavioural Inventory (FBI) or a score of≥10 on the Stereotypy Rating Inventory (SRI).							
Exclusion criteria	None stated							
Sex	75.7% male							
Age	Mean age 61.6 years (SD 6.6)							
Presentation	suspected bv-FTD							
Reference standard	Diagnoses were based on the published consensus guidelines for dementia (Rascovsky, 2011, for FTD; Gorno-Tempini, 2011, for PPA; McKhann, 2011, for AD; NINDS-AIREN for VaD; McKeith, 2005, for DLB and DSM-IV-TR for dementia) and the primary psychiatric diagnoses were based on current psychiatric criteria.							
bv-FTD versus non-bv-FTD								
Index Test: FDG-PET 18-F FDG-PET scans were made on an ECAT EXACT HR+ scanner (Siemens/CTI). [18F]FDG-PET-scans were assessed visually and interpreted by an experienced nuclear medicine physician on frontal and/or anterior temporal hypometabolism based on the summed images of all the frames.								
Results	**True positives:**	24	**False negatives:**	3	**False positives:**	27	**True negatives:**	57

Vijverberg EGB, Wattjes MP, Dols A, Krudop WA, Moller C, Peters A, Kerssens CJ et al. Diagnostic Accuracy of MRI and Additional [18F]FDG-PET for Behavioral Variant Frontotemporal Dementia in Patients with Late Onset Behavioral Changes. Journal of Alzheimer's Disease, 2016b; 53: 1287–1297.								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	High	**Flow and timing:**	High
Overall risk of bias	Serious (19% study population was excluded from analysis and it is unclear whether a consecutive or random group of patients was enrolled or whether inappropriate exclusions were avoided; all test results (including the index tests) were used to reach the clinical diagnosis.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: FDG-PET and MRI 18-F FDG-PET and MRI. MRI was carried out using 3T Signa HDxt whole-body MRI system GE Medical Systems. Image acquisition included an established standard MRI protocol for memory clinic patients. Sagittal 3D heavily T1-weighted gradient-echo sequence with coronal reformats, a sagittal 3D T2-weighted fluid-attenuated inversion-recovery (FLAIR) fast spin-echo with axial reformats, a transverse T2-weighted fast spin-echo, a transverse T2∗ susceptibility sequence, and diffusion weighted imaging/EPI were carried out. The images were evaluated with respect to global cortical atrophy (GCA) using a 4-point scale and classified as consistent with frontotemporal dementia or not. 18-F FDG-PET scans were made on an ECAT EXACT HR+ scanner (Siemens/CTI). [18F]FDG-PET-scans were assessed visually and interpreted by an experienced nuclear medicine physician on frontal and/or anterior temporal hypometabolism based on the summed images of all the frames.								
Results	**True positives:**	26	**False negatives:**	1	**False positives:**	23	**True negatives:**	61
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	High	**Flow and timing:**	High
Overall risk of bias	Serious (19% study population was excluded from analysis and it is unclear whether a consecutive or random group of patients was enrolled or whether inappropriate exclusions were avoided; all test results (including the index tests) were used to reach the clinical diagnosis.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Vijverberg EGB, Wattjes MP, Dols A, Krudop WA, Moller C, Peters A, Kerssens CJ et al. Diagnostic Accuracy of MRI and Additional [18F]FDG-PET for Behavioral Variant Frontotemporal Dementia in Patients with Late Onset Behavioral Changes. Journal of Alzheimer's Disease, 2016b; 53: 1287–1297.								
Index Test: MRI MRI was carried out using 3T Signa HDxt whole-body MRI system GE Medical Systems. Image acquisition included an established standard MRI protocol for memory clinic patients. Sagittal 3D heavily T1-weighted gradient-echo sequence with coronal reformats, a sagittal 3D T2-weighted fluid-attenuated inversion-recovery (FLAIR) fast spin-echo with axial reformats, a transverse T2-weighted fast spin-echo, a transverse T2∗ susceptibility sequence, and diffusion weighted imaging/EPI were carried out. The images were evaluated with respect to global cortical atrophy (GCA) using a 4-point scale and classified as consistent with frontotemporal dementia or not.								
Results	**True positives:**	19	**False negatives:**	8	**False positives:**	6	**True negatives:**	78
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	High	**Flow and timing:**	High
Overall risk of bias	Serious (19% study population was excluded from analysis and it is unclear whether a consecutive or random group of patients was enrolled or whether inappropriate exclusions were avoided; all test results (including the index tests) were used to reach the clinical diagnosis.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

P.1.21 W

Walker Z, Jaros E, Walker RWH, Lee L, Costa DC, Livingston, G et al. Dementia with Lewy bodies: a comparison of clinical diagnosis, FP-CIT single photon emission computed tomography imaging and autopsy. J Neurol Neurosurg Psychiatry 2007;78:1176–1181.	
Study type	Retrospective cohort
Country	UK
Setting	Not stated
Inclusion criteria	People diagnosed with dementia who have FP-CIT SPECT data and autopsy confirmation of diagnosis.
Exclusion criteria	None stated
Sex	30.0% male

Walker Z, Jaros E, Walker RWH, Lee L, Costa DC, Livingston, G et al. Dementia with Lewy bodies: a comparison of clinical diagnosis, FP-CIT single photon emission computed tomography imaging and autopsy. J Neurol Neurosurg Psychiatry 2007;78:1176–1181.								
Age	Mean age 77.3 years (SD 9.0)							
Presentation	Suspected dementia							
Reference standard	The neuropathological diagnostic criteria employed for AD included the following: CERAD (Consortium to Establish a Registry for Alzheimer's Disease) score and diagnosis, Braak stage18 and NIA-RI (National Institute on Aging and Reagan Institute) AD diagnosis. The neuropathological diagnostic criteria employed for DLB were those recommended by the Third report of the DLB Consortium (McKeith, 2005).							
DLB versus non-DLB dementias								
Index Test: 123I-FP-CIT SPECT FP-CIT SPECT, visual rating of scans. Imaged using a Strichman Medical Equipment 810.The Strichman camera consists of 12 individual detectors, each equipped with a focusing collimator.								
Results	**True positives:**	7	**False negatives:**	1	**False positives:**	2	**True negatives:**	10
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: 123I-FP-CIT SPECT FP-CIT SPECT, semi-quantitatively analysed scans. Imaged using a Strichman Medical Equipment 810.The Strichman camera consists of 12 individual detectors, each equipped with a focusing collimator. For the analysis of striatal binding, the ratio of specific to non-specific binding was calculated. An abnormal scan, signifying a more likely diagnosis of DLB, was defined as a scan with semi-quantitative binding in the posterior putamen (right and left), which was more than 2 SDs below the mean of the controls.								
Results	**True positives:**	7	**False negatives:**	1	**False positives:**	0	**True negatives:**	12
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient**	Low	**Index test:**	Low	**Reference**	Low		

Walker Z, Jaros E, Walker RWH, Lee L, Costa DC, Livingston, G et al. Dementia with Lewy bodies: a comparison of clinical diagnosis, FP-CIT single photon emission computed tomography imaging and autopsy. J Neurol Neurosurg Psychiatry 2007;78:1176–1181.								
	selection:				**standard:**			
Overall indirectness	Not serious							
Index Test: 123I-FP-CIT SPECT FP-CIT SPECT, semi-quantitatively analysed scans with abnormal binding on one side allowed. Imaged using a Strichman Medical Equipment 810.The Strichman camera consists of 12 individual detectors, each equipped with a focusing collimator. For the analysis of striatal binding, the ratio of specific to non-specific binding was calculated. An abnormal scan, signifying a more likely diagnosis of DLB, was defined as having posterior putamen binding on just one side (either right or left) more than 2 SDs below the mean of the controls (ie, ,2.91).								
Results	**True positives:**	8	**False negatives:**	0	**False positives:**	1	**True negatives:**	11
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Low	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Not serious							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Walker RWH, Walker Z. Dopamine transporter single photon emission computerized tomography in the diagnosis of dementia with Lewy bodies. Movement Disorders 2009; 24: S754–9.	
Study type	Retrospective cohort
Country	UK
Setting	Institute of Nuclear Medicine, University College London Medical School
Inclusion criteria	Patients with dementia fulfilling at least one of the Consensus DLB criteria or NINCDS-ADRDA criteria
Exclusion criteria	None stated
Sex	30.0% male

Walker RWH, Walker Z. Dopamine transporter single photon emission computerized tomography in the diagnosis of dementia with Lewy bodies. Movement Disorders 2009; 24: S754–9.								
Age	Not stated							
Presentation	Patients with previously diagnosed DLB or AD							
Reference standard	The neuropathological diagnostic criteria employed for AD included the following: CERAD (Consortium to Establish a Registry for Alzheimer's Disease) score and diagnosis, Braak stage and NIA-RI (National Institute on Aging and Reagan Institute) AD diagnosis. The neuropathological diagnostic criteria employed for DLB were those recommended by the Third report of the DLB Consortium.							
DLB vs no-DLB								
Index Test: 123I-FP-CIT SPECT 123I-FP-CIT SPECT scan using a Strichman Medical Equipment 810 camera. Scanning took place 3 to 4 hours after injection of DaTscanT M. All scans were subject to a semi-quantitative analysis, interpreted by a specialist in nuclear medicine. An abnormal scan on semi-quantitative analysis was defined as having binding > 2 SDs below that of healthy controls in the posterior putamen on 1 or both sides.								
Results	**True positives:**	10	**False negatives:**	0	**False positives:**	1	**True negatives:**	12
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Some of the included individuals had a presumed dementia diagnosis at baseline)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

P.1.22 Y

Yakushev I, Bartenstein, P, Siessmeier T, Hiemke C, Scheurich A, Lotz J, Fellgiebel A, Muller MJ. Cerebrospinal Fluid Tau Protein Levels and 18 F-Fluorodeoxyglucose Positron Emission Tomography in the Differential Diagnosis of Alzheimer's Disease.	
Study type	Prospective cohort
Country	Germany
Setting	Memory clinic

Yakushev I, Bartenstein, P, Siessmeier T, Hiemke C, Scheurich A, Lotz J, Fellgiebel A, Muller MJ. Cerebrospinal Fluid Tau Protein Levels and 18 F-Fluorodeoxyglucose Positron Emission Tomography in the Differential Diagnosis of Alzheimer's Disease.							
Inclusion criteria	Consecutive referrals to the memory clinic.						
Exclusion criteria	Not stated						
Sex	60.0% male						
Age	Mean age 67.0 years (SD 10.9)						
Presentation	Suspected dementia						
Reference standard	Patients were diagnosed with AD according to NINCDS-ADRDA criteria; MCI according to Petersen criteria; vascular dementia according to NINDS-AIREN criteria; frontotemporal dementia according to Lund-Manchester criteria.						
AD versus no dementia (excludes MCI)							
Index Test: Total Tau CSF total tau (INNOTEST hTau- Ag ELISA), cut-off >520ng/l							
Results	**True positives:**	11	**False negatives:**	13	**False positives:**	1	**True negatives:** 21
Additional comments	p-tau 181 data not analysed as AD versus non-dementia and AD versus other dementias do not have the same sensitivity despite sharing the same test cut-off (>65ng/l)						
Risk of bias	**Patient selection:**	Low	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:** High
Overall risk of bias	Very serious (Subgroup analysis with >10% population excluded; use of optimised thresholds for test)						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	
Overall indirectness	Not serious						
AD versus non-AD dementias (excludes MCI)							
Index Test: Total Tau CSF total tau (INNOTEST hTau- Ag ELISA), cut-off >440ng/l							
Results	**True positives:**	13	**False negatives:**	11	**False positives:**	1	**True negatives:** 12
Additional comments	p-tau 181 data not analysed as AD versus non-dementia and AD versus other dementias do not have the same sensitivity despite sharing the same test cut-off (>65ng/l)						
Risk of bias	**Patient**	Low	**Index test:**	High	**Reference**	Low	**Flow and** High

Yakushev I, Bartenstein, P, Siessmeier T, Hiemke C, Scheurich A, Lotz J, Fellgiebel A, Muller MJ. Cerebrospinal Fluid Tau Protein Levels and 18 F-Fluorodeoxyglucose Positron Emission Tomography in the Differential Diagnosis of Alzheimer's Disease.								
	selection:				**standard:**		**timing:**	
Overall risk of bias	Very serious (Subgroup analysis with >10% population excluded; use of optimised thresholds for test)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus no dementia (excludes MCI)								
Index Test: FDG-PET FDG-PET images taken using a Siemens ECAT EXACT scanner in 3-D mode. The PET scans were processed using Neurostat software. After image realignment and spatial normalization, grey matter activities were extracted to predefined surface pixels using a 3-D stereotactic surface projection (3D-SSP) technique. The findings were finally rated as AD-typical or not AD-typical.								
Results	**True positives:**	19	**False negatives:**	5	**False positives:**	2	**True negatives:**	20
Additional comments	p-tau 181 data not analysed as AD versus non-dementia and AD versus other dementias do not have the same sensitivity despite sharing the same test cut-off (>65ng/l)							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with >10% population excluded)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus non-AD dementias (excludes MCI)								
Index Test: FDG-PET FDG-PET images taken using a Siemens ECAT EXACT scanner in 3-D mode. The PET scans were processed using Neurostat software. After image realignment and spatial normalization, grey matter activities were extracted to predefined surface pixels using a 3-D stereotactic surface projection (3D-SSP) technique. The findings were finally rated as AD-typical or not AD-typical.								
Results	**True positives:**	19	**False negatives:**	5	**False positives:**	0	**True negatives:**	13
Additional comme	p-tau 181 data not analysed as AD versus non-dementia and AD versus other dementias do not have the same sensitivity despite							

Yakushev I, Bartenstein, P, Siessmeier T, Hiemke C, Scheurich A, Lotz J, Fellgiebel A, Muller MJ. Cerebrospinal Fluid Tau Protein Levels and 18 F-Fluorodeoxyglucose Positron Emission Tomography in the Differential Diagnosis of Alzheimer's Disease.								
nts	sharing the same test cut-off (>65ng/l)							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with >10% population excluded)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
AD versus other groups (non-AD dementias and no dementia, excludes MCI)								
Index Test: FDG-PET FDG-PET images taken using a Siemens ECAT EXACT scanner in 3-D mode. The PET scans were processed using Neurostat software. After image realignment and spatial normalization, grey matter activities were extracted to predefined surface pixels using a 3-D stereotactic surface projection (3D-SSP) technique. The findings were finally rated as AD-typical or not AD-typical.								
Results	**True positives:**	19	**False negatives:**	5	**False positives:**	2	**True negatives:**	33
Additional comments	p-tau 181 data not analysed as AD versus non-dementia and AD versus other dementias do not have the same sensitivity despite sharing the same test cut-off (>65ng/l) Data presented with different cut-offs for MCI so could not include MCI results in AD versus all other groups comparison.							
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Serious (Subgroup analysis with >10% population excluded)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Yeung PY, Wong LL, Chan CC, Leung JLM, Yung CY. A validation study of the Hong Kong version of Montreal Cognitive Assessment (HK-MoCA) in Chinese older adults in Hong Kong. Hong Kong Med J 2014; 20: 504–10.	
Study type	Prospective cohort
Country	China

Yeung PY, Wong LL, Chan CC, Leung JLM, Yung CY. A validation study of the Hong Kong version of Montreal Cognitive Assessment (HK-MoCA) in Chinese older adults in Hong Kong. Hong Kong Med J 2014; 20: 504–10.								
Setting	Cognition clinic and memory clinic of a public hospital in Hong Kong							
Inclusion criteria	Cantonese-speaking Chinese adults aged 60 years or above, who were seen for suspected cognitive impairment and gave consent, were recruited.							
Exclusion criteria	Patients were excluded if they had a history, as documented in medical records, of neurodegenerative disorders, central nervous system infection, brain tumour, significant head trauma, subdural haematoma, epilepsy, significant psychiatric disorders (such as major depression or schizophrenia), substance abuse, or alcoholism. People who were unable to use a pen or with communication barriers such as deafness or significant language or speech problem were also excluded. Last of all, advanced dementia patients with Global Deterioration Scale (GDS) stage 6 or above were not recruited.							
Sex	40.0% male							
Age	Mean age 77.4 years (SD 7.5)							
Presentation	Suspected dementia							
Reference standard	The DSM-IV criteria was used to diagnose dementia and the Petersen criteria (1999) for MCI.							
Dementia versus no dementia (including MCI)								
Index Test: Montreal Cognitive Assessment, MoCA (<22) Hong-Kong version of MoCA, cut off 21/22								
Results	**True positives:**	130	**False negatives:**	0	**False positives:**	90	**True negatives:**	52
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	Low
Overall risk of bias	Serious (Unclear whether patients were selected randomly or consecutively or whether inappropriate exclusions were avoided; the optimal index test thresholds were determined during the study; it is unclear whether the index test results and reference test results were assessed independently of each other.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Dementia versus no dementia (excluding MCI)								
Index Test: Montreal Cognitive Assessment, MoCA (<19)								

Yeung PY, Wong LL, Chan CC, Leung JLM, Yung CY. A validation study of the Hong Kong version of Montreal Cognitive Assessment (HK-MoCA) in Chinese older adults in Hong Kong. Hong Kong Med J 2014; 20: 504–10.								
Hong-Kong version of MoCA, cut off 18/19								
Results	**True positives:**	120	**False negatives:**	10	**False positives:**	4	**True negatives:**	45
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Very serious (Unclear whether patients were selected randomly or consecutively or whether inappropriate exclusions were avoided; the optimal index test thresholds were determined during the study; it is unclear whether the index test results and reference test results were assessed independently of each other: subgroup analysis was carried out with >10% population (MCI) being excluded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<25) Cantonese MMSE, cut off 24/25								
Results	**True positives:**	124	**False negatives:**	6	**False positives:**	5	**True negatives:**	44
Additional comments	Cantonese MMSE, cut off 26/27 -data for dementia plus MCI versus no dementia and MCI versus normal control cannot be used to calculate dementia versus no dementia (including MCI) as the specificity is not consistent between tests at with the same cut off and population.							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Very serious (Unclear whether patients were selected randomly or consecutively or whether inappropriate exclusions were avoided; the optimal index test thresholds were determined during the study; it is unclear whether the index test results and reference test results were assessed independently of each other: subgroup analysis was carried out with >10% population (MCI) being excluded.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

P.1.23 Z

Zerr I, Bodemer M, Gefeller O, et al. Detection of 14-3-3 protein in the cerebrospinal fluid supports the diagnosis of Creutzfeldt-Jakob disease. Ann Neurol 1998; 43: 32– 40.								
Study type	Prospective cohort							
Country	Germany							
Setting	German National Surveillance unit							
Inclusion criteria	People referred for diagnosis with suspected CJD							
Exclusion criteria	Not stated							
Sex	28.4% male							
Age	Median ages range from 38 to 67 across the diagnostic groups							
Presentation	Rapidly progressive dementia leading to suspected CJD							
Reference standard	Criteria for CJD based on Masters et al. (1979), Will et al. (1998), Zerr (1996) and Steinhoff et al. (1996)							
CJD (including possible CJD) versus not-CJD								
Index Test: CSF 14-3-3 immunoblotting CSF 14-3-3 protein detected by immunoblotting with any ambiguous results defined as positive								
Results	**True positives:**	161	**False negatives:**	24	**False positives:**	7	**True negatives:**	97
Additional comments	The healthy control group was excluded as they did not have suspected CJD at baseline							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Serious (The assay used an optimised cut-off. It was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
CJD (excluding possible CJD) versus not-CJD								

Zerr I, Bodemer M, Gefeller O, et al. Detection of 14-3-3 protein in the cerebrospinal fluid supports the diagnosis of Creutzfeldt-Jakob disease. Ann Neurol 1998; 43: 32– 40.								
Index Test: CSF 14-3-3 immunoblotting CSF 14-3-3 protein detected by immunoblotting with any ambiguous results defined as positive								
Results	**True positives:**	132	**False negatives:**	13	**False positives:**	7	**True negatives:**	97
Additional comments	The healthy control group was excluded as they did not have suspected CJD at baseline							
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Unclear	**Flow and timing:**	High
Overall risk of bias	Very serious (The assay used an optimised cut-off and a subgroup analysis was carried out with >10% population excluded. It was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Zerr I, Pocchiari M, Collins S, et al. Analysis of EEG and CSF 14-3-3 proteins as aids to the diagnosis of Creutzfeldt-Jakob disease. Neurology 2000; 55: 811– 815.	
Study type	Retrospective cohort
Country	Multi-country (Australia, UK, France, Italy, Germany, Austria, Spain)
Setting	Multiple National CJD surveillance units
Inclusion criteria	Patients referred to various National surveillance units with suspected CJD.
Exclusion criteria	Not stated
Sex	Not stated
Age	Not stated
Presentation	Rapidly progressive dementia leading to suspected CJD
Reference standard	Criteria for CJD based on Masters et al. (1979) and Will et al. (1998)

Zerr I, Pocchiari M, Collins S, et al. Analysis of EEG and CSF 14-3-3 proteins as aids to the diagnosis of Creutzfeldt-Jakob disease. Neurology 2000; 55: 811– 815.								
CJD versus not CJD								
Index Test: CSF 14-3-3 immunoblotting CSF 14-3-3 protein detected by immunoblotting								
Results	**True positives:**	497	**False negatives:**	114	**False positives:**	34	**True negatives:**	358
Risk of bias	**Patient selection:**	Unclear	**Index test:**	Unclear	**Reference standard:**	Low	**Flow and timing:**	Low
Overall risk of bias	Serious (It was unclear whether the index tests were interpreted independently of the reference test results; it was unclear whether a consecutive or random sample of people were enrolled or inappropriate exclusions avoided; or the index test threshold was pre-specified.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							

Zerr I, Kallenberg K, Summers DM, Romero C, Taraturo A, Heinemann U et al. Updated clinical diagnostic criteria for sporadic Creutzfeldt-Jakob disease. Brain 2009: 132; 2659–2668.	
Study type	Retrospective cohort
Country	Germany
Setting	National TSE reference centre
Inclusion criteria	Patients were recruited from 12 countries. For the CJD cases: (i) CJD diagnosis confirmed by brain pathology (definite cases) or fulfilling accepted case definition criteria for 'probable' sCJD (data used for a separate set of analyses); (ii) molecular subtype determined by codon 129 genotyping (MM, MV or VV) and western blot analysis of brain pathogenic prion protein (PrPSc) type (1 or 2) (corresponding to MM1, MM2, MV1, MV2, VV1 and VV2 subtype). For the control group: (i) cases in which the diagnosis of sCJD was suspected (patients classified at least as probable or possible CJD) but excluded on follow up by clinical investigations (improvement or recovery, inflammatory CSF findings, other diagnosis) or at autopsy; and (ii) available FLAIR or DWI brain MRI.
Exclusion criteria	Not stated
Sex	45.8% male
Age	Median age of CJD patients 64.0 years (range 35.3-85.0); non-CJD cases 65.9 years (range 25.9-91.5)
Presentation	Suspected CJD

Zerr I, Kallenberg K, Summers DM, Romero C, Taraturo A, Heinemann U et al. Updated clinical diagnostic criteria for sporadic Creutzfeldt-Jakob disease. Brain 2009: 132; 2659–2668.								
Reference standard	Patients were diagnosed using brain pathology or by clinician diagnosis using the criteria for probable CJD, codon 129 genotyping and W. blot analysis of brain pathogenic prion protein.							
CJD versus no CJD								
Index Test: WHO CJD criteria WHO criteria for sporadic CJD. 14-3-3 was detected by immunoblotting and EEG (periodic sharp wave complexes) were measured. EEG typical & 14-3-3 test positive for CJD.								
Results	**True positives:**	95	**False negatives:**	8	**False positives:**	15	**True negatives:**	37
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Unclear whether patients were selected randomly or consecutively or whether inappropriate exclusions were avoided; the optimal index test thresholds were determined during the study and a subgroup analysis was used to determine test sensitivity and specificity.)							
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low		
Overall indirectness	Not serious							
Index Test: New criteria for sporadic CJD New criteria for sporadic CJD (EEG, 14-3-3 and MRI FLAIR and DWI). 14-3-3 was detected by immunoblotting and EEG (periodic sharp wave complexes) were measured. For MRI a standardized protocol was used which included seven cerebral cortex regions. Current criteria positive & MRI positive for positive CJD diagnosis.								
Results	**True positives:**	49	**False negatives:**	1	**False positives:**	7	**True negatives:**	17
Additional comments								
Risk of bias	**Patient selection:**	Unclear	**Index test:**	High	**Reference standard:**	Low	**Flow and timing:**	High
Overall risk of bias	Very serious (Unclear whether patients were selected randomly or consecutively or whether inappropriate exclusions were avoided; the optimal index test thresholds were determined during the study and a subgroup analysis was used to determine test sensitivity and specificity.)							

Zerr I, Kallenberg K, Summers DM, Romero C, Taraturo A, Heinemann U et al. Updated clinical diagnostic criteria for sporadic Creutzfeldt-Jakob disease. Brain 2009: 132; 2659–2668.						
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low
Overall indirectness	Not serious					

Zwan MD, Bouwman FH, Konijnberg E, van der Flier WM, et al. Diagnostic impact of [18F]flutemetamol PET in early-onset dementia. Alzheimer's Research & Therapy 2017; 9: 2								
Study type	Prospective cohort							
Country	Netherlands							
Setting	Memory clinic							
Inclusion criteria	Consecutive series of patients visiting a memory clinic with suspected mild dementia (defined as Mini Mental State Examination (MMSE) score ≥ 18) or early-onset dementia (defined by age at diagnosis ≤ 70 years), who had no firm diagnosis after the standardized dementia evaluation or persisting diagnostic uncertainty (defined as pre-PET diagnostic confidence < 90% as measured by a standardised study questionnaire).							
Exclusion criteria	People with suspected dementia and diagnostic confidence after standardised work-up > 90%.							
Sex	55% male							
Age	Mean age 62 years (SD 6)							
Presentation	Suspected dementia							
Reference standard	Clinical diagnosis was established using clinical criteria (Roman et al. 1993, McKeith et al 2005, Boeve etal 2003, Litvan et al 1996) without knowledge of PET or CSF results or APOE carrier status.							
AD versus non-AD								
Index Test: [18F] flutemetamol PET [18F] flutemetamol PET scans were made on a Gemini TF-64 PET/CT scanner. Patients underwent a low-dose CT scan followed by a 20-minute (i.e., 4 frames of 5 minutes) PET scan. Scans were checked for movement and frames were summed to obtain a static (20-minute) image for each patient. Scans were visually assessed and dichotomously rated as either amyloid positive or amyloid-negative by the local nuclear medicine physician, who completed the training program for visual interpretation of [18F]flutemetamol images.								
Results	**True positives:**	110	**False negatives:**	34	**False positives:**	23	**True negatives:**	44
Risk of bias	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low	**Flow and timing:**	Low

Zwan MD, Bouwman FH, Konijnberg E, van der Flier WM, et al. Diagnostic impact of [18F]flutemetamol PET in early-onset dementia. Alzheimer's Research & Therapy 2017; 9: 2						
Overall risk of bias	Not serious					
Indirectness	**Patient selection:**	Low	**Index test:**	Low	**Reference standard:**	Low
Overall indirectness	Not serious					

P.2 GRADE tables

P.2.1 Dementia versus no dementia

P.2.1.1 10-point Cognitive Screener (10-CS) (≤5)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Apolinario 2015)	Prospective	230	0.69 (0.59, 0.77)	0.94 (0.88, 0.97)	**LR+**	10.67 (5.40, 21.12)	Serious	n/a	Serious	Not serious	-	LOW
					LR-	0.33 (0.25, 0.44)	Serious	n/a	Serious	Not serious		LOW

Notes on risk of bias
Apolinario 2015: Optimised thresholds were calculated and people with moderate to severe dementia were excluded from the study.
Notes on indirectness
Apolinario 2015: Included patients were selected to be ≥ 60 years old and had on average only 4.7 years of schooling

P.2.1.2 10-point Cognitive Screener (10-CS) (≤7)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Apolinario 2015)	Prospective	230	0.94 (0.88, 0.97)	0.60 (0.51, 0.68)	**LR+**	2.34 (1.88, 2.91)	Serious	n/a	Serious	Serious	-	VERY LOW
					LR-	0.09 (0.04, 0.21)	Serious	n/a	Serious	Not serious		LOW

Notes on risk of bias
Apolinario 2015: Optimised thresholds were calculated and people with moderate to severe dementia were excluded from the study.
Notes on indirectness
Apolinario 2015: Included patients were selected to be ≥ 60 years old and had on average only 4.7 years of schooling

P.2.1.3 10-point Cognitive Screener (10-CS) (≤8)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Apolinario 2015)	Prospective	230	0.97 (0.92, 0.99)	0.40 (0.32, 0.49)	**LR+**	1.63 (1.40, 1.89)	Serious	n/a	Serious	Not serious	-	LOW
					LR-	0.07 (0.02, 0.22)	Serious	n/a	Serious	Not serious		LOW

Notes on risk of bias
Apolinario 2015: Optimised thresholds were calculated and people with moderate to severe dementia were excluded from the study.
Notes on indirectness
Apolinario 2015: Included patients were selected to be ≥ 60 years old and had on average only 4.7 years of schooling

P.2.1.4 6 item screener (≥0)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Callahan 2002)	Prospective	651	1.00 (0.98, 1.00)	0.00 (0.00, 0.03)	**LR+**	1.00 (0.99, 1.01)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.89 (0.02, 44.58)	Serious	n/a	Not serious	V. serious		VERY LOW
Notes on risk of bias Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.												

P.2.1.5 6 item screener (≥1)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Callahan 2002)	Prospective	651	0.97 (0.94, 0.98)	0.53 (0.48, 0.59)	**LR+**	2.07 (1.84, 2.34)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.06 (0.03, 0.11)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.												

P.2.1.6 6 item screener (≥2)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Callahan 2002)	Prospective	651	0.90 (0.86, 0.92)	0.79 (0.75, 0.84)	**LR+**	4.35 (3.48, 5.44)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.13 (0.10, 0.18)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.												

P.2.1.7 6 item screener (≥3)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Callahan 2002)	Prospective	651	0.81 (0.76, 0.84)	0.91 (0.87, 0.94)	**LR+**	8.81 (6.16, 12.58)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.21 (0.17, 0.27)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.												

P.2.1.8 6 item screener (≥4)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Callahan 2002)	Prospective	651	0.68 (0.62, 0.72)	0.96 (0.93, 0.98)	**LR+**	17.22 (9.84, 30.13)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.34 (0.29, 0.39)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.												

P.2.1.9 6 item screener (≥5)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Callahan 2002)	Prospective	651	0.49 (0.44, 0.54)	0.99 (0.97, 1.00)	**LR+**	37.47 (14.07, 99.80)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.52 (0.47, 0.57)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.												

P.2.1.10 6 item screener (≥6)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Callahan 2002)	Prospective	651	0.30 (0.26, 0.35)	0.99 (0.97, 1.00)	**LR+**	46.57 (11.59, 187.06)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.70 (0.65, 0.75)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.												

P.2.1.11 6-item Cognitive Impairment Test (6CIT) (>9)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Abdel-Aziz 2015)	Prospective	245	0.88 (0.75, 0.94)	0.78 (0.72, 0.83)	**LR+**	4.01 (3.01, 5.33)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.16 (0.08, 0.34)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.1.12 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA												
1 study (Dobert 2005)	Prospective	24	0.89 (0.65, 0.97)	0.33 (0.08, 0.73)	**LR+**	1.33 (0.74, 2.40)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.33 (0.06, 1.88)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Dobert 2005: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided.												

P.2.1.13 Addenbrooke's Cognitive Examination, ACE (<75)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Larner 2007)	Prospective	285	0.85 (0.78, 0.90)	0.83 (0.76, 0.88)	**LR+**	4.93 (3.43, 7.09)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.18 (0.12, 0.27)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.1.14 Addenbrooke's Cognitive Examination, ACE (<83)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Larner 2007; Mathuranath 2000)	2 × prospective	424	0.91 (0.67, 0.98)	0.84 (0.29, 0.98)	**LR+**	5.62 (0.81, 39.07)	Serious	Serious	Not serious	Serious	-	VERY LOW
					LR-	0.12 (0.04, 0.33)	Serious	Serious	Not serious	Not serious		LOW
Notes on risk of bias Mathuranath 2000: Optimised test-threshold used and it was unclear whether the index test results were interpreted without knowledge of the results of the reference standard.												

P.2.1.15 Addenbrooke's Cognitive Examination, ACE (<88)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Larner 2007; Mathuranath 2000)	2 × prospective	424	0.98 (0.71, 1.00)	0.56 (0.29, 0.80)	**LR+**	2.18 (1.23, 3.85)	Serious	Serious	Not serious	Serious	-	VERY LOW
					LR-	0.04 (0.00, 0.42)	Serious	Serious	Not serious	Not serious		LOW
Notes on risk of bias Mathuranath 2000: Optimised test-threshold used and it was unclear whether the index test results were interpreted without knowledge of the results of the reference standard.												

P.2.1.16 Addenbrooke's Cognitive Examination-III, ACE- III (<81)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Jubb 2015)	Prospective	59	0.81 (0.61, 0.92)	0.97 (0.81, 1.00)	**LR+**	26.65 (3.83, 185.32)	Serious	n/a	Serious	Not serious	-	LOW
					LR-	0.20 (0.09, 0.44)	Serious	n/a	Serious	Not serious		LOW
Notes on risk of bias Jubb 2015: Optimised threshold used for analysis. **Notes on indirectness** Jubb 2015: Study population was confined to >75 years												

P.2.1.17 Addenbrooke's Cognitive Examination-III, ACE- III (<82)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Jubb 2015)	Prospective	59	0.81 (0.61, 0.92)	0.70 (0.52, 0.83)	**LR+**	2.67 (1.54, 4.62)	Not serious	n/a	Serious	Serious	-	LOW
					LR-	0.28 (0.12, 0.63)	Not serious	n/a	Serious	Serious		LOW
Notes on indirectness Jubb 2015: Study population was confined to >75 years												

P.2.1.18 Addenbrooke's Cognitive Examination-III, ACE- III (<84)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Jubb 2015)	Prospective	59	0.92 (0.74, 0.98)	0.61 (0.43, 0.76)	**LR+**	2.34 (1.51, 3.63)	Serious	n/a	Serious	Serious	-	VERY LOW
					LR-	0.13 (0.03, 0.49)	Serious	n/a	Serious	Not serious		LOW
Notes on risk of bias Jubb 2015: Optimised threshold used for analysis. **Notes on indirectness** Jubb 2015: Study population was confined to >75 years												

P.2.1.19 Addenbrooke's Cognitive Examination-III, ACE- III (<88)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Jubb 2015)	Prospective	60	0.96 (0.77, 0.99)	0.50 (0.34, 0.66)	**LR+**	1.92 (1.36, 2.71)	Not serious	n/a	Serious	Serious	-	LOW
					LR-	0.08 (0.01, 0.54)	Not serious	n/a	Serious	Serious		LOW
Notes on indirectness Jubb 2015: Study population was confined to >75 years												

P.2.1.20 Addenbrooke's Cognitive Examination-Revised, ACE-R (<74)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Hancock 2011)	Prospective	140	0.90 (0.76, 0.96)	0.93 (0.86, 0.97)	**LR+**	12.95 (6.29, 26.67)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.11 (0.04, 0.28)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Hancock 2011: Optimised test threshold.												

P.2.1.21 Addenbrooke's Cognitive Examination-Revised, ACE-R (<83)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Bastide 2012; Terpening 2011)	2 × prospective	442	0.87 (0.69, 0.95)	0.73 (0.61, 0.82)	**LR+**	3.04 (2.48, 3.73)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.18 (0.08, 0.39)	Serious	Serious	Not serious	Not serious		LOW
Notes on risk of bias Terpening 2011: Patients lacking a clinical diagnosis were excluded from the analysis Bastide 2012: Optimised test cut-offs used.												

P.2.1.22 Addenbrooke's Cognitive Examination-Revised, ACE-R (<85)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Terpening 2011)	Prospective	122	0.85 (0.76, 0.91)	0.80 (0.65, 0.90)	**LR+**	4.27 (2.28, 7.98)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.18 (0.11, 0.32)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Terpening 2011: Patients lacking a clinical diagnosis were excluded from the analysis												

P.2.1.23 Addenbrooke's Cognitive Examination-Revised, ACE-R (<89)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Terpening 2011)	Prospective	122	0.91 (0.83, 0.96)	0.68 (0.52, 0.80)	**LR+**	2.81 (1.79, 4.42)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.13 (0.06, 0.27)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Terpening 2011: Patients lacking a clinical diagnosis were excluded from the analysis												

P.2.1.24 AD8 (≥2)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Larner 2015)	Prospective	212	0.97 (0.89, 0.99)	0.11 (0.07, 0.17)	**LR+**	1.09 (1.02, 1.17)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.26 (0.06, 1.10)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.1.25 Abbreviated Mental Test, AMT (<10)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Flicker 1997)	Prospective	299	0.97 (0.94, 0.99)	0.28 (0.19, 0.38)	**LR+**	1.34 (1.17, 1.54)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.10 (0.04, 0.24)	V. serious	n/a	Not serious	Not serious		LOW

Notes on risk of bias

Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.

P.2.1.26 Abbreviated Mental Test, AMT (<7)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Flicker 1997)	Prospective	299	0.58 (0.52, 0.65)	0.87 (0.78, 0.93)	**LR+**	4.40 (2.51, 7.72)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.48 (0.40, 0.57)	V. serious	n/a	Not serious	Serious		VERY LOW

Notes on risk of bias

Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.

P.2.1.27 Abbreviated Mental Test, AMT (<8)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Flicker 1997)	Prospective	299	0.73 (0.66, 0.78)	0.71 (0.60, 0.80)	**LR+**	2.51 (1.78, 3.56)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.38 (0.30, 0.50)	V. serious	n/a	Not serious	Not serious		LOW

Notes on risk of bias

Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.

P.2.1.28 Abbreviated Mental Test, AMT (<9)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Flicker 1997)	Prospective	299	0.88 (0.82, 0.91)	0.53 (0.42, 0.63)	**LR+**	1.86 (1.47, 2.35)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.24 (0.16, 0.35)	V. serious	n/a	Not serious	Not serious		LOW

Notes on risk of bias

Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.

P.2.1.29 Amyloid Beta 1-42 and total tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Frisoni 2009)	Prospective	94	0.42 (0.31, 0.55)	0.79 (0.60, 0.90)	**LR+**	1.98 (0.92, 4.25)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.73 (0.55, 0.97)	Serious	n/a	Not serious	Not serious		MODERATE

Notes on risk of bias

Frisoni 2009: Patients whose cognitive deficit reverted (regarded as primarily depressed with secondary cognitive impairment) were excluded from the study; unclear whether reference test was interpreted without knowledge of index test and unclear whether results of index test interpreted without knowledge of reference test.

P.2.1.30 Applause sign (<3)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Bonello 2016)	Prospective	275	0.54 (0.40, 0.67)	0.85 (0.80, 0.89)	**LR+**	3.64 (2.43, 5.45)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.54 (0.40, 0.73)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.1.31 Boston Naming Test, BNT (<13)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.39 (0.28, 0.52)	0.93 (0.88, 0.96)	**LR+**	5.94 (3.12, 11.33)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.65 (0.53, 0.79)	Serious	n/a	Not serious	Not serious		MODERATE

Notes on risk of bias

Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.

P.2.1.32 Boston Naming Test, BNT (<14)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.55 (0.43, 0.66)	0.84 (0.77, 0.89)	**LR+**	3.35 (2.23, 5.05)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.54 (0.41, 0.71)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.												

P.2.1.33 Boston Naming Test, BNT (<15)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.71 (0.59, 0.81)	0.63 (0.55, 0.70)	**LR+**	1.91 (1.49, 2.45)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.46 (0.31, 0.68)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.												

P.2.1.34 Brief Neuropsychological Test Battery

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Coutinho 2013)	Prospective	131	0.91 (0.79, 0.96)	0.83 (0.73, 0.90)	**LR+**	5.43 (3.28, 8.99)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.11 (0.05, 0.26)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.1.35 Clock Drawing Test, CDT, Shulman scoring method (>0)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.86 (0.76, 0.93)	0.52 (0.45, 0.60)	**LR+**	1.81 (1.51, 2.19)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.26 (0.14, 0.49)	Serious	n/a	Not serious	Not serious		MODERATE

Notes on risk of bias

Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.

P.2.1.36 Clock Drawing Test, CDT, Shulman scoring method (>1)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.71 (0.59, 0.81)	0.88 (0.82, 0.92)	**LR+**	5.91 (3.81, 9.17)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.33 (0.22, 0.48)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.												

P.2.1.37 Clock Drawing Test, CDT, Shulman scoring method (>2)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Beinhoff 2005; Milian 2012)	1xprospective 1x retrospective	734	0.55 (0.13, 0.91)	0.97 (0.94, 0.99)	**LR+**	15.66 (6.85, 35.82)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.41 (0.13, 1.28)	Serious	Serious	Not serious	Serious		VERY LOW
Notes on risk of bias Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other. Milian 2012: Unclear whether inappropriate exclusions were avoided; whether the patients were a random or consecutive sample and whether the reference standard result was interpreted without knowledge of the results of the index test.												

P.2.1.38 Clock Drawing Test, CDT, Shulman scoring method (>3)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Berger 2008)	Prospective	462	0.90 (0.86, 0.93)	0.56 (0.48, 0.65)	**LR+**	2.06 (1.69, 2.51)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.18 (0.12, 0.25)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Berger 2008: People who received a final diagnosis of FTD, DLB or MCI were excluded from the study.												

P.2.1.39 Clock Drawing Test, CDT, Watson scoring method (>4)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Berger 2008)	Prospective	462	0.72 (0.67, 0.76)	0.64 (0.55, 0.72)	**LR+**	2.00 (1.57, 2.54)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.44 (0.35, 0.54)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Berger 2008: People who received a final diagnosis of FTD, DLB or MCI were excluded from the study.												

P.2.1.40 Clock Drawing Test, CDT, Wolf-Klein scoring method (<7)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Berger 2008)	Prospective	462	0.58 (0.53, 0.63)	0.81 (0.74, 0.87)	**LR+**	3.10 (2.14, 4.49)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.52 (0.44, 0.60)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Berger 2008: People who received a final diagnosis of FTD, DLB or MCI were excluded from the study.												

P.2.1.41 Clock Drawing Test, CDT, scoring method unclear (<8)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Sager 2006)	Prospective	364	0.72 (0.66, 0.77)	0.83 (0.74, 0.89)	**LR+**	4.10 (2.68, 6.28)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.34 (0.28, 0.42)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.1.42 Clock Drawing Test, CDT, Manos and Wu scoring method (<8)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Berger 2008)	Prospective	462	0.81 (0.77, 0.85)	0.60 (0.51, 0.68))	**LR+**	2.04 (1.64, 2.54)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.31 (0.24, 0.41)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Berger 2008: People who received a final diagnosis of FTD, DLB or MCI were excluded from the study												

P.2.1.43 Clock Drawing Test, Clock Drawing Test, CDT, Manos and Wu scoring method (<9)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Berger 2008)	Prospective	462	0.93 (0.90, 0.95)	0.37 (0.29, 0.45)	**LR+**	1.47 (1.29, 1.68)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.19 (0.12, 0.30)	V. serious	n/a	Not serious	Not serious		LOW
Notes on risk of bias Berger 2008: People who received a final diagnosis of FTD, DLB or MCI were excluded from the study and an optimised threshold was used.												

P.2.1.44 Clock Drawing Test, CDT, Lin scoring method (<3)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Berger 2008)	Prospective	462	0.88 (0.84, 0.91)	0.49 (0.41, 0.58)	**LR+**	1.73 (1.45, 2.07)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.24 (0.17, 0.34)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Berger 2008: People who received a final diagnosis of FTD, DLB or MCI were excluded from the study.												

P.2.1.45 CERAD battery

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Hentschel 2005)	Prospective	100	0.74 (0.60, 0.84)	0.98 (0.87, 1.00)	**LR+**	37.00 (5.28, 259.34)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.27 (0.17, 0.42)	V. serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Hentschel 2005: The index tests were carried out with knowledge of the primary care diagnosis and it is unclear whether pre-specified thresholds were used; the reference standard diagnosis used all available data including the index test results												

P.2.1.46 Computed Tomography, CT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (O'Brien 2000)	Prospective	116	0.54 (0.45, 0.64)	0.77 (0.48, 0.92)	**LR+**	2.36 (0.86, 6.46)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.59 (0.41, 0.85)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.1.47 Functional Activities Questionnaire, FAQ (<9)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Cruz-Orduna 2012)	Prospective	160	0.87 (0.59, 0.97)	0.82 (0.75, 0.87)	**LR+**	4.83 (3.24, 7.22)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.16 (0.04, 0.59)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Cruz-Orduna 2012: Thresholds were not pre-specified but were calculated to give optimum sensitivity and specificity.												

P.2.1.48 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
3 studies (Dobert 2005; Frisoni 2009; Silverman 2001)	3 × prospective	386	0.87 (0.46, 0.98)	0.77 (0.69, 0.84)	**LR+**	3.70 (2.62, 5.22)	Not serious	Not serious	Not serious	Not serious	-	HIGH
					LR-	0.16 (0.03, 0.79)	Serious	Serious	Not serious	Serious		VERY LOW
Notes on risk of bias Dobert 2005: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided. Frisoni 2009: Patients whose cognitive deficit reverted (regarded as primarily depressed with secondary cognitive impairment) were excluded from the study; unclear whether reference test was interpreted without knowledge of index test and unclear whether results of index test interpreted without knowledge of reference test.												

P.2.1.49 Free recall score of 5- word test, ≤ 6 for all dementia

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Mormont 2012)	Prospective	145	0.78 (0.69, 0.85)	0.90 (0.78, 0.96)	**LR+**	7.66 (3.31, 17.69)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.24 (0.16, 0.36)	V. serious	n/a	Not serious	Not serious		LOW
Notes on risk of bias Mormont 2012: Exclusion of >35% population at analysis and use of optimised test thresholds.												

P.2.1.50 Informant Questionnaire on Cognitive Decline, IQCODE (16 item, >3.5)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Garcia 2002; Knaefelc 2003)	2 × prospective	436	0.93 (0.90, 0.96)	0.65 (0.27, 0.91)	**LR+**	2.80 (0.97, 8.10)	Serious	Serious	Not serious	Serious	-	VERY LOW
					LR-	0.12 (0.07, 0.18)	Serious	Not serious	Not serious	Not serious		MODERATE

Notes on risk of bias
Garcia 2002: Inappropriate exclusions at patient selection stage.
Knaefelc 2003: Unclear whether all patients were included in the analysis; unclear interval between index and reference tests; lack of a pre-specified threshold.

P.2.1.51 Informant Questionnaire on Cognitive Decline, IQCODE (16 item, >4.1)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Goncalves 2011)	Prospective	204	0.72 (0.64, 0.78)	0.67 (0.54, 0.79)	**LR+**	2.19 (1.47, 3.28)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.42 (0.31, 0.58)	Serious	n/a	Not serious	Serious		LOW

Notes on risk of bias
Goncalves 2011: The reference diagnosis was not independent of the index tests; optimised test thresholds were used.

P.2.1.52 Informant Questionnaire on Cognitive Decline, IQCODE (26 item, >3.5)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Flicker 1997; Hancock 2009)	2 × prospective	443	0.87 (0.82, 0.90)	0.49 (0.31, 0.67)	**LR+**	1.69 (1.16, 2.47)	V. serious	Serious	Not serious	Serious	-	VERY LOW
					LR-	0.27 (0.17, 0.42)	V. serious	Not serious	Not serious	Not serious		LOW

Notes on risk of bias

Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.
Hancock 2009: An optimised test threshold was used.

P.2.1.53 Informant Questionnaire on Cognitive Decline, IQCODE (26 item, >3.6)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Cruz-Orduna 2012)	Prospective	160	0.80 (0.53, 0.93)	0.77 (0.69, 0.83)	**LR+**	3.14 (2.31, 5.03)	Serious	n/a	Not serious	Not serious		MODERATE
					LR-	0.26 (0.09, 0.72)	Serious	n/a	Not serious	Serious		LOW
SECONDARY CARE												
1 study (Flicker 1997)	Prospective	299	0.81 (0.76, 0.86)	0.61 (0.51, 0.71)	**LR+**	2.11 (1.60, 2.79)	V. serious	n/a	Not serious	Serious		VERY LOW
					LR-	0.30 (0.22, 0.42)	V. serious	n/a	Not serious	Not serious		LOW
ALL EVIDENCE POOLED V. serious												
2 studies (Cruz-Orduna 2012; Flicker 1997)	2x prospective	459	0.81 (0.76, 0.86)	0.70 (0.53, 0.82	**LR+**	2.63 (1.65, 4.20)	V. serious	Serious	Not serious	Serious	-	VERY LOW
					LR-	0.30 (0.22, 0.41)	V. serious	Not serious	Not serious	Not serious		LOW

Notes on risk of bias

Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.
Cruz-Orduna 2012: Thresholds were not pre-specified but were calculated to give optimum sensitivity and specificity

P.2.1.54 Informant Questionnaire on Cognitive Decline, IQCODE (26 item, >3.7)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Flicker 1997)	Prospective	299	0.78 (0.72, 0.83)	0.65 (0.54, 0.75)	**LR+**	2.23 (1.65, 3.01)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.34 (0.25, 0.46)	V. serious	n/a	Not serious	Not serious		LOW

Notes on risk of bias

Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.

P.2.1.55 Informant Questionnaire on Cognitive Decline, IQCODE (26 item, >3.8)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Flicker 1997)	Prospective	299	0.75 (0.68, 0.80)	0.71 (0.60, 0.80)	**LR+**	2.58 (1.82, 3.64)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.36 (0.27, 0.47)	V. serious	n/a	Not serious	Not serious		LOW

Notes on risk of bias

Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.

P.2.1.56 Informant Questionnaire on Cognitive Decline, IQCODE (26 item, >3.9)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Flicker 1997)	Prospective	299	0.70 (0.64, 0.76)	0.75 (0.64, 0.83)	**LR+**	2.78 (1.90, 4.07)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.40 (0.31, 0.50)	V. serious	n/a	Not serious	Serious		VERY LOW

Notes on risk of bias

Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.

P.2.1.57 Informant Questionnaire on Cognitive Decline, IQCODE (26 item, >4.0)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Flicker 1997)	Prospective	299	0.65 (0.58, 0.71)	0.80 (0.69, 0.87)	**LR+**	3.16 (2.05, 4.89)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.44 (0.36, 0.55)	V. serious	n/a	Not serious	Serious		VERY LOW

Notes on risk of bias

Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.

P.2.1.58 Informant Questionnaire on Cognitive Decline, IQCODE (26 item, >4.1)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Flicker 1997)	Prospective	299	0.58 (0.52, 0.65)	0.83 (0.74, 0.90)	**LR+**	3.46 (2.12, 5.65)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.50 (0.42, 0.60)	V. serious	n/a	Not serious	Serious		VERY LOW

Notes on risk of bias

Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.

P.2.1.59 Letter Sorting Test, LST (<1)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.12 (0.06, 0.22)	0.99 (0.95, 1.00)	**LR+**	10.06 (2.19, 46.14)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.89 (0.81, 0.97)	Serious	n/a	Not serious	Not serious		MODERATE

Notes on risk of bias

Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.

P.2.1.60 Letter Sorting Test, LST (<2)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.44 (0.33, 0.56)	0.93 (0.88, 0.96)	**LR+**	6.08 (3.30, 11.18)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.60 (0.49, 0.75)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.												

P.2.1.61 Letter Sorting Test, LST (<3)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.80 (0.69, 0.88)	0.69 (0.61, 0.75)	**LR+**	2.56 (1.99, 3.31)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.29 (0.17, 0.47)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.												

P.2.1.62 Mini-ACE (<26)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Larner 2017)	Prospective	260	0.98 (0.85, 1.00)	0.35 (0.29, 0.42)	**LR+**	1.50 (1.35, 1.67)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.07 (0.01, 0.46)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.1.63 Mini-Cog (≤2)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnero-Pardo 2013)	Prospective	142	0.99 (0.86, 1.00)	0.40 (0.31, 0.50)	**LR+**	1.65 (1.39, 1.95)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.03 (0.00, 0.40)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Carnero-Pardo 2013: The test threshold was not pre-specified, but was optimised based on the data obtained.												

P.2.1.64 Mini-Cog (Scanlan and Borson algorithm)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Milian 2012)	Retrospective	502	0.87 (0.83, 0.90)	0.99 (0.89, 1.00)	**LR+**	112.68 (7.12, 1782.71)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.13 (0.11, 0.17)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Milian 2012: Unclear whether inappropriate exclusions were avoided; whether the patients were a random or consecutive sample and whether the reference standard result was interpreted without knowledge of the results of the index test.												

P.2.1.65 Memory Impairment Screen, MIS (<4)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnero-Pardo 2011)	Prospective	117	0.93 (0.77, 0.98)	0.80 (0.71, 0.87)	**LR+**	4.78 (3.09, 7.39)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.08 (0.02, 0.32)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.1.66 Memory Impairment Screen, MIS (<5)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnero-Pardo 2011)	Prospective	117	0.97 (0.80, 1.00)	0.71 (0.61, 0.80)	**LR+**	3.36 (2.40, 4.71)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.05 (0.01, 0.32)	Not serious	n/a	Not serious	Not serious		HIGH
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.82 (0.71, 0.89)	0.81 (0.75, 0.87)	**LR+**	4.38 (3.13, 6.14)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.22 (0.13, 0.37)	Serious	n/a	Not serious	Not serious		MODERATE
ALL EVIDENCE POOLED												
2 studies (Beinhoff 2005; Carnero-Pardo 2011)	2 × prospective	349	0.90 (0.61, 0.98)	0.77 (0.66, 0.85)	**LR+**	3.84 (2.96, 4.97)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.14 (0.03, 0.57)	Serious	Serious	Not serious	Serious		VERY LOW

Notes on risk of bias
Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.

P.2.1.67 Memory Impairment Screen, MIS (<6)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.88 (0.78, 0.94)	0.70 (0.62, 0.76)	**LR+**	2.92 (2.28, 3.74)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.17 (0.09, 0.33)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.												

P.2.1.68 Memory Impairment Screen, MIS (<7)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.92 (0.83, 0.97)	0.53 (0.45, 0.60)	**LR+**	1.97 (1.65, 2.34)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.14 (0.06, 0.34)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.												

P.2.1.69 Memory Impairment Screen, MIS (<8)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.98 (0.90, 1.00)	0.32 (0.25, 0.39)	**LR+**	1.45 (1.30, 1.61)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.05 (0.01, 0.34)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.												

P.2.1.70 MMSE (<17)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnero-Pardo 2013)	Prospective	360	0.70 (0.59, 0.79)	0.93 (0.89, 0.95)	**LR+**	9.92 (6.35, 15.52)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.32 (0.23, 0.45)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Carnero-Pardo 2013: Multiple test thresholds were used												

P.2.1.71 MMSE (<18)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Cruz-Orduna 2012)	Prospective	360	0.81 (0.70, 0.88)	0.92 (0.88, 0.95)	**LR+**	9.91 (6.60, 14.88)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.21 (0.13, 0.33)	Serious	n/a	Not serious	Not serious		MODERATE
SECONDARY CARE												
1 study (Flicker 1997)	Prospective	299	0.50, 0.43, 0.57)	0.90 (0.82, 0.95)	**LR+**	5.19 (2.65, 10.16)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.55 (0.48, 0.64)	V. serious	n/a	Not serious	Serious		VERY LOW
ALL EVIDENCE POOLED V. serious												
2 studies (Cruz-Orduna 2012; Flicker 1997)	2x prospective	659	0.67 (0.33, 0.89)	0.92 (0.88, 0.94)	**LR+**	7.59 (4.07, 14.17)	V. serious	Serious	Not serious	Not serious	-	VERY LOW
					LR-	0.35 (0.14, 0.90	V. serious	Serious	Not serious	Serious		VERYLOW

Notes on risk of bias

Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.
Cruz-Orduna 2012: Thresholds were not pre-specified but were calculated to give optimum sensitivity and specificity

P.2.1.72 MMSE (<19)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
2 studies (Carnero-Pardo 2013, Cruz-Orduna 2012)	2x prospective	520	0.87 (0.78, 0.92)	0.87 (0.83, 0.90)	**LR+**	6.46 (4.97, 8.38)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.16 (0.09, 0.26)	Serious	Not serious	Not serious	Not serious		MODERATE
SECONDARY CARE												
1 study (Flicker 1997)	Prospective	299	0.56 (0.49, 0.62)	0.97 (0.78, 0.93)	**LR+**	4.19 (2.39, 7.36)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.51 (0.43, 0.61)	V. serious	n/a	Not serious	Serious		VERY LOW
ALL EVIDENCE POOLED V. serious												
2 studies (Carnero-Pardo 2013; Cruz-Orduna 2012; Flicker 1997)	3x prospective	819	0.76 (0.46, 0.93)	0.87 (0.83, 0.89)	**LR+**	5.95 (4.64, 7.62)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.26 (0.10, 0.70)	V. serious	Serious	Not serious	Serious		VERYLOW

Notes on risk of bias

Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.
Cruz-Orduna 2012: Thresholds were not pre-specified but were calculated to give optimum sensitivity and specificity

Carnero-Pardo 2013: Multiple test thresholds were used

P.2.1.73 MMSE (<20)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnero-Pardo 2013)	Prospective	360	0.94 (0.85, 0.97)	0.82 (0.77, 0.86)	**LR+**	5.19 (4.02, 6.70)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.08 (0.03, 0.19)	Serious	n/a	Not serious	Not serious		MODERATE
SECONDARY CARE												
1 study (Flicker 1997)	Prospective	299	0.62 (0.55, 0.68)	0.84 (0.75, 0.91)	**LR+**	3.96 (2.38, 6.60)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.45 (0.37, 0.55)	V. serious	n/a	Not serious	Serious		VERY LOW
ALL EVIDENCE POOLED V. serious												
2 studies (Carnero-Pardo 2013; Flicker 1997)	2x prospective	659	0.82 (0.36, 0.98)	0.82 (0.78, 0.86)	**LR+**	4.92 (3.91, 6.18)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.20 (0.04, 1.09)	V. serious	Serious	Not serious	Serious		VERYLOW

Notes on risk of bias

Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.

Carnero-Pardo 2013: Multiple test thresholds were used

P.2.1.74 MMSE (<21)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnero-Pardo 2013)	Prospective	360	0.95 (0.87, 0.98)	0.73 (0.68, 0.78)	**LR+**	3.53 (2.89, 4.31)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.07 (0.03, 0.18)	Serious	n/a	Not serious	Not serious		MODERATE
SECONDARY CARE												
1 study (Flicker 1997)	Prospective	299	0.69 (0.63, 0.75)	0.76 (0.66, 0.84)	**LR+**	2.86 (1.93, 4.24)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.41 (0.32, 0.52)	V. serious	n/a	Not serious	Serious		VERY LOW
ALL EVIDENCE POOLED V. serious												
2 studies (Carnero-Pardo 2013; Flicker 1997)	2x prospective	659	0.86 (0.43, 0.98)	0.74 (0.69, 0.78)	**LR+**	3.38 (2.83, 4.04)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.18 (0.03, 1.00)	V. serious	Serious	Not serious	Serious		VERYLOW

Notes on risk of bias

Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.

Carnero-Pardo 2013: Multiple test thresholds were used

P.2.1.75 MMSE (<22)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnero-Pardo 2013)	Prospective	360	0.96 (0.89, 0.99)	0.67 (0.61, 0.72)	**LR+**	2.92 (2.46, 3.48)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.06 (0.02, 0.18)	Serious	n/a	Not serious	Serious		MODERATE
3 studies (Callahan 2002; Flicker 1997; Kukull 1994)	3x prospective	1,089	0.69 (0.60, 0.78)	0.94 (0.64, 0.99)	**LR+**	12.43 (1.75, 88.49)	Very serious	Serious	Not serious	Serious	-	VERY LOW
					LR-	0.35 (0.26, 0.46)	Serious	Serious	Not serious	Serious		LOW
ALL EVIDENCE POOLED												
4 studies (Callahan 2002; Carnero-Pardo 2013; Flicker 1997; Kukull 1994)	4 × prospective	1,443	0.76 (0.64, 0.85)	0.89 (0.67, 0.97)	**LR+**	6.54 (2.67, 16.01)	Serious	Serious	Not serious	Not serious	-	LOW
					LR-	0.30 (0.21, 0.43)	Serious	Serious	Not serious	Not serious		LOW

Notes on risk of bias

Kukull 1994: It is unclear whether the index test results were interpreted without knowledge of the results of the reference standard; multiple pre-specified cut offs were used to determine the optimal cut off; the index test result was known during the reference standard diagnosis.
Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.
Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.
Carnero-Pardo 2013: Multiple test thresholds were used

P.2.1.76 MMSE (<23)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnero-Pardo 2013)	1 × prospective	360	0.99 (0.91, 1.00)	0.57 (0.51, 0.63)	**LR+**	2.29 (2.00, 2.62)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.02 (0.00, 0.16)	Serious	n/a	Not serious	Not serious		MODERATE
SECONDARY CARE												
5 studies (Abdel-Aziz 2015; Callahan 2002; Flicker 1997; Kukull 1994; Nielsen 2013)	5 × prospective	1,364	0.67 (0.55, 0.77)	0.89 (0.75, 0.96)	**LR+**	6.79 (2.70, 15.00)	Very serious	Serious	Not serious	Not serious	-	VERY LOW
					LR-	0.38 (0.26, 0.52)	Very serious	Serious	Not serious	Serious		VERY LOW
ALL EVIDENCE POOLED												
6 studies (Abdel-Aziz 2015; Callahan 2002; Carnero-Pardo 2013; Flicker 1997; Kukull 1994; Nielsen 2013)	6 × prospective	1,724	0.75 (0.54, 0.88)	0.85 (0.69, 0.94)	**LR+**	5.47 (2.60, 10.80)	V. serious	Serious	Not serious	Not serious	-	VERY LOW
					LR-	0.31 (0.15, 0.51)	V. serious	Serious	Not serious	Serious		VERY LOW

Notes on risk of bias

Kukull 1994: It is unclear whether the index test results were interpreted without knowledge of the results of the reference standard; multiple pre-specified cut offs were used to determine the optimal cut off; the index test result was known during the reference standard diagnosis.
Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.
Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.
Carnero-Pardo 2013: Multiple test thresholds were used
Nielsen 2013: The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; the test threshold was not pre-specified.
Abdel-Aziz 2015: Subgroup of 6 CIT tested patients were tested with MMSE as well; MMSE cut off was not pre-specified as chosen for comparison to 6CIT test.

P.2.1.77 MMSE (<24)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnero-Pardo 2013)	Prospective	360	0.99 (0.91, 1.00)	0.46 (0.40, 0.52)	**LR+**	1.84 (1.65 2.05)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.08 (0.01, 1.32)	Serious	n/a	Not serious	Not serious		MODERATE
SECONDARY CARE												
11 studies (Bastide 2012; Callahan 2002; Goncalves 2011; Flicker 1997; Hancock 2011; Knaefelc 2003; Kukull 1994; Mathuranath 2000; Nielsen 2013; Postel-Vinay 2014; Sager 2006)	11 × prospective	2,975	0.73 (0.63, 0.81)	0.91 (0.83, 0.96)	**LR+**	8.43 (4.47, 14.80)	Serious	Serious	Not serious	Not serious	-	LOW
					LR-	0.31 (0.23, 0.40)	Serious	Serious	Not serious	Not serious		LOW
ALL EVIDENCE POOLED												
12 studies (Bastide 2012; Callahan 2002; Carnero-Pardo 2013; Flicker 1997; Goncalves 2011; Hancock 2011; Knaefelc 2003; Kukull 1994; Mathuranath 2000; Nielsen 2013; Postel-Vinay 2014; Sager 2006)	12 × prospective	3,335	0.75 (0.65, 0.84)	0.88 (0.78, 0.94)	**LR+**	6.65 (3.70, 11.00)	Serious	Serious	Not serious	Not serious	-	LOW
					LR-	0.29 (0.20, 0.38)	Serious	Serious	Not serious	Not serious		LOW

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
Notes on risk of bias Kukull 1994: It is unclear whether the index test results were interpreted without knowledge of the results of the reference standard; multiple pre-specified cut offs were used to determine the optimal cut off; the index test result was known during the reference standard diagnosis. Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test. Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified. Knaefelc 2003: Unclear whether all patients were included in the analysis; unclear interval between index and reference tests; lack of a pre-specified threshold. Goncalves 2011: The reference diagnosis was not independent of the index tests; optimised test thresholds were used. Goncalves 2011: The reference diagnosis was not independent of the index tests; optimised test thresholds were used. Hancock 2011: Optimised test threshold. Bastide 2012: Optimised test cut-offs used. Carnero-Pardo 2013: Multiple test thresholds were used Nielsen 2013: The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; the test threshold was not pre-specified. Postel-Vinay 2014: Optimised cut-off was used; the study was not downgraded for exclusions as <10% population was excluded												

P.2.1.78 MMSE (<25)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnero-Pardo 2013)	1 × prospective	360	0.99 (0.91, 1.00)	0.38 (0.33, 0.44)	**LR+**	1.61 (1.46, 1.76)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.02 (0.00, 0.27)	Serious	n/a	Not serious	Serious		MODERATE
SECONDARY CARE												
7 studies (Callahan 2002; Flicker 1997; Kukull 1994; Larner 2015; Milian 2012; Nielsen 2013; Yeung 2014)	6 × prospective; 1 × retrospective	2,020	0.82 (0.73, 0.87)	0.83 (0.70, 0.91)	**LR+**	5.18 (2.74, 9.37)	V. serious	Serious	Not serious	Not serious	-	VERY LOW
					LR-	0.22 (0.14, 0.33)	V. serious	Serious	Not serious	Not serious		VERY LOW
ALL EVIDENCE POOLED												
8 studies (Callahan 2002; Carnero-Pardo 2013; Flicker 1997; Kukull 1994; Larner 2015; Milian 2012; Nielsen 2013; Yeung 2014)	7 × prospective; 1 × retrospective	2,380	0.85 (0.75, 0.91)	0.80 (0.62, 0.90)	**LR+**	4.41 (2.31, 8.1)	V. serious	Serious	Not serious	Not serious	-	VERY LOW
					LR-	0.20 (0.12, 0.31)	V. serious	Serious	Not serious	Not serious		VERY LOW

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
Notes on risk of bias Kukull 1994: It is unclear whether the index test results were interpreted without knowledge of the results of the reference standard; multiple pre-specified cut-offs were used to determine the optimal cut-off; the index test result was known during the reference standard diagnosis. Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test. Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified. Milian 2012: Unclear whether inappropriate exclusions were avoided; whether the patients were a random or consecutive sample and whether the reference standard result was interpreted without knowledge of the results of the index test. Carnero-Pardo 2013: Multiple test thresholds were used Nielsen 2013: The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; the test threshold was not pre-specified. Yeung 2014: Unclear whether patients were selected randomly or consecutively or whether inappropriate exclusions were avoided; the optimal index test thresholds were determined during the study; it is unclear whether the index test results and reference test results were assessed independently of each other: subgroup analysis was carried out with >10% population (MCI) being excluded.											

P.2.1.79 MMSE (<26)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 studies (Callahan 2002; Flicker 1997; Milian 2012; Nielsen 2013)	3 × prospective; 1 × retrospective	1,583	0.85 (0.77, 0.91)	0.78 (0.53, 0.92)	**LR+**	3.84 (1.68, 8.76)	V. serious	Serious	Not serious	Serious	-	VERY LOW
					LR-	0.19 (0.14, 0.28)	V. serious	Serious	Not serious	Not serious		VERY LOW

Notes on risk of bias

Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.
Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.
Milian 2012: Unclear whether inappropriate exclusions were avoided; whether the patients were a random or consecutive sample and whether the reference standard result was interpreted without knowledge of the results of the index test.
Nielsen 2013: The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; the test threshold was not pre-specified.

P.2.1.80 MMSE (<27)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 studies (Bastide 2012; Callahan 2002; Mathuranath 2000; Nielsen 2013)	4 × prospective	1,241	0.86 (0.73, 0.94)	0.75 (0.66, 0.82)	**LR+**	3.43 (2.43, 4.85)	Serious	Serious	Not serious	Not serious	-	LOW
					LR-	0.17 (0.09, 0.33)	Serious	Serious	Not serious	Not serious		LOW

Notes on risk of bias

Mathuranath 2000: Optimised test-threshold used and it was unclear whether the index test results were interpreted without knowledge of the results of the reference standard.
Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.
Bastide 2012: Optimised test cut-offs used.
Nielsen 2013: The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; the test threshold was not pre-specified.

P.2.1.81 MMSE (<28)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Callahan 2002; Mormont 2012)	2 × prospective	796	0.96 (0.87, 0.99)	0.70 (0.57, 0.81)	**LR+**	3.13 (2.22, 4.41)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.05 (0.02, 0.16)	V. serious	Serious	Not serious	Not serious		VERY LOW

Notes on risk of bias

Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.
Mormont 2012: Exclusion of >35% population at analysis and use of optimised test thresholds.

P.2.1.82 Montreal Cognitive Assessment, MoCA (<19)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Chen 2011; Yeung 2014)	2 × prospective	495	0.93 (0.90, 0.96)	0.81 (0.44, 0.96)	**LR+**	5.18 (1.32, 20.41)	V. serious	Serious	Not serious	Serious	-	VERY LOW
					LR-	0.09 (0.06, 0.13)	V. serious	Not serious	Not serious	Not serious		LOW

Notes on risk of bias

Chen 2011: Unclear whether inappropriate exclusions were avoided or if a pre-specified test threshold was used; unclear whether index and reference tests were interpreted without knowledge of each other and whether all participants were included in the analysis.
Yeung 2014: Unclear whether patients were selected randomly or consecutively or whether inappropriate exclusions were avoided; the optimal index test thresholds were determined during the study; it is unclear whether the index test results and reference test results were assessed independently of each other: subgroup analysis was carried out with >10% population (MCI) being excluded.

P.2.1.83 Montreal Cognitive Assessment, MoCA (<22)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Yeung 2014)	Prospective	272	1.00 (0.94, 1.00)	0.37 (0.29, 0.45)	**LR+**	1.57 (1.39, 1.78)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.01 (0.00, 0.17)	Serious	n/a	Not serious	Not serious		MODERATE

Notes on risk of bias
Yeung 2014: Unclear whether patients were selected randomly or consecutively or whether inappropriate exclusions were avoided; the optimal index test thresholds were determined during the study; it is unclear whether the index test results and reference test results were assessed independently of each other.

P.2.1.84 Montreal Cognitive Assessment , MoCA (<24)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Goldstein 2014)	Prospective	81	0.96 (0.78, 0.99)	0.31 (0.21, 0.45)	**LR+**	1.41 (1.16, 1.71)	Not serious	n/a	Serious	Not serious	-	MODERATE
					LR-	0.12 (0.02, 0.84)	Not serious	n/a	Serious	Serious		LOW

Notes on indirectness
Goldstein 2014: Study only recruited African Americans ≥ 50 years old.

P.2.1.85 Montreal Cognitive Assessment , MoCA (<25)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Goldstein 2014)	Prospective	81	0.98 (0.77, 1.00)	0.23 (0.14, 0.36)	**LR+**	1.27 (1.09, 1.48)	Not serious	n/a	Serious	Not serious	-	MODERATE
					LR-	0.08 (0.00, 1.28)	Not serious	n/a	Serious	Serious		LOW
Notes on indirectness Goldstein 2014: Study only recruited African Americans ≥ 50 years old.												

P.2.1.86 Montreal Cognitive Assessment , MoCA (<26)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Larner 2017)	Prospective	260	0.99 (0.84, 1.00)	0.31 (0.25, 0.37)	**LR+**	1.43 (1.30, 1.57)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.04 (0.00, 0.58)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.1.87 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Frisoni 2009; Hentschel 2005)	2 × prospective	234	0.83 (0.49, 0.96)	0.57 (0.47, 0.66)	**LR+**	1.87 (1.45, 2.37)	V. serious	Not serious	Not serious	Serious	-	VERY LOW
					LR-	0.30 (0.09, 1.04)	V. serious	Serious	Not serious	Serious		VERY LOW

Notes on risk of bias

Hentschel 2005: The index tests were carried out with knowledge of the primary care diagnosis and it is unclear whether pre-specified thresholds were used; the reference standard diagnosis used all available data including the index test results.

P.2.1.88 Orientation, OR (<7)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.39 (0.28, 0.52)	0.99 (0.95, 1.00)	**LR+**	32.70 (7.99, 133.88)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.61 (0.50, 0.75)	Serious	n/a	Not serious	Not serious		MODERATE

Notes on risk of bias

Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.

P.2.1.89 Orientation, OR (<8)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.65 (0.53, 0.76)	0.90 (0.85, 0.94)	**LR+**	6.76 (4.11, 11.12)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.39 (0.28, 0.54)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.												

P.2.1.90 Palmo-Mental Reflex

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Streit 2015)	Retrospective	154	0.41 (0.21, 0.65)	0.82 (0.74, 0.87)	**LR+**	2.26 (1.16, 4.41)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.72 (0.48, 1.08)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Streit 2015: Patients had to have cognitive complaints, but normal MMSE and CDT tests at baseline.												

P.2.1.91 Palmo-Mental Reflex and Short smell test, 1 positive

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Streit 2015)	Retrospective	154	0.71 (0.46, 0.87)	0.64 (0.55, 0.71)	**LR+**	1.93 (1.33, 2.82)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.46 (0.22, 0.98)	Serious	n/a	Not serious	Serious		LOW

Notes on risk of bias
Streit 2015: Patients had to have cognitive complaints, but normal MMSE and CDT tests at baseline..

P.2.1.92 Palmo-Mental Reflex and Short smell test, both positive

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Streit 2015)	Retrospective	154	0.24 (0.09, 0.49)	0.93 (0.88, 0.97)	**LR+**	3.58 (1.24, 10.38)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.82 (0.63, 1.07)	Serious	n/a	Not serious	Not serious		MODERATE

Notes on risk of bias
Streit 2015: Patients had to have cognitive complaints, but normal MMSE and CDT tests at baseline.
Notes on indirectness
Streit 2015: Patients had to have cognitive complaints, but score as normal on the MMSE and CDT tests.

P.2.1.93 Phototest (<27)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnero-Pardo 2011)	Prospective	140	0.81 (0.68, 0.90)	0.89 (0.81, 0.94)	**LR+**	7.48 (4.10, 13.63)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.21 (0.12, 0.38)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.1.94 Rowland Universal Dementia Assessment Scale, RUDAS (<21)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Goncalves 2011)	Prospective	204	0.66 (0.58, 0.73)	0.90 (0.79, 0.96)	**LR+**	6.84 (2.95, 15.87)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.38 (0.30, 0.48)	Serious	n/a	Not serious	Not serious		MODERATE

Notes on risk of bias
Nielsen 2013: The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; a variety of test thresholds are reported.

P.2.1.95 Rowland Universal Dementia Assessment Scale, RUDAS (<22)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Nielsen 2013)	Prospective	137	0.49 (0.37, 0.60)	0.91 (0.81, 0.96)	**LR+**	5.27 (2.37, 11.70)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.57 (0.45, 0.72)	V. serious	n/a	Not serious	Serious		VERY LOW

Notes on risk of bias
Nielsen 2013: The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; a variety of test thresholds are reported.

P.2.1.96 Rowland Universal Dementia Assessment Scale, RUDAS (<23)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Nielsen 2013)	Prospective	137	0.64 (0.52, 0.74)	0.83 (0.72, 0.90)	**LR+**	3.78 (2.14, 6.65)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.43 (0.31, 0.60)	V. serious	n/a	Not serious	Serious		VERY LOW

Notes on risk of bias
Nielsen 2013: The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; a variety of test thresholds are reported.

P.2.1.97 Rowland Universal Dementia Assessment Scale, RUDAS (<24)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Nielsen 2013)	Prospective	137	0.69 (0.58, 0.79)	0.80 (0.69, 0.88)	**LR+**	3.47 (2.09, 5.78)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.38 (0.26, 0.55)	V. serious	n/a	Not serious	Serious		VERY LOW

Notes on risk of bias
Nielsen 2013: The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; a variety of test thresholds are reported.

P.2.1.98 Rowland Universal Dementia Assessment Scale, RUDAS (<25)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Nielsen 2013)	Prospective	137	0.76 (0.65, 0.85)	0.66 (0.54, 0.77)	**LR+**	2.26 (1.57, 3.25)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.36 (0.23, 0.56)	V. serious	n/a	Not serious	Serious		VERY LOW

Notes on risk of bias
Nielsen 2013: The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; the test threshold was not pre-specified.

P.2.1.99 Rowland Universal Dementia Assessment Scale, RUDAS (<26)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Nielsen 2013)	Prospective	137	0.82 (0.71, 0.89)	0.65 (0.52, 0.75)	**LR+**	2.32 (1.64, 3.27)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.28 (0.17, 0.47)	V. serious	n/a	Not serious	Not serious		LOW

Notes on risk of bias

Nielsen 2013: The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; the test threshold was not pre-specified.

P.2.1.100 Seven Minute Screen (P>0.6)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skjerve 2008)	Prospective	95	0.72 (0.61, 0.82)	0.65 (0.46, 0.81)	**LR+**	2.09 (1.21, 3.62)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.42 (0.26, 0.68)	Serious	n/a	Not serious	Serious		LOW

Notes on risk of bias

Skjerve 2008: Use of an alternative threshold to the standard one and that was not pre-specified.

P.2.1.101 Seven Minute Screen (P>0.7)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skjerve 2008)	Prospective	95	0.72 (0.61, 0.82)	0.69 (0.49, 0.84)	**LR+**	2.36 (1.30, 4.27)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.40 (0.25, 0.63)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.1.102 Seven Minute Screen (P>0.8)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skjerve 2008)	Prospective	95	0.71 (0.59, 0.80)	0.73 (0.53, 0.87)	**LR+**	2.64 (1.38, 5.06)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.40 (0.26, 0.61)	Serious	n/a	Not serious	Serious		LOW

Notes on risk of bias
Skjerve 2008: Use of an alternative threshold to the standard one and that was not pre-specified.

P.2.1.103 Short smell test

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Streit 2015)	Retrospective	154	0.53 (0.30, 0.74)	0.75 (0.67, 0.82)	**LR+**	2.13 (1.25, 3.64)	Serious	n/a	Serious	Serious	-	VERY LOW
					LR-	0.63 (0.37, 1.05)	Serious	n/a	Serious	Serious		VERY LOW

Notes on risk of bias
Streit 2015: Patients had to have cognitive complaints, but normal MMSE and CDT tests at baseline.
Notes on indirectness
Streit 2015: Patients had to have cognitive complaints, but score as normal on the MMSE and CDT tests.

P.2.1.104 Short Portable Mental Status Questionnaire, SPMSQ (≥4)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Malhotra 2013)	Prospective	127	0.79 (0.70, 0.86)	0.75 (0.54, 0.88)	**LR+**	3.15 (1.56, 6.34)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.28 (0.18, 0.44)	V. serious	n/a	Not serious	Not serious		LOW

Notes on risk of bias
Malhotra 2013: It was unclear whether the study avoided inappropriate exclusions; optimised test cut-offs were calculated and a subgroup analysis was used which excluded 60% study population (people with <6 years education).
Notes on indirectness
Malhotra 2013: Participants had ≥ 6 years education

P.2.1.105 Short Portable Mental Status Questionnaire, SPMSQ (≥5)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Malhotra 2013)	Prospective	127	0.78 (0.69, 0.85)	0.75 (0.54, 0.88)	**LR+**	3.11 (1.54, 6.26)	Serious	n/a	Serious	Serious	-	VERY LOW
					LR-	0.30 (0.19, 0.46)	Serious	n/a	Serious	Not serious		LOW

Notes on risk of bias
Malhotra 2013: It was unclear whether the study avoided inappropriate exclusions and optimised test cut-offs were used.
Notes on indirectness
Malhotra 2013: 60% participants had < 6 years education

P.2.1.106 Short Portable Mental Status Questionnaire, SPMSQ (≥6)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Malhotra 2013)	Prospective	127	0.72 (0.62, 0.80)	0.42 (0.24, 0.62)	**LR+**	1.23 (0.86, 1.76)	V. serious	n/a	Serious	Not serious	-	VERY LOW
					LR-	0.68 (0.38, 1.19)	V. serious	n/a	Serious	Serious		VERY LOW

Notes on risk of bias
Malhotra 2013: It was unclear whether the study avoided inappropriate exclusions; optimised test cut-offs were calculated and a subgroup analysis was used which excluded 40% study population (people with ≥ 6 years education).
Notes on indirectness
Malhotra 2013: Participants had < 6 years education

P.2.1.107 Syndrom Kurztest (≥7)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skjerve 2008)	Prospective	95	0.71 (0.59, 0.80)	0.54 (0.35, 0.72)	**LR+**	1.54 (0.99, 2.39)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.54 (0.32, 0.90)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Skjerve 2008: Use of an alternative threshold to the standard one and that was not pre-specified.												

P.2.1.108 Syndrom Kurztest (≥8)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skjerve 2008)	Prospective	95	0.65 (0.53, 0.75)	0.65 (0.46, 0.81)	**LR+**	1.88 (1.08, 3.28)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.53 (0.35, 0.82)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Skjerve 2008: Use of an alternative threshold to the standard one and that was not pre-specified.												

P.2.1.109 Syndrom Kurztest (≥9)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skjerve 2008)	Prospective	95	0.58 (0.46, 0.69)	0.69 (0.49, 0.84)	**LR+**	1.88 (1.02, 3.47)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.61 (0.42, 0.89)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.1.110 Total recall score of 5-word test, ≤ 9

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Mormont 2012)	Prospective	145	0.81 (0.72, 0.88)	0.90 (0.78, 0.96)	**LR+**	7.96 (3.45, 18.37)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.21 (0.14, 0.32)	V. serious	n/a	Not serious	Not serious		LOW
Notes on risk of bias Mormont 2012: Exclusion of >35% population at analysis and use of optimised test thresholds.												

P.2.1.111 Total weighted score of 5-word test, ≤ 15

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Mormont 2012)	Prospective	145	0.75 (0.65, 0.83)	0.96 (0.85, 0.99)	**LR+**	18.38 (4.71, 71.75)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.26 (0.18, 0.37)	V. serious	n/a	Not serious	Not serious		LOW
Notes on risk of bias Mormont 2012: Exclusion of >35% population at analysis and use of optimised test thresholds.												

P.2.1.112 Test Your Memory, TYM (≤30)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Hancock 2011)	Prospective	224	0.73 (0.62, 0.82)	0.88 (0.81, 0.92)	**LR+**	5.93 (3.77, 9.32)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.31 (0.21, 0.44)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Hancock 2011: Optimised test threshold.												

P.2.1.113 Test Your Memory, TYM (≤42)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Hancock 2011)	Prospective	224	0.95 (0.87, 0.98)	0.45 (0.37, 0.53)	**LR+**	1.73 (1.48, 2.02)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.11 (0.04, 0.30)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.1.114 Test Your Memory (≤39)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Postel-Vinay 2014)	Prospective	201	0.90 (0.80, 0.95)	0.70 (0.62, 0.77)	**LR+**	2.98 (2.27, 3.91)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.15 (0.07, 0.30)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Postel-Vinay 2014: Optimised cut-off was used; the study was not downgraded for exclusions as <10% population was excluded												

P.2.1.115 Verbal category fluency (animal naming), VF (<14)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Sager 2006)	Prospective	364	0.85 (0.80, 0.89)	0.60 (0.50, 0.69)	**LR+**	2.14 (1.68, 2.72)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.25 (0.18, 0.35)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.1.116 Verbal category fluency (animal naming), VF (<19)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.85 (0.74, 0.92)	0.63 (0.56, 0.70)	**LR+**	2.31 (1.85, 2.89)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.24 (0.13, 0.43)	Serious	n/a	Not serious	Not serious		MODERATE

Notes on risk of bias

Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.

P.2.1.117 Verbal category fluency (animal naming), VF (<20)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.94 (0.85, 0.98)	0.58 (0.50, 0.65)	**LR+**	2.23 (1.85, 2.69)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.10 (0.04, 0.27)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.												

P.2.1.118 Verbal category fluency (animal naming), VF (<21)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.94 (0.85, 0.98)	0.52 (0.45, 0.60)	**LR+**	1.97 (1.66, 2.34)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.12 (0.04, 0.30)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.												

P.2.1.119 Verbal category fluency (animal naming), VF (<22)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.95 (0.87, 0.99)	0.46 (0.38, 0.53)	**LR+**	1.76 (1.52, 2.04)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.10 (0.03, 0.30)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.												

P.2.1.120 Verbal category fluency (animal naming), VF (<23)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.97 (0.89, 0.99)	0.39 (0.31, 0.46)	**LR+**	1.58 (1.39, 1.79)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.08 (0.02, 0.31)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.												

P.2.1.121 Verbal category fluency (animal naming), VF (<24)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.98 (0.90, 1.00)	0.31 (0.24, 0.38)	**LR+**	1.42 (1.28, 1.58)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.05 (0.01, 0.35)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.												

P.2.2 AD versus DLB

P.2.2.1 Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Andreasen 2001)	Prospective	172	0.65 (0.57, 0.72)	0.67 (0.33, 0.89)	**LR+**	1.95 (0.77, 4.95)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.52 (0.32, 0.87)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.2.2 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ossenkoppele 2013)	Prospective	70	0.58 (0.46, 0.70)	0.20 (0.03, 0.69)	**LR+**	0.73 (0.45, 1.19)	V. serious	n/a	Serious	Serious	-	VERY LOW
					LR-	2.08 (0.35, 12.27)	V. serious	n/a	Serious	V. serious		VERY LOW

Notes on risk of bias

Ossenkoppele 2013: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the index test was interpreted with knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.

Notes on indirectness

Ossenkoppele 2013: It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.

P.2.2.3 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	270	0.29 (0.24, 0.35)	0.72 (0.58, 0.83)	**LR+**	1.05 (0.64, 1.75)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.98 (0.81, 1.19)	Serious	n/a	Not serious	Not serious		MODERATE

Notes on risk of bias

Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.

P.2.3 AD versus FTD

P.2.3.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
2 studies (Launes 1991; Velakoulis 1997)	2 × prospective	59	0.73 (0.42, 0.91)	0.71 (0.43, 0.89)	**LR+**	2.78 (1.20, 6.42)	V. serious	Not serious	Not serious	Serious	-	VERY LOW
					LR-	0.41 (0.23, 0.74)	Serious	Not serious	Not serious	Serious		LOW
MULTIPLE CAMERA												
1 study (Boutoleau-Bretonniere 2012)	Prospective	29	0.78 (0.54, 0.91)	0.73 (0.41, 0.91)	**LR+**	2.85 (1.05, 7.72)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.31 (0.12, 0.78)	V. serious	n/a	Not serious	Serious		VERY LOW
ALL EVIDENCE POOLED												
3 studies (Boutoleau-Bretonniere 2012; Launes 1991; Velakoulis 1997)	3 × prospective	88	0.72 (0.56, 0.83)	0.72 (0.51, 0.86)	**LR+**	2.81 (1.48, 5.33)	V. serious	Not serious	Not serious	Serious	-	VERY LOW
					LR-	0.38 (0.23, 0.62)	V. serious	Not serious	Not serious	Serious		VERY LOW

Notes on risk of bias

Launes 1991: Subgroup analysis used with >10% study population excluded.
Velakoulis 1997: Subgroup analysis where >10% study population excluded and it was unclear whether: the index test results were interpreted without knowledge of the results of the reference standard; the index test threshold was pre-specified or the reference standard results interpreted without knowledge of the results of the index test.
Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded

P.2.3.2 Amyloid Beta 1-42 and Total Tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Toledo 2012)	Retrospective	100	0.90 (0.81, 0.95)	0.83 (0.65, 0.93)	**LR+**	5.23 (2.35, 11.65)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.12 (0.06, 0.25)	Serious	n/a	Not serious	Not serious		MODERATE

Notes on risk of bias

Toledo 2012: >10% population excluded from analysis; the index test thresholds used are not stated and it is unclear if they were pre-specified

P.2.3.3 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ossenkoppele 2013)	Prospective	83	0.58 (0.46, 0.70)	0.78 (0.54, 0.91)	**LR+**	2.63 (1.08, 6.39)	V. serious	n/a	Serious	Serious	-	VERY LOW
					LR-	0.53 (0.37, 0.78)	V. serious	n/a	Serious	Serious		VERY LOW

Notes on risk of bias

Ossenkoppele 2013: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the index test was interpreted with knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.

Notes on indirectness

Ossenkoppele 2013: It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.

P.2.3.4 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	315	0.29 (0.24, 0.35)	0.77 (0.68, 0.85)	**LR+**	1.28 (0.83, 1.96)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.92 (0.80, 1.06)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.												

P.2.3.5 p-tau 181

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Toledo 2012)	Retrospective	100	0.99 (0.90, 1.00)	0.85 (0.68, 0.94)	**LR+**	6.62 (2.82, 15.52)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.01 (0.00, 0.13)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Toledo 2012: >10% population excluded from analysis; the index test thresholds used are not stated and it is unclear if they were pre-specified												

P.2.4 AD versus no dementia

P.2.4.1 Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Maddalena 2003)	Prospective	70	0.84 (0.72, 0.92)	0.84 (0.61, 0.95)	**LR+**	5.34 (1.88, 15.19)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.19 (0.10, 0.36)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Maddalena 2003: It was unclear whether inappropriate exclusions had been made; an optimised threshold was used for each test and within each test for different analyses; it was unclear whether the index and reference tests were interpreted independently of each other.												

P.2.4.2 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Yakushev 2010)	Prospective	46	0.79 (0.59, 0.91)	0.91 (0.70, 0.98)	**LR+**	8.71 (2.29, 33.17)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.23 (0.10, 0.51)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Yakushev 2010: Subgroup analysis with >10% population excluded												

P.2.5 Free recall score of 5- word test, ≤ 5 for AD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Mormont 2012)	Prospective	110	0.81 (0.70, 0.89)	0.99 (0.86, 1.00)	**LR+**	81.45 (5.15, 1287.53)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.19 (0.11, 0.32)	V. serious	n/a	Not serious	Not serious		LOW
Notes on risk of bias Mormont 2012: Exclusion of >35% population at analysis and use of optimised test thresholds.												

P.2.5.1 Informant Questionnaire on Cognitive Decline, IQCODE (16 item, >3.2)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Sikkes 2010)	Prospective	269	0.96 (0.92, 0.98)	0.42 (0.32, 0.52)	**LR+**	1.64 (1.38, 1.96)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.09 (0.04, 0.20)	V. serious	n/a	Not serious	Not serious		LOW
Notes on risk of bias Sikkes 2010: Use of subgroup analysis where >10% study population excluded (MCI group); lack of a pre-specified test threshold; unclear that index and reference tests are interpreted without knowledge of each other.												

P.2.5.2 Informant Questionnaire on Cognitive Decline, IQCODE (16 item, >3.3)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Sikkes 2010)	Prospective	269	0.96 (0.91, 0.98)	0.47 (0.37, 0.58)	**LR+**	1.81 (1.48, 2.21)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.09 (0.05, 0.19)	V. serious	n/a	Not serious	Not serious		LOW
Notes on risk of bias Sikkes 2010: Use of subgroup analysis where >10% study population excluded (MCI group); lack of a pre-specified test threshold; unclear that index and reference tests are interpreted without knowledge of each other.												

P.2.5.3 Informant Questionnaire on Cognitive Decline, IQCODE (16 item, >3.4)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Sikkes 2010)	Prospective	269	0.92 (0.87, 0.95)	0.63 (0.52, 0.72)	**LR+**	2.47 (1.88, 3.25)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.13 (0.08, 0.22)	V. serious	n/a	Not serious	Not serious		LOW
Notes on risk of bias Sikkes 2010: Use of subgroup analysis where >10% study population excluded (MCI group); lack of a pre-specified test threshold; unclear that index and reference tests are interpreted without knowledge of each other.												

P.2.5.4 Informant Questionnaire on Cognitive Decline, IQCODE (16 item, >3.5)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Sikkes 2010)	Prospective	269	0.89 (0.84, 0.93)	0.69 (0.58, 0.77)	**LR+**	2.84 (2.08, 3.88)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.15 (0.10, 0.24)	V. serious	n/a	Not serious	Not serious		LOW

Notes on risk of bias

Sikkes 2010: Use of subgroup analysis where >10% study population excluded (MCI group); lack of a pre-specified test threshold; unclear that index and reference tests are interpreted without knowledge of each other.

P.2.5.5 Informant Questionnaire on Cognitive Decline, IQCODE (16 item, >3.6)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Sikkes 2010)	Prospective	269	0.86 (0.80, 0.90)	0.74 (0.64, 0.82)	**LR+**	3.31 (2.32, 4.73)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.19 (0.13, 0.28)	V. serious	n/a	Not serious	Not serious		LOW

Notes on risk of bias

Sikkes 2010: Use of subgroup analysis where >10% study population excluded (MCI group); lack of a pre-specified test threshold; unclear that index and reference tests were interpreted without knowledge of each other.

P.2.5.6 MMSE (<28)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Mormont 2012)	Prospective	110	0.98 (0.89, 1.00)	0.78 (0.64, 0.87)	**LR+**	4.38 (2.60, 7.38)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.02 (0.00, 0.15)	V. serious	n/a	Not serious	Not serious		LOW
Notes on risk of bias Mormont 2012: Exclusion of >35% population at analysis and use of optimised test thresholds.												

P.2.5.7 p-tau 181

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Maddalena 2003)	Prospective	70	0.67 (0.53, 0.78)	0.63 (0.40, 0.81)	**LR+**	1.81 (0.97, 3.36)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.53 (0.31, 0.89)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Maddalena 2003: It was unclear whether inappropriate exclusions had been made; an optimised threshold was used for each test and within each test for different analyses; it was unclear whether the index and reference tests were interpreted independently of each other.												

P.2.5.8 p-tau/Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Maddalena 2003)	Prospective	70	0.80 (0.67, 0.89)	0.89 (0.66, 0.97)	**LR+**	7.64 (2.04, 28.53)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.22 (0.12, 0.39)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Maddalena 2003: It was unclear whether inappropriate exclusions had been made; an optimised threshold was used for each test and within each test for different analyses; it was unclear whether the index and reference tests were interpreted independently of each other.												

P.2.5.9 Total recall score of 5-word test, ≤ 9

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Mormont 2012)	Prospective	110	0.92 (0.82, 0.97)	0.90 (0.78, 0.96)	**LR+**	9.00 (3.91, 20.71)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.09 (0.04, 0.21)	V. serious	n/a	Not serious	Not serious		LOW
Notes on risk of bias Mormont 2012: Exclusion of >35% population at analysis and use of optimised test thresholds.												

P.2.5.10 Total Tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Yakushev 2010)	Prospective	46	0.46 (0.27, 0.65)	0.95 (0.74, 0.99)	**LR+**	10.08 (1.42, 71.85)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.57 (0.39, 0.83)	V. serious	n/a	Not serious	Serious		VERY LOW
Notes on risk of bias Yakushev 2010: Subgroup analysis with >10% population excluded; use of optimised thresholds for test												

P.2.5.11 Total weighted score of 5-word test, ≤ 15

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Mormont 2012)	Prospective	110	0.90 (0.80, 0.96)	0.96 (0.85, 0.99)	**LR+**	22.09 (5.67, 86.05)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.10 (0.05, 0.22)	V. serious	n/a	Not serious	Not serious		LOW
Notes on risk of bias Mormont 2012: Exclusion of >35% population at analysis and use of optimised test thresholds.												

P.2.6 AD versus non-AD dementia plus unclassifiable

P.2.6.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA												
1 study (Boutoleau-Bretonniere 2012)	Prospective	56	0.78 (0.54, 0.91)	0.66 (0.50, 0.79)	**LR+**	2.27 (1.37, 3.77)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.34 (0.14, 0.83)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear whether consecutive or random enrolment of patients was employed; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used but <10% study population discarded												

P.2.6.2 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Boutoleau-Bretonniere 2012)	Prospective	56	0.33 (0.16, 0.57)	0.66 (0.50, 0.79)	**LR+**	0.97 (0.44, 2.14)	Serious	n/a	Not serious	V. serious	-	VERY LOW
					LR-	1.01 (0.68, 1.51)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases												

P.2.7 AD versus non-AD

P.2.7.1 ≥ 2 of 3 biomarkers abnormal (Amyloid Beta 1-42, t-tau, p-tau)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Duits 2014)	Prospective	1,149	0.86 (0.83, 0.89)	0.72 (0.68, 0.76)	**LR+**	3.10 (2.68, 3.57)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.19 (0.16, 0.24)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.7.2 2 out of 3 abnormal (Amyloid Beta 1–42, Total Tau, p-tau)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Brandt 2008)	Retrospective	147	0.42 (0.29, 0.56)	0.90 (0.82, 0.94)	**LR+**	4.13 (2.10, 8.11)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.65 (0.51, 0.83)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.7.3 Amyloid Beta 1–42, Total Tau, p-tau abnormal

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Brandt 2008; Jahn 2011)	1x prospective, 1x retrospective	225	0.62 (0.08, 0.97)	0.93 (0.22, 1.00)	**LR+**	6.85 (0.73, 64.28)	Serious	Serious	Not serious	Serious	-	VERY LOW
					LR-	0.39 (0.10, 1.50)	Serious	Serious	Not serious	Serious		VERY LOW
Notes on risk of bias Jahn 2011: >10% population excluded from analysis; unclear whether the patients were a random or consecutive sample or whether inappropriate exclusions were avoided; unclear whether the reference standard was interpreted without knowledge of the index tests results												

P.2.7.4 99mTc-ECD SPECT, visual assessment method

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA												
2 studies (Kaneta 2016; Tripathi 2010)	2x prospective	206	0.72 (0.09, 0.99)	0.87 (0.49, 0.98)	**LR+**	4.56 (0.31, 66.33)	Serious	Serious	Not serious	V serious		VERY LOW
					LR-	0.26 (0.02, 3.24)	Serious	Serious	Not serious	V. serious		VERY LOW
Notes on risk of bias Tripathi 2010: 14% of participants were lost to follow up and did not receive a reference standard; it is unclear whether the index test was interpreted without knowledge of the reference standard.												

P.2.7.5 99mTc-ECD SPECT, all information method

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA												
1 study (Kaneta 2016)	Prospective	89	0.71 (0.57, 0.82)	0.68 (0.53, 0.81)	**LR+**	2.31 (1.38, 3.63)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.43 (0.26, 0.7)	Serious	n/a	Not serious	Serious		LOW

Notes on risk of bias
Kaneta 2016: The SMH was defined based on the data and it was unclear whether the index test results were interpreted without knowledge of the results of the reference standard or whether the reference standard results were interpreted without knowledge of the results of the index test.

P.2.7.6 99mTc-ECD SPECT, automated method

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA												
1 study (Kaneta 2016)	Prospective	89	0.40 (0.27, 0.54)	0.83 (0.68, 0.92)	**LR+**	2.32 (1.08, 4.96)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.73 (0.56, 0.95)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.7.7 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
5 studies (Bergman 1997; Holman 1992; Launes 1991; Masterman 1997; McMurdo 1994)	5 × prospective	505	0.70 (0.55, 0.81)	0.62 (0.30, 0.86)	**LR+**	2.07 (1.08, 4.47)	Not serious	Serious	Not serious	Serious	-	LOW
					LR-	0.52 (0.37, 0.84)	Not serious	Serious	Not serious	Serious		LOW
MULTIPLE CAMERA												
2 studies (Dobert 2005; Rollin-Sillaire 2012)	1x prospective 1x retrospective	72	0.45 (0.24, 0.69)	0.93 (0.77, 0.98)	**LR+**	6.80 (1.98, 23.36)	Not serious	Not serious	Not serious	Serious	-	MODERATE
					LR-	0.60 (0.40, 0.90)	Serious	Not serious	Not serious	Serious		LOW
ALL EVIDENCE POOLED												
7 studies (Bergman 1997; Dobert 2005; Holman 1992; Launes 1991; Masterman 1997; McMurdo 1994; Rollin-Sillaire 2012)	6 × prospective; 1 × retrospective	577	0.63 (0.49, 0.75)	0.74 (0.45, 0.90)	**LR+**	2.10 (1.29, 3.43)	Not serious	Serious	Not serious	Serious	-	LOW
					LR-	0.56 (0.43, 0.73)	Not serious	Not serious	Not serious	Serious		MODERATE

Notes on risk of bias

Holman 1992: People with uncertain clinical diagnoses (> 10% population) were excluded from analysis

Dobert 2005: It is unclear whether a consecutive or random sample of patients was enrolled or whether inappropriate exclusions were avoided.

P.2.7.8 Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
ALL EVIDENCE POOLED												
10 studies (Andreasen 2001; Brandt 2008; Duits 2014; Dumurgier 2015 (Lille); Dumurgier 2015 (Paris); Dumurgier 2015 (Montpellier); Gabelle 2012 (Lille and Paris); Gabelle 2012 (Montpellier); Knapskgog 2016; Mulder 2010)	8 × prospective; 2 × retrospective	3,685	0.76 (0.67, 0.83)	0.74 (0.68, 0.79)	**LR+**	2.88 (2.23, 3.67)	Serious	Serious	Not serious	Not serious	-	LOW
					LR-	0.34 (0.23, 0.46)	Serious	Serious	Not serious	Not serious		LOW

Notes on risk of bias

Mulder 2010: It is unclear whether participants were consecutively or randomly recruited; the test cut offs were not pre-specified but selected to obtain 85% sensitivity; the timing between the reference and index tests is unclear and it is unclear whether the index test was interpreted independently of the reference test results

Gabelle 2012: Test thresholds were not pre-specified, but optimised based on the data; it was unclear whether the study enrolled random or consecutive people or avoided inappropriate exclusions. A subgroup analysis was carried out but as < 10% population was excluded the study was not downgraded for this.

Dumurgier 2015: The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study and the timing of the reference and index tests is unclear.

Additional notes: the Dumurgier study had 3 independent data sets from 3 different clinics; the Gabelle study had 2 independent data sets from 2 clinics.

P.2.7.9 Amyloid Beta 1-42 and total tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Frisoni 2009)	Prospective	94	0.71 (0.55, 0.83)	0.88 (0.76, 0.94)	**LR+**	5.68 (2.76, 11.70)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.33 (0.20, 0.55)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Frisoni 2009: Patients whose cognitive deficit reverted (regarded as primarily depressed with secondary cognitive impairment) were excluded from the study; unclear whether reference test was interpreted without knowledge of index test and unclear whether results of index test interpreted without knowledge of reference test.												

P.2.7.10 Amyloid Beta 1-42 and t-tau and/or p-tau abnormal

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Duits 2014)	Prospective	1,149	0.74 (0.70, 0.77)	0.86 (0.83, 0.89)	**LR+**	5.40 (4.33, 6.73)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.30 (0.26, 0.35)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.7.11 Amyloid Beta 1-42/p-tau 181

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
2 studies (Gabelle 2012 (Lille); Gabelle 2012 (Montpellier))	2 × prospective	1,200	0.83 (0.78, 0.87)	0.83 (0.79, 0.86)	LR+	4.74 (3.67, 6.12)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.21 (0.15, 0.28)	Serious	Serious	Not serious	Not serious		LOW

Notes on risk of bias

Gabelle 2012: Test thresholds were not pre-specified, but optimised based on the data; it was unclear whether the study enrolled random or consecutive people or avoided inappropriate exclusions. A subgroup analysis was carried out but as < 10% population was excluded the study was not downgraded for this.
Additional notes: the Gabelle study had 2 independent data sets from 2 different clinics.

P.2.7.12 Amyloid Beta 1-42/Total Tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
2 studies (Gabelle 2012 (Lille and Paris); Gabelle 2012 (Montpellier))	2 × prospective	1,200	0.85 (0.82, 0.88)	0.78 (0.74, 0.81)	LR+	3.79 (3.21, 4.46)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.19 (0.15, 0.25)	Serious	Not serious	Not serious	Not serious		MODERATE

Notes on risk of bias

Gabelle 2012: Test thresholds were not pre-specified, but optimised based on the data; it was unclear whether the study enrolled random or consecutive people or avoided inappropriate exclusions. A subgroup analysis was carried out but as < 10% population was excluded the study was not downgraded for this.
Additional notes: the Gabelle study had 2 independent data sets from 2 different clinics.

P.2.7.13 Amyloid Beta 1-42/1- 40

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
3 studies (Dumurgier 2015 (Lille); Dumurgier 2015 (Paris); Dumurgier 2015 (Montpellier))	3 × prospective	367	0.83 (0.60, 0.94)	0.77 (0.66, 0.85)	**LR+**	3.33 (2.31, 4.78)	V. serious	Not serious	Not serious	Not serious	-	LOW
					LR-	0.22 (0.09, 0.54)	V. serious	Serious	Not serious	Serious		VERY LOW

Notes on risk of bias

Dumurgier 2015: The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study and the timing of the reference and index tests is unclear.
Additional notes: the Dumurgier study had 3 independent data sets from 3 different clinics.

P.2.7.14 EEG

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Engedal 2015)	Prospective	372	0.70 (0.61, 0.77)	0.40 (0.34, 0.46)	**LR+**	1.16 (1.00, 1.35)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.76 (0.56, 1.02)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.7.15 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
6 studies (Dobert 2005; Frisoni 2009; Ossenkoppele 2013; Panegyres 2009; Silverman 2001; Yakushev 2010)	6 × prospective	544	0.72 (0.53, 0.86)	0.77 (0.70, 0.83)	**LR+**	3.19 (2.05, 4.60)	Serious	Serious	Serious	Not serious	-	VERY LOW
					LR-	0.37 (0.18, 0.62)	Serious	Serious	Serious	Serious		VERY LOW

Notes on risk of bias

Dobert 2005: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided.

Frisoni 2009: Patients whose cognitive deficit reverted (regarded as primarily depressed with secondary cognitive impairment) were excluded from the study; unclear whether reference test was interpreted without knowledge of index test and unclear whether results of index test interpreted without knowledge of reference test.

Yakushev 2010: Subgroup analysis with >10% population excluded

Ossenkoppele 2013: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the index test was interpreted with knowledge of the reference diagnosis.

Notes on indirectness

Panegyres 2009: The study only recruited people with early onset dementia (<65 years old).

Ossenkoppele 2013: It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.

P.2.7.16 FDG-PET/CT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Motara 2017)	Retrospective	98	0.87 (0.74, 0.94)	0.96 (0.86, 0.99)	**LR+**	22.61 (5.78, 88.40)	Serious	n/a	Serious	Not serious	-	LOW
					LR-	0.14 (0.06, 0.29)	Serious	n/a	Serious	Not serious		LOW

Notes on risk of bias

Motara 2017: There were 22 unstated reasons for exclusion; it was unclear whether a random or consecutive sample of patients was enrolled; whether the reference standard was likely to correctly classify the target condition or if it was interpreted without knowledge of the results of the index test.

Notes on indirectness

Motara 2017: There were 22 unstated reasons for exclusion

P.2.7.17 [18F] flutemetamol PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Zwan 2017)	Prospective	211	0.76 (0.69, 0.83)	0.66 (0.54, 0.76)	**LR+**	2.23 (1.58, 3.14)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.36 (0.26, 0.51)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.7.18 Formula Hulstaert (biomarkers)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Duits 2014)	Prospective	1,149	0.93 (0.91,0.95)	0.74 (0.70, 0.77)	**LR+**	3.54 (3.06, 4.10)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.09 (0.07, 0.13)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.7.19 Formula Mattson (biomarkers)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Duits 2014)	Prospective	1,149	0.80 (0.77, 0.83)	0..85 (0.81, 0.88)	**LR+**	5.26 (4.28,6.47)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.24 (0.20, 0.28)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.7.20 Formula Mulder (biomarkers)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Duits 2014)	Prospective	1,149	0.93 (0.91, 0.95)	0.73 (0.68, 0.76)	**LR+**	3.38 (2.93, 3.91)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.10 (0.07, 0.13)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.7.21 Formula Schoonenboom (biomarkers)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Duits 2014)	Prospective	1,149	0.91 (0.88, 0.93)	0.78 (0.74, 0.81)	**LR+**	4.10 (3.48, 4.82)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.12 (0.09, 0.15)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.7.22 Mass Spectrometry

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Jahn 2011)	Prospective	86	0.87 (0.77, 0.94)	0.83 (0.62, 0.93)	**LR+**	5.02 (2.05, 12.29)	Serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.15 (0.08, 0.30)	Serious	n/a	Not serious	Serious		MODERATE

P.2.7.23 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Frisoni 2009; Koikkalainen 2016)	2 × prospective	637	0.62 (0.09, 0.96)	0.72 (0.39, 0.91)	**LR+**	1.91 (1.56, 2.35)	Not serious	Not serious	Not serious	Serious	-	MODERATE
					LR-	0.47 (0.13, 1.66)	Not serious	Serious	Not serious	Serious		LOW

P.2.7.24 MRI Total Hippocampal grey matter volume, Hv. Cut off 4.95ml.

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Suppa 2015)	Retrospective	100	0.61 (0.46, 0.74)	0.86 (0.74, 0.93)	**LR+**	4.30 (2.17, 8.50)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.45 (0.31, 0.66)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Suppa 2015: It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; assay cut-offs were determined using ROC analysis.												

P.2.7.25 MRI Hippocampal grey matter volume left, HVL. Cut- off 2.69 ml

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Suppa 2015)	Retrospective	100	0.70 (0.56, 0.82)	0.71 (0.58, 0.82)	**LR+**	2.47 (1.56, 3.89)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.41 (0.25, 0.67)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Suppa 2015: It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; assay cut-offs were determined using ROC analysis.												

P.2.7.26 MRI Hippocampal grey matter volume left/ total grey matter volume (HVL/GMV). Cut-off 4.69 per mille.

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Suppa 2015)	Retrospective	100	0.80 (0.65, 0.89)	0.66 (0.53, 0.77)	**LR+**	2.34 (1.58, 3.48)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.31 (0.17, 0.57)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Suppa 2015: It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; assay cut-offs were determined using ROC analysis.												

P.2.7.27 MRI Hippocampal grey matter volume right, HVR. Cut off 2.70ml.

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Suppa 2015)	Retrospective	100	0.75 (0.60, 0.86)	0.77 (0.64, 0.86)	**LR+**	3.23 (1.95, 5.36)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.33 (0.19, 0.55)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Suppa 2015: It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; assay cut-offs were determined using ROC analysis.												

P.2.7.28 MRI Hippocampal grey matter volume right/ total grey matter volume (HVR/GMV). Cut-off 4.54 per mille.

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Suppa 2015)	Retrospective	100	0.80 (0.65, 0.89)	0.80 (0.68, 0.89)	**LR+**	4.05 (2.34, 7.02)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.25 (0.14, 0.46)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Suppa 2015: It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; assay cut-offs were determined using ROC analysis.												

P.2.7.29 MRI Total hippocampal grey matter volume/total grey matter volume (HV/GMV). Cut-off 8.36 per mille.

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Suppa 2015)	Retrospective	100	0.66 (0.51, 0.78)	0.88 (0.76, 0.94)	**LR+**	5.27 (2.55, 10.88)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.39 (0.26, 0.59)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Suppa 2015: It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; assay cut-offs were determined using ROC analysis.												

P.2.7.30 Olfactory Test ≥ 3 errors

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Christensen 2017)	Prospective	50	0.79 (0.59, 0.91)	0.46 (0.28, 0.65)	**LR+**	1.47 (0.97, 2.22)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.45 (0.19, 1.09)	Not serious	n/a	Not serious	Serious		MODERATE
Notes on risk of bias Christensen 2017: Although the threshold was not pre-specified, data was presented for all possible cut offs.												

P.2.7.31 Olfactory Test ≥ 4 errors

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Christensen 2017)	Prospective	50	0.50 (0.31, 0.69)	0.73 (0.53, 0.87)	**LR+**	1.86 (0.88, 3.93)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.68 (0.43, 1.09)	Not serious	n/a	Not serious	Serious		MODERATE
Notes on risk of bias Christensen 2017: Although the threshold was not pre-specified, data was presented for all possible cut offs.												

P.2.7.32 Olfactory Test ≥ 5 errors

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Christensen 2017)	Prospective	50	0.21 (0.09, 0.41)	0.85 (0.65, 0.94)	**LR+**	1.35 (0.41, 4.46)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.94 (0.72, 1.22)	Not serious	n/a	Not serious	Serious		MODERATE

Notes on risk of bias
Christensen 2017: Although the threshold was not pre-specified, data was presented for all possible cut offs..

P.2.7.33 p-tau 181

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
ALL EVIDENCE POOLED												
9 studies (Brandt 2008; Duits 2014; Dumurgier 2015 (Lille); Dumurgier 2015 (Paris); Dumurgier 2015 (Montpellier); Gabelle 2012 (Lille and Paris); Gabelle 2012 (Montpellier); Knapskgog 2016; Mulder 2010)	7 × prospective; 2 × retrospective	3,448	0.75 (0.62, 0.84)	0.84 (0.76, 0.90)	**LR+**	4.87 (3.37, 6.92)	V. serious	Serious	Not serious	Not serious	-	VERY LOW
					LR-	0.30 (0.20, 0.43)	V. serious	Serious	Not serious	Not serious		VERY LOW

Notes on risk of bias
Mulder 2010: It is unclear whether participants were consecutively or randomly recruited; the test cut offs were not pre-specified but selected to obtain 85% sensitivity; the timing between the reference and index tests is unclear and it is unclear whether the index test was interpreted independently of the reference test results
Gabelle 2012: Test thresholds were not pre-specified, but optimised based on the data; it was unclear whether the study enrolled random or consecutive people or avoided inappropriate exclusions. A subgroup analysis was carried out but as < 10% population was excluded the study was not downgraded for this.
Dumurgier 2015: The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study and the timing of the reference and index tests is unclear.
Additional notes: the Dumurgier study had 3 independent data sets from 3 different clinics; the Gabelle study had 2 independent data sets from 2 clinics.

P.2.7.34 p-tau and Amyloid Beta 1-42 combined then in case of discrepancy between p-tau and Amyloid Beta 1-42 the Amyloid Beta 42/40 ratio was used in place of Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Dumurgier 2015)	Prospective	329	0.88 (0.82, 0.92)	0.91 (0.86, 0.95)	**LR+**	10.29 (6.41, 16.50)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.13 (0.08, 0.20)	V. serious	n/a	Not serious	Not serious		LOW

Notes on risk of bias

Dumurgier 2015: The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study; the timing of the reference and index tests is unclear and a subgroup analysis was carried out that excluded >10% population (with indeterminate results).

P.2.7.35 p-tau and Amyloid Beta 42/40

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Dumurgier 2015)	Prospective	303	0.87 (0.81, 0.92)	0.91 (0.86, 0.95)	**LR+**	9.79 (6.01, 15.93)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.14 (0.09, 0.22)	V. serious	n/a	Not serious	Not serious		LOW

Notes on risk of bias

Dumurgier 2015: The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study; the timing of the reference and index tests is unclear and a subgroup analysis was carried out that excluded >10% population (with indeterminate results).

P.2.7.36 p-tau/Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Duits 2014; Dumurgier 2015)	2 × prospective	1,434	0.87 (0.81, 0.92)	0.90 (0.74, 0.97)	**LR+**	8.77 (2.95, 26.08)	V. serious	Serious	Not serious	Not serious	-	VERY LOW
					LR-	0.14 (0.08, 0.25)	V. serious	Serious	Not serious	Not serious		VERY LOW
Notes on risk of bias Dumurgier 2015: The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study; the timing of the reference and index tests is unclear and a subgroup analysis was carried out that excluded >10% population (with indeterminate results).												

P.2.7.37 Total Tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
ALL EVIDENCE POOLED												
9 studies (Brandt 2008; Duits 2014; Dumurgier (Lille) 2015; Dumurgier 2015 (Paris); Dumurgier 2015 (Montpellier); Gabelle 2012 (Lille and Paris); Gabelle 2012 (Montpellier); Knapskgog 2016; Mulder 2010)	7 × prospective; 2 × retrospective	3,447	0.78 (0.71, 0.84)	0.78 (0.74, 0.82)	**LR+**	3.62 (3.14, 4.17)	Serious	Serious	Not serious	Not serious	-	LOW
					LR-	0.28 (0.21, 0.36)	V. serious	Serious	Not serious	Not serious		VERY LOW

Notes on risk of bias

Mulder 2010: It is unclear whether participants were consecutively or randomly recruited; the test cut offs were not pre-specified but selected to obtain 85% sensitivity; the timing between the reference and index tests is unclear and it is unclear whether the index test was interpreted independently of the reference test results

Gabelle 2012: Test thresholds were not pre-specified, but optimised based on the data; it was unclear whether the study enrolled random or consecutive people or avoided inappropriate exclusions. A subgroup analysis was carried out but as < 10% population was excluded the study was not downgraded for this.

Dumurgier 2015: The reference standard diagnosis included consideration of the CSF results; the test cut-offs were optimised; patients with unknown clinical diagnoses or MCI were excluded from the study and the timing of the reference and index tests is unclear and it is unclear whether a consecutive or random sample of patients was enrolled.

Additional notes: the Dumurgier study had 3 independent data sets from 3 different clinics; the Gabelle study had 2 independent data sets from 2 clinics.

P.2.7.38 Total Tau/Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Duits 2014)	Prospective	1,149	0.85 (0.82, 0.88)	0.82 (0.79, 0.85)	**LR+**	4.78 (3.96, 5.77)	Not serious	Not serious	Not serious	Not serious	-	HIGH
					LR-	0.18 (0.15, 0.22)	Not serious	Not serious	Not serious	Not serious		HIGH

P.2.7.39 Urinary AD7c-NTP (22ug/ml)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Goodman 2007)	Retrospective	168	0.59 (0.49, 0.69)	0.73 (0.62, 0.81)	**LR+**	2.15 (1.45, 3.19)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.56 (0.42, 0.75)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.8 AD versus other dementias

P.2.8.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
1 study (Velakoulis 1997)	Prospective	33	0.89 (0.50, 0.98)	0.71 (0.50, 0.85)	**LR+**	3.05 (1.57, 5.93)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.16 (0.02, 1.01)	V. serious	n/a	Not serious	Serious		VERY LOW

Notes on risk of bias
Velakoulis 1997: Subgroup analysis where >10% study population excluded and it was unclear whether: the index test results were interpreted without knowledge of the results of the reference standard; the index test threshold was pre-specified or the reference standard results interpreted without knowledge of the results of the index test.

P.2.8.2 AD scale (≥6)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Gustafson 2010)	Prospective	190	0.80 (0.71, 0.87)	0.87 (0.78, 0.93)	**LR+**	6.18 (3.53, 10.82)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.23 (0.16, 0.34)	Not serious	n/a	Not serious	Not serious		HIGH

Notes on risk of bias
Gustafson 2010: The study was not downgraded for subgroup analysis as <10% population was excluded.

P.2.8.3 Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
3 studies (Boutoleau-Bretonniere 2012; Ibach 2006; Maddalena 2003)	3 × prospective	249	0.74 (0.67, 0.81)	0.62 (0.53, 0.71)	**LR+**	1.96 (1.46, 2.62)	V. serious	Not serious	Not serious	Serious	-	VERY LOW
					LR-	0.41 (0.29, 0.58)	V. serious	Not serious	Not serious	Serious		VERY LOW

Notes on risk of bias
Maddalena 2003: It was unclear whether inappropriate exclusions had been made; an optimised threshold was used for each test and within each test for different analyses; it was unclear whether the index and reference tests were interpreted independently of each other.
Ibach 2006: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the test thresholds were not pre-specified and it is unclear whether the index test was interpreted without knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.
Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.

P.2.8.4 Amyloid Beta 1-42 and total tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Frisoni 2009)	Prospective	66	0.71 (0.55, 0.83)	0.96 (0.79, 0.99)	**LR+**	19.89 (2.87, 137.80)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.30 (0.18, 0.50)	V. serious	n/a	Not serious	Not serious		LOW

Notes on risk of bias

Frisoni 2009: Subgroup analysis with >10% population excluded; patients whose cognitive deficit reverted (regarded as primarily depressed with secondary cognitive impairment) were excluded from the study; unclear whether reference test was interpreted without knowledge of index test and unclear whether results of index test interpreted without knowledge of reference test.

P.2.8.5 Apo E (≥1 allele)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Mayeux 1998)	Retrospective	2,188	0.65 (0.62, 0.67)	0.68 (0.64, 0.72)	**LR+**	2.03 (1.75, 2.34)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.52 (0.48, 0.57)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.8.6 CSF 14-3-3, total Tau and p-tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Boutoleau-Bretonniere 2012)	Prospective	44	0.97 (0.69, 1.00)	0.69 (0.49, 0.83)	**LR+**	3.09 (1.76, 5.42)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.04 (0.00, 0.60)	V. serious	n/a	Not serious	Serious		VERY LOW
Notes on risk of bias Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.												

P.2.8.7 Computed Tomography, CT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (O'Brien 2000)	Prospective	103	0.51 (0.39, 0.62)	0.38 (0.24, 0.55)	**LR+**	0.82 (0.58, 1.17)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	1.29 (0.79, 2.10)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias O'Brien 2000: Subgroup analysis with >10% population excluded												

P.2.8.8 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
6 studies (Arslan 2015; Frisoni 2009; Hoffman 2000; Jagust 2007; Ossenkoppele 2013; Yakushev 2010)	4 × prospective; 2 × retrospective	300	0.71 (0.60, 0.80)	0.66 (0.57, 0.74)	**LR+**	2.07 (1.52, 2.78)	Serious	Not serious	Not serious	Serious	-	LOW
					LR-	0.46 (0.30, 0.64)	Serious	Serious	Not serious	Serious		VERY LOW

Notes on risk of bias

Frisoni 2009: Subgroup analysis with >10% population excluded; patients whose cognitive deficit reverted (regarded as primarily depressed with secondary cognitive impairment) were excluded from the study; unclear whether reference test was interpreted without knowledge of index test and unclear whether results of index test interpreted without knowledge of reference test.
Yakushev 2010: Subgroup analysis with >10% population excluded
Ossenkoppele 2013: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the index test was interpreted with knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.
Arslan 2015: Unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard and if the imaging patterns were pre-specified; the reference standard results were interpreted independently of the index test results.

Notes on indirectness

Ossenkoppele 2013: It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.

P.2.8.9 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Frisoni 2009; Koikkalainen 2016)	2 × prospective	471	0.62 (0.09, 0.96)	0.67 (0.40, 0.86)	**LR+**	1.54 (1.08, 2.19)	Serious	Serious	Not serious	Serious	-	VERY LOW
					LR-	0.50 (0.14, 1.84)	Serious	Serious	Not serious	Serious		VERY LOW
Notes on risk of bias Frisoni 2009: Subgroup analysis with >10% population excluded; patients whose cognitive deficit reverted (regarded as primarily depressed with secondary cognitive impairment) were excluded from the study; unclear whether reference test was interpreted without knowledge of index test. Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.												

P.2.8.10 p-tau 181

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
3 studies (Boutoleau-Bretonniere 2012; Ibach 2006; Maddalena 2003)	3 × prospective	2249	0.75 (0.64, 0.84)	0.74 (0.61, 0.83)	**LR+**	2.97 (1.73, 5.09)	V. serious	Serious	Not serious	Serious	-	VERY LOW
					LR-	0.35 (0.21, 0.57)	V. serious	Not serious	Not serious	Serious		VERY LOW

Notes on risk of bias

Maddalena 2003: It was unclear whether inappropriate exclusions had been made; an optimised threshold was used for each test and within each test for different analyses; it was unclear whether the index and reference tests were interpreted independently of each other.
Ibach 2006: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the test thresholds were not pre-specified and it is unclear whether the index test was interpreted without knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.
Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.

P.2.8.11 p-tau/Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Ibach 2006; Maddalena 2003)	2 × prospective	205	0.79 (0.71, 0.85)	0.74 (0.64, 0.83)	**LR+**	3.07 (2.08, 4.52)	V. serious	Not serious	Not serious	Not serious	-	LOW
					LR-	0.29 (0.20, 0.41)	V. serious	Not serious	Not serious	Not serious		LOW

Notes on risk of bias

Maddalena 2003: It was unclear whether inappropriate exclusions had been made; an optimised threshold was used for each test and within each test for different analyses; it was unclear whether the index and reference tests were interpreted independently of each other.
Ibach 2006: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the test thresholds were not pre-specified and it is unclear whether the index test was interpreted without knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.

P.2.8.12 Total tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
3 studies (Boutoleau-Bretonniere 2012; Ibach 2006; Yakushev 2010)	3 × prospective	205	0.71 (0.52, 0.85)	0.82 (0.63, 0.93)	**LR+**	4.28 (1.75, 9.99)	V. serious	Not serious	Not serious	Not serious	-	LOW
					LR-	0.38 (0.24, 0.61)	V. serious	Serious	Not serious	Serious		VERY LOW

Notes on risk of bias

Ibach 2006: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the test thresholds were not pre-specified and it is unclear whether the index test was interpreted without knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.
Yakushev 2010: Subgroup analysis with >10% population excluded; use of optimised thresholds for test
Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.

P.2.8.13 Total Tau/Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ibach 2006)	Prospective	124	0.75 (0.64, 0.83)	0.75 (0.61, 0.85)	**LR+**	3.00 (1.81, 4.98)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.33 (0.22, 0.51)	V. serious	n/a	Not serious	Serious		VERY LOW

Notes on risk of bias

Ibach 2006: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the test thresholds were not pre-specified and it is unclear whether the index test was interpreted without knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.

P.2.9 AD versus VaD

P.2.9.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
2 studies (Launes 1991; McMurdo 1994)	2 × prospective	97	0.61 (0.49, 0.72)	0.85 (0.69, 0.93)	**LR+**	4.13 (1.85, 9.21)	Serious	Not serious	Not serious	Serious	-	LOW
					LR-	0.45 (0.31, 0.66)	Serious	Not serious	Not serious	Serious		LOW
MULTIPLE CAMERA												
1 study (Boutoleau-Bretonniere 2012)	Prospective	26	0.78 (0.54, 0.91)	0.50 (0.20, 0.80)	**LR+**	1.56 (0.75, 3.25)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.44 (0.15, 1.35)	V. serious	n/a	Not serious	Serious		VERY LOW
ALL EVIDENCE POOLED												
3 studies (Boutoleau-Bretonniere 2012; Launes 1991; McMurdo 1994)	3 × prospective	123	0.64 (0.53, 0.74)	0.74 (0.45, 0.91)	**LR+**	2.54 (1.19, 5.41)	V. serious	Not serious	Not serious	Serious	-	VERY LOW
					LR-	0.45 (0.32, 0.64)	Serious	Not serious	Not serious	Serious		LOW

Notes on risk of bias

Launes 1991: Subgroup analysis used with >10% study population excluded.
McMurdo 1994: Subgroup analysis used with >10% study population discarded.
Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded

P.2.9.2 Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Andreasen 2001)	Prospective	186	0.65 (0.57, 0.72)	0.48 (0.29, 0.68)	**LR+**	1.25 (0.83, 1.87)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.73 (0.45, 1.18)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.9.3 Computed Tomography, CT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (O'Brien 2000)	Prospective	94	0.51 (0.39, 0.62)	0.32 (0.17, 0.52)	**LR+**	0.75 (0.52, 1.06)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	1.54 (0.83, 2.86)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias O'Brien 2000: Subgroup analysis with >10% population excluded												

P.2.9.4 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	247	0.29 (0.24, 0.35)	0.88 (0.68, 0.96)	LR+	2.33 (0.79, 6.85)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.81 (0.68, 0.96)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.												

P.2.10 bv-FTD versus non-bv-FTD

P.2.10.1 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Vijverberg 2016b)	Prospective	111	0.89 (0.71, 0.96)	0.68 (0.57, 0.77)	LR+	2.77 (1.97, 3.88)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.16 (0.06, 0.48)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Vijverberg 2016b: 19% study population was excluded from analysis and it is unclear whether a consecutive or random group of patients was enrolled or whether inappropriate exclusions were avoided; all test results (including the index tests) were used to reach the clinical diagnosis.												

P.2.10.2 FDG-PET and MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Vijverberg 2016b)	Prospective	111	0.96 (0.78, 0.99)	0.73 (0.62, 0.81)	**LR+**	3.52 (2.46, 5.02)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.05 (0.01, 0.35)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Vijverberg 2016b: 19% study population was excluded from analysis and it is unclear whether a consecutive or random group of patients was enrolled or whether inappropriate exclusions were avoided; all test results (including the index tests) were used to reach the clinical diagnosis.												

P.2.10.3 FTDC criteria for bv FTD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Harris 2013)	Retrospective	147	0.79 (0.69, 0.87)	0.96 (0.88, 0.99)	**LR+**	18.48 (6.07, 56.26)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.22 (0.14, 0.34)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Harris 2013: Study excludes third of sample at initial screening												

P.2.10.4 FTDC criteria for possible bvFTD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Vijverberg 2016a)	Prospective	116	0.85 (0.67, 0.94)	0.27 (0.19, 0.37)	**LR+**	1.17 (0.95, 1.43)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.55 (0.21, 1.44)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Vijverberg 2016a: 19% study population was excluded from analysis and it is unclear whether a consecutive or random group of patients was enrolled or whether the reference standard results were interpreted without knowledge of the results of the index test.												

P.2.10.5 FTDC criteria for probable bvFTD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Vijverberg 2016a)	Prospective	116	0.85 (0.67, 0.94)	0.82 (0.73, 0.89)	**LR+**	4.74 (2.96, 7.59)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.18 (0.07, 0.45)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Vijverberg 2016a: 19% study population was excluded from analysis and it is unclear whether a consecutive or random group of patients was enrolled or whether the reference standard results were interpreted without knowledge of the results of the index test.												

P.2.10.6 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Vijverberg 2016b)	Prospective	111	0.70 (0.51, 0.84)	0.93 (0.85, 0.97)	**LR+**	9.85 (4.39, 22.12)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.32 (0.18, 0.57)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Vijverberg 2016b: 19% study population was excluded from analysis and it is unclear whether a consecutive or random group of patients was enrolled or whether inappropriate exclusions were avoided; all test results (including the index tests) were used to reach the clinical diagnosis.												

P.2.11 bvFTD/fd+ versus non-bvFTD/fd+

P.2.11.1 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Kerklaan 2014)	Retrospective	52	0.47 (0.24, 0.71)	0.92 (0.78, 0.97)	**LR+**	5.76 (1.71, 19.34)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.58 (0.36, 0.94)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.12 CADASIL versus CADASIL-like syndromes

P.2.12.1 Skin biopsy

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ampuero 2009)	Prospective	90	0.96 (0.78, 0.99)	0.68 (0.56, 0.79)	**LR+**	3.03 (2.10, 4.39)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.05 (0.01, 0.37)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.13 CBD versus non-CBD

P.2.13.1 CBD consensus criteria

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Alexander 2014)	Retrospective	33	0.93 (0.70, 0.98)	0.03 (0.00, 0.37)	**LR+**	0.96 (0.82, 1.12)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	2.25 (0.10, 51.46)	Not serious	n/a	Not serious	V. serious		LOW

P.2.14 CJD versus non-CJD

P.2.14.1 Amyloid Beta 1-42 and total tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Van Everbroeck 2003)	Retrospective	250	0.87 (0.74, 0.93)	0.98 (0.95, 0.99)	**LR+**	42.84 (16.14, 113.67)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.14 (0.07, 0.27)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.14.2 CSF 14-3-3 Automated Capillary Western Assay

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Fourier 2017)	Retrospective	268	0.94 (0.85, 0.97)	0..95 (0.91, 0.98)	**LR+**	19.84 (10.46, 37.65)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.07 (0.03, 0.16)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.14.3 CSF 14-3-3 (multiple methods)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Tschampa 2005)	Retrospective	174	0.91 (0.86, 0.95)	0.44 (0.29, 0.61)	**LR+**	1.64 (1.21, 2.21)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.19 (0.10, 0.38)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.14.4 CSF 14-3-3 ELISA

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Kenney 2000; Leitao 2016)	1 × prospective; 1 × retrospective	292	0.94 (0.78, 0.98)	0.96 (0.91, 0.98)	**LR+**	22.61 (10.33, 49.47)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.07 (0.02, 0.24)	Serious	Serious	Not serious	Not serious		LOW

Notes on risk of bias

Kenney 2000: The test threshold was not pre-specified and it was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test.
Leitao 2016: It was unclear whether: a consecutive or random sample of patients was enrolled; the study avoided inappropriate exclusions; test thresholds were pre-specified.

P.2.14.5 CSF 14-3-3 immunoblotting

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
17 studies (Bahl 2008; Beudry 1998; Burkhard 2001; Chohan 2010; Coulthart 2011; Cuadrado-Corrales 2006; Fourier 2017, Foutz 2017; Hamlin 2012; Kenney 2000; Lattanzio 2017; Lemstra 2000; Rohan 2015; Tagliapietra 2013; Van Everbroeck 2003; Zerr 1998; Zerr 2000)	8 × prospective; 9 × retrospective	6,086	0.87 (0.84, 0.90)	0.83 (0.73, 0.90)	**LR+**	5.44 (3.28, 8.78)	Serious	Serious	Not serious	Not serious	-	LOW
					LR-	0.16 (0.13, 0.19)	Serious	Not serious	Not serious	Not serious		MODERATE

Notes on risk of bias

Beudry 1998: Optimised test cut-offs were used and it was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test.
Zerr 1998: The assay used an optimised cut-off. It was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test.
Kenney 2000: It was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test.
Lemstra 2000: Unclear whether the reference and index tests were carried out blind to each other; it is unclear whether the index test (as carried out) was able to detect 14-3-3 protein at an appropriate threshold level.
Zerr 2000: It was unclear whether the index tests were interpreted independently of the reference test results; it was unclear whether a consecutive or random sample of people were enrolled or inappropriate exclusions avoided; or the index test threshold was pre-specified.
Cuadrado-Corrales 2006: 20% drop out due to problems with samples; <10 % excluded from analysis for possible CJD so not downgraded for this issue.
Bahl 2008: Exclusion of possible CJD group from index tests may inflate test sensitivity
Chohan 2010: Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.
Coulthart 2011: Not downgraded for exclusions during data analysis as <10% population excluded.
Hamlin 2012: > 28% population excluded as 14-3-3 results were ambiguous; multiple thresholds were tested and unclear whether researchers were blind to reference test results or that the reference test was interpreted without knowledge of index test.
Rohan 2015: It was unclear whether: a consecutive or random sample of patients was enrolled; the index test results were interpreted without knowledge of the results of the reference standard; a pre-specified cut-off was used for the index tests; the reference standard results were interpreted without knowledge of the index test results.

Notes on indirectness

Burkhard 2001: Patients do not have suspected CJD at baseline

P.2.14.6 CSF 14-3-3 (presence) and S100B (>1.0ng/ml)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Chohan 2010)	Retrospective	411	0.62 (0.56, 0.68)	0.95 (0.90, 0.97)	**LR+**	11.72 (6.16, 22.29)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.40 (0.34, 0.47)	Serious	n/a	Not serious	Not serious		MODERATE

Notes on risk of bias

Chohan 2010: Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.

P.2.14.7 CSF 14-3-3 and Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Van Everbroeck 2003)	Retrospective	250	0.99 (0.87, 1.00)	0.98 (0.94, 0.99)	**LR+**	43.81 (17.57, 109.24)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.01 (0.00, 0.15)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.14.8 CSF 14-3-3 and total Tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Chohan 2010)	Retrospective	351	0.75 (0.69, 0.80)	0.88 (0.82, 0.93)	**LR+**	6.33 (3.97, 10.09)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.28 (0.22, 0.36)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Chohan 2010: Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.												

P.2.14.9 CSF 14-3-3, total Tau and S100B

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Chohan 2010)	Retrospective	351	0.57 (0.50, 0.63)	0.96 (0.90, 0.98)	**LR+**	12.81 (5.81, 28.25)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.45 (0.38, 0.53)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Chohan 2010: Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.												

P.2.14.10 EEG

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Tagliapietra 2013; Tschampa 2005)	2 × retrospective	202	0.71 (0.05, 0.99)	0.49 (0.00, 1.00)	**LR+**	1.95 (0.42, 9.15)	Not serious	Serious	Not serious	V. serious	-	VERY LOW
					LR-	0.73 (0.63, 0.84)	Not serious	Not serious	Not serious	Not serious		HIGH

P.2.14.11 European criteria for CJD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Brandel 2000)	Retrospective	236	0.91 (0.86, 0.95)	0.28 (0.16, 0.43)	**LR+**	1.26 (1.04, 1.53)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.32 (0.16, 0.62)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.14.12 French criteria for CJD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Brandel 2000)	Retrospective	236	0.88 (0.83, 0.92)	0.50 (0.35, 0.65)	**LR+**	1.77 (1.29, 2.42)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.23 (0.14, 0.38)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.14.13 Master's criteria for CJD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Brandel 2000)	Retrospective	236	0.98 (0.95, 1.00)	0.10 (0.04, 0.24)	**LR+**	1.09 (0.99, 1.21)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.15 (0.04, 0.66)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.14.14 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 studies (Schroter 2000; Tagliapietra 2013; Tschampa 2005; Van Everbroeck 2004)	1 × prospective; 3 × retrospective	564	0.54 (0.40, 0.67)	0.90 (0.79, 0.96)	**LR+**	5.40 (2.46, 11.88)	Not serious	Serious	Not serious	Not serious	-	MODERATE
					LR-	0.52 (0.37, 0.72)	Not serious	Serious	Not serious	Serious		LOW
Notes on risk of bias Van Everbroeck 2004: > 10% population excluded from analysis												

P.2.14.15 MRI, DWI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Tagliapietra 2013)	Retrospective	31	0.73 (0.41, 0.91)	0.95 (0.72, 0.99)	**LR+**	14.55 (2.08, 101.66)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.29 (0.11, 0.76)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.14.16 Neuron-specific enolase

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Bahl 2008; Beudry 1998)	2 × prospective	295	0.74 (0.65, 0.82)	0.90 (0.85, 0.94)	**LR+**	8.00 (5.05, 12.69)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.28 (0.20, 0.40)	Serious	Not serious	Not serious	Not serious		MODERATE

Notes on risk of bias

Beudry 1998: Optimised test cut-offs were used and it was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test.
Bahl 2008: Exclusion of possible CJD group from index tests may inflate test sensitivity

P.2.14.17 New criteria for sporadic CJD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Zerr 2009)	Retrospective	74	0.98 (0.87, 1.00)	0.71 (0.50, 0.85)	**LR+**	3.36 (1.80, 6.28)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.03 (0.00, 0.20)	V. serious	n/a	Not serious	Not serious		LOW

Notes on risk of bias

Zerr 2009: Unclear whether patients were selected randomly or consecutively or whether inappropriate exclusions were avoided; the optimal index test thresholds were determined during the study and a subgroup analysis was used to determine test sensitivity and specificity.

P.2.14.18 p-tau 181/total tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Bahl 2008; Leitao 2016)	1 × prospective; 1 × retrospective	282	0.93 (0.71, 0.99)	0.89 (0.84, 0.93)	**LR+**	8.10 (5.35, 12.26)	V. serious	Not serious	Not serious	Not serious	-	LOW
					LR-	0.08 (0.02, 0.37)	V. serious	Serious	Not serious	Not serious		VERY LOW
Notes on risk of bias Bahl 2008: Exclusion of possible CJD group from index tests may inflate test sensitivity; test cut off not pre-specified Leitao 2016: It was unclear whether: a consecutive or random sample of patients was enrolled; the study avoided inappropriate exclusions; test thresholds were pre-specified.												

P.2.14.19 RT-QuIC

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Foutz 2017; Lattanzio 2017)	1 × prospective; 1 × retrospective	779	0.89 (0.69, 0.97)	0.99 (0.96, 1.00)	**LR+**	99.38 (26.52, 372.49)	Not serious	Not serious	Not serious	Not serious	-	HIGH

P.2.14.20 S100B, 1.0ng/ml

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Chohan 2010)	Retrospective	412	0.65 (0.59, 0.71)	0.90 (0.84, 0.94)	**LR+**	6.46 (4.08, 10.24)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.39 (0.33, 0.47)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Chohan 2010: Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.												

P.2.14.21 S100B, 2.5ng/ml

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Beudry 1998; Coulthart 2011)	2 × prospective	1,053	0.87 (0.82, 0.91)	0.87 (0.84, 0.89)	**LR+**	6.65 (5.52, 8.00)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.15 (0.10, 0.21)	Serious	Not serious	Not serious	Not serious		MODERATE

Notes on risk of bias

Beudry 1998: Optimised test cut-offs were used and it was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test.
Coulthart 2011: Optimised threshold used to analyse S100B results; unclear whether the reference standards would correctly classify non-CJD cases as not specified; not downgraded for exclusions during data analysis as <10% population excluded.

P.2.14.22 S100B, 4.2ng/ml

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Coulthart 2011)	Prospective	924	0.52 (0.43, 0.60)	0.97 (0.96, 0.98)	**LR+**	17.26 (11.23, 26.52)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.50 (0.41, 0.60)	Not serious	n/a	Not serious	Serious		MODERATE

Notes on risk of bias

Coulthart 2011: Unclear whether the reference standards would correctly classify non-CJD cases as not specified; not downgraded for exclusions during data analysis as <10% population excluded and standard threshold used to analyse S100B results.

P.2.14.23 Total Tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
11 studies (Bahl 2008; Chohan 2010; Coulthart 2011; Foutz 2017; Hamlin 2012; Lattanzio 2017; Leitao 2016; Rohan 2015; Tagliapietra 2013; Van Everbroeck 2003; Van Everbroeck 2004)	4 × prospective; 7 × retrospective	3,614	0.87 (0.84, 0.90)	0.88 (0.80, 0.93)	**LR+**	7.22 (4.34, 11.60)	Serious	Serious	Not serious	Not serious	-	LOW
					LR-	0.15 (0.12, 0.19)	Serious	Serious	Not serious	Not serious		LOW

Notes on risk of bias

Van Everbroeck 2004: > 10% population excluded from analysis
Bahl 2008: Exclusion of possible CJD group from index tests may inflate test sensitivity; test cut off not pre-specified
Chohan 2010: Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.
Coulthart 2011: Optimised threshold used to analyse Tau results; unclear whether the reference standards would correctly classify non-CJD cases as not specified; not downgraded for exclusions during data analysis as <10% population excluded.
Hamlin 2012: Multiple thresholds were tested and unclear whether researchers were blind to reference test results or that the reference test was interpreted without knowledge of index test.
Rohan 2015: It was unclear whether: a consecutive or random sample of patients was enrolled; the index test results were interpreted without knowledge of the results of the reference standard; a pre-specified cut-off was used for the index tests; the reference standard results were interpreted without knowledge of the index test results.
Leitao 2016: It was unclear whether: a consecutive or random sample of patients was enrolled; the study avoided inappropriate exclusions; test thresholds were pre-specified.
Lattanzio 2017: An optimised threshold was used for the assay.

P.2.14.24 Total Tau and S100B

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Chohan 2010)	Retrospective	351	0.59 (0.52, 0.65)	0.95 (0.90, 0.98)	**LR+**	11.34 (5.46, 23.53)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.43 (0.37, 0.51)	Serious	n/a	Not serious	Serious		LOW

Notes on risk of bias

Chohan 2010: Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.

P.2.14.25 WHO CJD criteria

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Heath 2010; Zerr 2009)	2 × retrospective	306	0.90 (0.85, 0.94)	0.71 (0.61, 0.79)	**LR+**	3.14 (2.29, 4.30)	V. serious	Not serious	Serious	Not serious	-	VERY LOW
					LR-	0.14 (0.09, 0.21)	V. serious	Not serious	Serious	Not serious		VERY LOW

Notes on risk of bias

Zerr 2009: Unclear whether patients were selected randomly or consecutively or whether inappropriate exclusions were avoided; the optimal index test thresholds were determined during the study and a subgroup analysis was used to determine test sensitivity and specificity.
Heath 2010: It was unclear whether the index test was interpreted without knowledge of the results of the reference test; whether a consecutive or random sample of patients was enrolled or inappropriate exclusions were avoided.

Notes on indirectness

Heath 2010: Mean age at onset< 40 years old

P.2.15 DLB versus AD

P.2.15.1 Lewy body composite risk score, LBCRS, ≥ 3

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Galvin 2015)	Prospective	153	0.94 (0.84, 0.98)	0.78 (0.69, 0.85)	**LR+**	4.29 (2.95, 6.24)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.07 (0.02, 0.22)	Serious	n/a	Not serious	Not serious		MODERATE

Notes on risk of bias
Galvin 2015: Subgroup analysis was carried out excluding >30% study population.

P.2.15.2 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	270	0.43 (0.29, 0.57)	0.71 (0.65, 0.77)	**LR+**	1.48 (1.00, 2.19)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.81 (0.62, 1.04)	Serious	n/a	Not serious	Not serious		MODERATE

Notes on risk of bias
Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.

P.2.16 DLB versus FTD

P.2.16.1 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	139	0.43 (0.29, 0.57)	0.86 (0.77, 0.92)	**LR+**	3.01 (1.65, 5.51)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.67 (0.52, 0.87)	Serious	n/a	Not serious	Not serious		MODERATE

Notes on risk of bias

Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.

P.2.17 DLB versus non-DLB

P.2.17.1 123I-FP-CIT SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
1 study (Walker 2009)	Retrospective	23	0.95 (0.55, 1.00)	0.89 (0.61, 0.98)	**LR+**	8.91 (1.95, 40.64)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.05 (0.00, 0.77)	Serious	n/a	Not serious	Serious		LOW
MULTIPLE CAMERA												
2 studies (Kemp 2011; O'Brien 2009; Thomas 2017)	1x prospective, 2x retrospective	161	0.78 (0.59, 0.89)	0.95 (0.87, 0.98)	**LR+**	15.40 (6.24, 38.01)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.25 (0.13, 0.48)	Not serious	Serious	Not serious	Not serious		MODERATE
ALL EVIDENCE POOLED												
3 studies (Kemp 2011; O'Brien 2009; Walker 2009; Thomas 2017)	1x prospective, 2 × retrospective	184	0.83 (0.52, 0.96))	0.94 (0.86, 0.98)	**LR+**	13.34 (6.14, 29.01)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.22 (0.11, 0.44)	Not serious	Not serious	Not serious	Not serious		HIGH
Notes on risk of bias Walker 2009: Some of the included individuals had a presumed dementia diagnosis at baseline Kemp 2011: Index test used as part of the reference standard												

P.2.17.2 123I-IMP SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA												
1 study (Sakamoto 2014)	Retrospective	101	0.62 (0.42, 0.78)	0.75 (0.64, 0.83)	**LR+**	2.43 (1.48, 3.98)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.52 (0.31, 0.85)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Sakamoto 2014: It was unclear whether the study avoided inappropriate exclusions or whether the reference standard results were interpreted without knowledge of the results of the index test.												

P.2.17.3 123I-IMP SPECT and 123I-MIBG cardiac scintigraphy combined

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA												
1 study (Sakamoto 2014)	Retrospective	100	0.88 (0.70, 0.96)	0.86 (0.77, 0.93)	**LR+**	6.55 (3.62, 11.84)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.13 (0.05, 0.39)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Sakamoto 2014: It was unclear whether the study avoided inappropriate exclusions or whether the reference standard results were interpreted without knowledge of the results of the index test.												

P.2.17.4 123I-MIBG cardiac scintigraphy

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
5 studies (Estorch 2008; Manabe 2017; Sakamoto 2014; Sakamoto 2017, Slaets 2015)	4 × prospective; 1 × retrospective	607	0.89 (0.81, 0.93)	0.91 (0.82, 0.96)	**LR+**	10.80 (4.89, 21.50)	Serious	Serious	Not serious	Not serious	-	LOW
					LR-	0.13 (0.07, 0.21)	V. serious	Not serious	Not serious	Not serious		LOW

Notes on risk of bias

Estorch 2008: Significant proportion of people not given a final reference standard diagnosis

Sakamoto 2014: It was unclear whether the study avoided inappropriate exclusions or whether the reference standard results were interpreted without knowledge of the results of the index test.

Slaets 2015: The diagnosing physicians were not blind to the index test results.

Manabe 2017: Optimised test cut-offs were calculated and it was unclear whether the reference standard was interpreted without knowledge of the results of the index test or the index test was interpreted without knowledge of the results of the reference test.

Sakamoto 2017: Selective reporting of sensitivity and specificity of outcome variables and it was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; whether the reference standard results were interpreted without knowledge of the results of the index test or whether the test cut-off was pre-specified.

P.2.17.5 EEG

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Engedal 2015)	Prospective	387	0.87 (0.59, 0.97)	0.88 (0.84, 0.91)	**LR+**	7.01 (5.01, 9.80)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.15 (0.04, 0.55)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.17.6 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Ossenkoppele 2013; Panegyres 2009)	2 × prospective	255	0.53 (0.06, 0.96)	0.97 (0.91, 0.99)	**LR+**	19.64 (1.28, 301.23)	Serious	Serious	Serious	Serious	-	VERY LOW
					LR-	0.48 (0.11, 2.13)	Serious	Serious	Serious	V. serious		VERY LOW

Notes on risk of bias

Ossenkoppele 2013: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the index test was interpreted with knowledge of the reference diagnosis.

Notes on indirectness

Panegyres 2009: The study only recruited people with early onset dementia (<65 years old).
Ossenkoppele 2013: It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.

P.2.17.7 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	504	0.43 (0.29, 0.57)	0.76 (0.72, 0.80)	**LR+**	1.80 (1.24, 2.61)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.75 (0.59, 0.97)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.17.8 RBD or two or more of visual hallucinations, Parkinsonism, and fluctuating attention and concentration

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ferman 2011)	Prospective	234	0.90 (0.82, 0.94)	0.73 (0.65, 0.80)	**LR+**	3.30 (2.49, 4.38)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.14 (0.08, 0.25)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.17.9 Two or more of fluctuating attention and concentration, visual hallucinations and Parkinsonism

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ferman 2011)	Prospective	234	0.85 (0.76, 0.91)	0.73 (0.65, 0.80)	**LR+**	3.11 (2.34, 4.15)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.21 (0.13, 0.34)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.17.10 Two or more of visual hallucinations, Parkinsonism or RBD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ferman 2011)	Prospective	234	0.83 (0.74, 0.89)	0.85 (0.77, 0.90)	**LR+**	5.35 (3.58, 8.01)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.21 (0.13, 0.32)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.17.11 Two or more of visual hallucinations, Parkinsonism, fluctuating attention and concentration or RBD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ferman 2011)	Prospective	234	0.88 (0.80, 0.93)	0.73 (0.65, 0.80)	**LR+**	3.23 (2.43, 4.29)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.17 (0.10, 0.29)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.18 DLB versus other dementias

P.2.18.1 123I-FP-CIT SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
1 study (Treglia 2012)	Prospective	31	0.90 (0.68, 0.97)	0.91 (0.56, 0.99)	**LR+**	9.90 (1.52, 64.52)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.11 (0.03, 0.42)	Not serious	n/a	Not serious	Not serious		HIGH
MULTIPLE CAMERA												
1 study (Walker 2007)	Retrospective	20	0.83 (0.46, 0.97)	0.96 (0.60, 1.00)	**LR+**	21.67 (1.43, 333.42)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.17 (0.04, 0.75)	Not serious	n/a	Not serious	Serious		MODERATE
ALL EVIDENCE POOLED												
2 studies (Treglia 2012; Walker 2007)	1 × prospective; 1 × retrospective	51	0.88 (0.70, 0.96)	0.93 (0.72 0.99)	**LR+**	12.72 (2.71, 59.68)	Not serious	Not serious	Not serious	Not serious	-	HIGH
					LR-	0.14 (0.05, 0.36)	Not serious	Not serious	Not serious	Not serious		HIGH

Notes on risk of bias
Treglia 2012: Specific criteria used as the reference standard not reported

P.2.18.2 123I-MIBG cardiac scintigraphy

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Treglia 2012)	Prospective	31	0.90 (0.68, 0.97)	0.91 (0.56, 0.99)	**LR+**	9.90 (1.52, 64.52)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.11 (0.03, 0.42)	Not serious	n/a	Not serious	Not serious		HIGH
Notes on risk of bias Treglia 2012: Specific criteria used as the reference standard not reported												

P.2.18.3 DLB consensus criteria

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skogseth 2017)	Prospective	55	0.80 (0.57, 0.92)	0.89 (0.74, 0.96)	**LR+**	7.20 (2.79, 18.61)	Serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.23 (0.09, 0.54)	Serious	n/a	Not serious	Serious		LOW

P.2.18.4 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ossenkoppele 2013)	Prospective	98	0.20 (0.03, 0.69)	0.95 (0.88, 0.98)	**LR+**	3.72 (0.53, 26.13)	V. serious	n/a	Serious	Serious	-	VERY LOW
					LR-	0.85 (0.54, 1.31)	V. serious	n/a	Serious	Not serious		VERY LOW

Notes on risk of bias
Ossenkoppele 2013: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the index test was interpreted with knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.
Notes on indirectness
Ossenkoppele 2013: It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.

P.2.18.5 Lewy body composite risk score, LBCRS, ≥ 3

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Galvin 2015)	Prospective	177	0.98 (0.88, 1.00)	0.86 (0.79, 0.91)	**LR+**	7.16 (4.59, 11.15)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.02 (0.00, 0.15)	Serious	n/a	Not serious	Not serious		MODERATE

Notes on risk of bias
Galvin 2015: Subgroup analysis was carried out excluding >30% study population.

P.2.18.6 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	386	0.43 (0.29, 0.57)	0.76 (0.72, 0.81)	**LR+**	1.80 (1.23, 2.65)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.75 (0.58, 0.97)	Serious	n/a	Not serious	Not serious		MODERATE

Notes on risk of bias

Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.

P.2.19 DLB versus VaD

P.2.19.1 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	71	0.43 (0.29, 0.57)	0.88 (0.68, 0.96)	**LR+**	3.40 (1.12, 10.32)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.66 (0.49, 0.88)	Serious	n/a	Not serious	Serious		LOW

Notes on risk of bias

Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.

P.2.20 FTD versus AD

P.2.20.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
4 studies (Launes 1991; Read 1995; Talbot 1998; Velakoulis 1997)	3 × prospective; 1 × retrospective	291	0.51 (0.35, 0.67)	0.96 (0.92, 0.98)	**LR+**	13.11 (6.13, 28.05)	V. serious	Not serious	Not serious	Not serious	-	LOW
					LR-	0.55 (0.45, 0.66)	V. serious	Not serious	Not serious	Serious		VERY LOW
MULTIPLE CAMERA												
2 studies (Boutoleau-Bretonniere 2012; Rollin-Sillaire 2012)	1 × prospective; 1 × retrospective	64	0.73 (0.52, 0.87)	0.96 (0.82, 0.99)	**LR+**	18.12 (3.71, 88.60)	V. serious	Not serious	Not serious	Not serious	-	LOW
					LR-	0.28 (0.15, 0.54)	V. serious	Not serious	Not serious	Serious		VERY LOW
ALL EVIDENCE POOLED												
6 studies (Boutoleau-Bretonniere 2012; Launes 1991; Read 1995; Rollin-Sillaire 2012; Talbot 1998; Velakoulis 1997)	4 × prospective; 2 × retrospective	355	0.58 (0.44, 0.72)	0.96 (0.92, 0.98)	**LR+**	13.50 (6.77, 24.20)	V. serious	Not serious	Not serious	Not serious	-	LOW
					LR-	0.44 (0.30, 0.59)	V. serious	Not serious	Not serious	Serious		VERY LOW

Studies	Design	Tota l N	Sens (95%CI)	Spec (95%CI)	Measu re	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality

Notes on risk of bias

Launes 1991: Subgroup analysis used with >10% study population excluded.
Read 1995: Subgroup analysis used with >10% study population excluded; unclear whether random or consecutive patient enrolment was used; unclear if inappropriate exclusions avoided.
Velakoulis 1997: Subgroup analysis where >10% study population excluded and it was unclear whether: the index test results were interpreted without knowledge of the results of the reference standard; the index test threshold was pre-specified or the reference standard results interpreted without knowledge of the results of the index test.
Talbot 1998: Unclear if avoided inappropriate exclusions; unclear whether the reference standard results were interpreted without knowledge of the index test and whether the index test was carried out without knowledge of reference test result; no pre-specified index test threshold; subgroup analysis used with >10% study population excluded.
Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.
Rollin-Sillaire 2012: Subgroup analysis where >10% study population excluded

P.2.20.2 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	315	0.50 (0.40, 0.60)	0.72 (0.66, 0.78)	**LR+**	1.80 (1.34, 2.41)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.69 (0.56, 0.86)	Serious	n/a	Not serious	Not serious		MODERATE

Notes on risk of bias

Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.

P.2.20.3 FTD versus DLB

P.2.20.4 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ossenkoppele 2013)	Prospective	23	0.34 (0.17, 0.57)	0.92 (0.38, 0.99)	**LR+**	4.11 (0.27, 62.70)	V. serious	n/a	Serious	V. serious	-	VERY LOW
					LR-	0.72 (0.48, 1.08)	V. serious	n/a	Serious	Serious		VERY LOW

Notes on risk of bias

Ossenkoppele 2013: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the index test was interpreted with knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.

Notes on indirectness

Ossenkoppele 2013: It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.

P.2.20.5 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	139	0.50 (0.40, 0.60)	0.94 (0.82, 0.98)	**LR+**	7.83 (2.57, 23.86)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.53 (0.43, 0.66)	Serious	n/a	Not serious	Serious		LOW

Notes on risk of bias

Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.

P.2.21 FTD versus non-FTD dementia plus unclassifiable

P.2.21.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA												
1 study (Boutoleau-Bretonniere 2012)	Prospective	56	0.73 (0.41, 0.91)	0.78 (0.63, 0.88)	**LR+**	3.27 (1.70, 6.30)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.35 (0.13, 0.93)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used but <10% study population discarded												

P.2.22 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Boutoleau-Bretonniere 2012)	Prospective	56	0.18 (0.05, 0.51)	0.62 (0.47, 0.75)	**LR+**	0.48 (0.13, 1.78)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	1.31 (0.92, 1.88)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases.												

P.2.23 FTD versus non-FTD

P.2.23.1 99mTc-ECD SPECT, visual assessment

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA												
1 study (Tripathi 2010)	Prospective	117	0.96 (0.78, 0.99)	0.99 (0.93, 1.00)	**LR+**	86.67 (12.32, 609.43)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.04 (0.01, 0.26)	Serious	n/a	Not serious	Not serious		MODERATE

Notes on risk of bias
Tripathi 2010: 14% of participants were lost to follow up and did not receive a reference standard; it is unclear whether the index test was interpreted without knowledge of the reference standard.

P.2.23.2 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
3 studies (Launes 1991; Read 1995; Talbot 1998)	2 × prospective; 1 × retrospective	501	0.51 (0.20, 0.81)	0.93 (0.90, 0.95)	**LR+**	6.05 (2.77, 13.22)	V. serious	Not serious	Not serious	Not serious	-	LOW
					LR-	0.63 (0.40, 1.01)	V. serious	Not serious	Not serious	Serious		VERY LOW
MULTIPLE CAMERA												
2 studies (Boutoleau-Bretonniere 2012; Rollin-Sillaire 2012)	1 × prospective; 1 × retrospective	108	0.74 (0.53, 0.88)	0.90 (0.53, 0.99)	**LR+**	7.88 (1.14, 54.71)	Serious	Serious	Not serious	Serious	-	VERY LOW
					LR-	0.30 (0.15, 0.59)	Serious	Not serious	Not serious	Serious		LOW
ALL EVIDENCE POOLED												
5 studies (Boutoleau-Bretonniere 2012; Launes 1991; Read 1995; Rollin-Sillaire 2012; Talbot 1998)	3 × prospective; 2 × retrospective	609	0.59 (0.37, 0.78)	0.91 (0.84, 0.95)	**LR+**	7.03 (3.36, 13.10)	V. serious	Not serious	Not serious	Not serious	-	LOW
					LR-	0.46 (0.24, 0.69)	V. serious	Serious	Not serious	Serious		VERY LOW

Notes on risk of bias

Talbot 1998: Unclear if avoided inappropriate exclusions; unclear whether the reference standard results were interpreted without knowledge of the index test and whether the index test was carried out without knowledge of reference test result; no pre-specified index test threshold; subgroup analysis used as data on 'other' clinical diagnosis group is not reported.
Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases

P.2.23.3 SPECT/PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
1 study (Mendez 2007)	Prospective	134	0.90 (0.80, 0.96)	0.75 (0.63, 0.83)	**LR+**	3.57 (2.38, 5.36)	Not serious	n/a	Serious	Not serious	-	HIGH
					LR-	0.13 (0.06, 0.28)	Not serious	n/a	Serious	Not serious		HIGH

P.2.23.4 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Ossenkoppele 2013; Panegyres 2009)	2 × prospective	255	0.43 (0.25, 0.63)	0.93 (0.87, 0.96)	**LR+**	6.20 (2.12, 18.11)	Serious	Serious	Serious	Not serious	-	VERY LOW
					LR-	0.63 (0.43, 0.92)	Serious	Not serious	Serious	Serious		VERY LOW

Notes on risk of bias

Ossenkoppele 2013: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the index test was interpreted with knowledge of the reference diagnosis.

Notes on indirectness

Panegyres 2009: The study only recruited people with early onset dementia (<65 years old).
Ossenkoppele 2013: It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.

P.2.23.5 FTD consensus criteria

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Mendez 2007)	Retrospective	134	0.37 (0.26, 0.49)	0.99 (0.90, 1.00)	**LR+**	52.88 (3.28, 853.00)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.64 (0.53, 0.77)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.23.6 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Koikkalainen 2016; Mendez 2007)	1 × prospective; 1 × retrospective	638	0.56 (0.43, 0.69)	0.78 (0.63, 0.89)	**LR+**	2.66 (1.85, 3.82)	Not serious	Serious	Not serious	Serious	-	LOW
					LR-	0.57 (0.48, 0.69)	Not serious	Not serious	Not serious	Serious		MODERATE

P.2.24 FTD versus other dementias

P.2.24.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
1 study (Velakoulis 1997)	Prospective	33	0.56 (0.25, 0.82)	0.96 (0.76, 0.99)	**LR+**	13.33 (1.79, 99.08)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.46 (0.22, 0.97)	V. serious	n/a	Not serious	Serious		VERY LOW

Notes on risk of bias

Velakoulis 1997: Subgroup analysis where >10% study population excluded and it was unclear whether: the index test results were interpreted without knowledge of the results of the reference standard; the index test threshold was pre-specified or the reference standard results interpreted without knowledge of the results of the index test.

P.2.24.2 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Arslan 2015; Ossenkoppele 2013)	1 × prospective; 1 × retrospective	146	0.40 (0.25, 0.57)	0.78 (0.49, 0.93)	**LR+**	1.78 (0.91, 3.51)	V. serious	Not serious	Serious	Serious	-	VERY LOW
					LR-	0.78 (0.59, 1.03)	V. serious	Not serious	Serious	Not serious		VERY LOW

Notes on risk of bias

Ossenkoppele 2013: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the index test was interpreted with knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.
Arslan 2015: Unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard and if the imaging patterns were pre-specified; the reference standard results were interpreted independently of the index test results.

Notes on indirectness

Ossenkoppele 2013: It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.

P.2.24.3 FTD scale (≥6)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Gustafson 2010)	Prospective	190	0.92 (0.81, 0.97)	0.92 (0.86, 0.96)	**LR+**	11.58 (6.53, 20.52)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.08 (0.03, 0.21)	Not serious	n/a	Not serious	Not serious		HIGH

Notes on risk of bias

Gustafson 2010: The study was not downgraded for subgroup analysis as <10% population was excluded.

P.2.24.4 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	386	0.50 (0.40, 0.60)	0.78 (0.72, 0.82)	**LR+**	2.23 (1.66, 2.99)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.64 (0.52, 0.80)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.												

P.2.25 FTD versus VaD

P.2.25.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
2 studies (Launes 1991; Talbot 1998)	2 × prospective	196	0.46 (0.36, 0.57)	0.85 (0.51, 0.97)	**LR+**	2.58 (0.77, 8.64)	V. serious	Serious	Not serious	Serious	-	VERY LOW
					LR-	0.72 (0.58, 0.91)	V. serious	Not serious	Not serious	Not serious		LOW
MULTIPLE CAMERA												
1 study (Boutoleau-Bretonniere 2012)	Prospective	19	0.73 (0.41, 0.91)	0.75 (0.38, 0.94)	**LR+**	2.91 (0.83, 10.19)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.36 (0.13, 1.03)	V. serious	n/a	Not serious	Serious		VERY LOW
ALL EVIDENCE POOLED												
3 studies (Boutoleau-Bretonniere 2012; Launes 1991; Talbot 1998)	3 × prospective	215	0.51 (0.35, 0.67)	0.82 (0.61, 0.93)	**LR+**	2.23 (1.20, 4.16)	V. serious	Not serious	Not serious	Serious	-	VERY LOW
					LR-	0.70 (0.56, 0.88)	V. serious	Not serious	Not serious	Not serious		LOW

Notes on risk of bias
Launes 1991: Subgroup analysis used with >10% study population excluded.
Talbot 1998: Unclear if avoided inappropriate exclusions; unclear whether the reference standard results were interpreted without knowledge of the index test and whether the index test was carried out without knowledge of reference test result; no pre-specified index test threshold; subgroup analysis used with >10% study population excluded.
Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.

P.2.25.2 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	116	0.50 (0.40, 0.60)	0.96 (0.76, 0.99)	**LR+**	12.00 (1.74, 82.64)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.52 (0.42, 0.65)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.												

P.2.26 HAND versus other neurological disorders in HIV+ people

P.2.26.1 HIV dementia scale (<10)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skinner 2009)	Prospective	33	0.46 (0.22, 0.72)	0.80 (0.57, 0.92)	**LR+**	2.31 (0.80, 6.63)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.67 (0.39, 1.17)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.26.2 HIV dementia scale (<11)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skinner 2009)	Prospective	33	0.62 (0.34, 0.83)	0.80 (0.57, 0.92)	**LR+**	3.08 (1.16, 8.17)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.48 (0.23, 0.99)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Skinner 2009: Use of an optimised threshold.												

P.2.26.3 International HIV Dementia scale (IHDS) (<10)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skinner 2009)	Prospective	33	0.77 (0.48, 0.92)	0.65 (0.43, 0.82)	**LR+**	2.20 (1.13, 4.28)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.36 (0.13, 1.01)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.26.4 Grooved pegboard test

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Davis 2002)	Prospective	455	0.71 (0.63, 0.78)	0.46 (0.41, 0.52)	**LR+**	1.31 (1.13, 1.52)	Serious	n/a	Serious	Not serious	-	LOW
					LR-	0.63 (0.48, 0.84)	Serious	n/a	Serious	Serious		VERY LOW

P.2.26.5 Modified HIV dementia scale (m-HDS) (<7.5)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Davis 2002)	Prospective	455	0.70 (0.62, 0.77)	0.71 (0.66, 0.76)	**LR+**	2.42 (1.98, 2.97)	Serious	n/a	Serious	Serious	-	VERY LOW
					LR-	0.42 (0.32, 0.55)	Serious	n/a	Serious	Serious		VERY LOW

P.2.26.6 Modified HIV dementia scale (m-HDS) and grooved pegboard combined.

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Davis 2002)	Prospective	455	0.77 (0.70, 0.83)	0.40 (0.35, 0.45)	**LR+**	1.28 (1.13, 1.46)	Serious	n/a	Serious	Not serious	-	LOW
					LR-	0.57 (0.41, 0.80)	Serious	n/a	Serious	Serious		VERY LOW

P.2.27 Neurosyphilis versus not neurosyphilis

P.2.27.1 CSF EIA

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Chan 2014)	Prospective	45	0.97 (0.68, 1.00)	0.47 (0.30, 0.64)	**LR+**	1.82 (1.28, 2.58)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.06 (0.00, 0.94)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.27.2 FTA-ABS

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Dumaresq 2013)	Retrospective	100	0.97 (0.65, 1.00)	0.11 (0.06, 0.20)	**LR+**	1.09 (0.97, 1.22)	Not serious	n/a	Serious	Not serious	-	MODERATE
					LR-	0.28 (0.02, 4.62)	Not serious	n/a	Serious	V. serious		VERY LOW
Notes on indirectness Dumaresq 2013: >99% men who have sex with men												

P.2.27.3 INNO-LIA

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Dumaresq 2013)	Retrospective	83	0.96 (0.60, 1.00)	0.12 (0.06, 0.21)	**LR+**	1.09 (0.95, 1.25)	Not serious	n/a	Serious	Not serious	-	MODERATE
					LR-	0.33 (0.02, 5.31)	Not serious	n/a	Serious	V. serious		VERY LOW
Notes on indirectness Dumaresq 2013: >99% men who have sex with men												

P.2.27.4 PCR for T. pallidum genes: polA, Tpp47, and bmp.

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Dumaresq 2013)	Retrospective	108	0.40 (0.19, 0.65)	0.61 (0.51, 0.71)	**LR+**	1.03 (0.53, 2.02)	Not serious	n/a	Serious	Serious	-	LOW
					LR-	0.98 (0.63, 1.53)	Not serious	n/a	Serious	Not serious		MODERATE
Notes on indirectness Dumaresq 2013: >99% men who have sex with men												

P.2.27.5 TPPA

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Dumaresq 2013)	Retrospective	100	0.67 (0.41, 0.85)	0.47 (0.37, 0.58)	**LR+**	1.26 (0.84, 1.90)	Not serious	n/a	Serious	Not serious	-	MODERATE
					LR-	0.71 (0.33, 1.50)	Not serious	n/a	Serious	Serious		LOW
Notes on indirectness Dumaresq 2013: >99% men who have sex with men												

P.2.28 PDD and DLB versus other dementias

P.2.28.1 123I-MIBG cardiac scintigraphy

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Hanyu 2006)	Prospective	96	0.95 (0.82, 0.99)	0.87 (0.76, 0.94)	**LR+**	7.47 (3.73, 14.98)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.06 (0.01, 0.22)	Serious	n/a	Not serious	Not serious		MODERATE

Notes on risk of bias
Hanyu 2006: It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard and whether the reference standard results were interpreted without knowledge of the results of the index test.

P.2.29 PDD versus non-PDD

P.2.29.1 FCSRT-IR 3- FR (≤22)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Kiesman 2013)	Prospective	40	0.84 (0.67, 0.93)	0.78 (0.42, 0.94)	**LR+**	3.77 (1.10, 12.94)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.21 (0.09, 0.50)	Serious	n/a	Not serious	Not serious		MODERATE

Notes on risk of bias
Kiesman 2013: Test threshold was not pre-specified.

P.2.29.2 Movement disorders criteria for PDD (≤120)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Kiesman 2013)	Prospective	40	0.80 (0.62, 0.90)	0.95 (0.53, 1.00)	**LR+**	15.94 (1.06, 238.88)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.21 (0.11, 0.43)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Kiesman 2013: Test threshold was not pre-specified.												

P.2.29.3 Movement disorders criteria for PDD (≤123)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Kiesman 2013)	Prospective	40	0.94 (0.78, 0.98)	0.78 (0.42, 0.94)	**LR+**	4.21 (1.24, 14.34)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.08 (0.02, 0.33)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Kiesman 2013: Test threshold was not pre-specified.												

P.2.29.4 Movement disorders criteria for PDD (≤132)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Kiesman 2013)	Prospective	40	0.98 (0.79, 1.00)	0.45 (0.19, 0.74)	**LR+**	1.79 (1.02, 3.14)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.03 (0.00, 0.59)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Kiesman 2013: Test threshold was not pre-specified.												

P.2.29.5 Rey-Osterrieth complex figure test, ROCF (≤22)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Kiesman 2013)	Prospective	40	0.90 (0.74, 0.97)	0.78 (0.42, 0.94)	**LR+**	4.06 (1.19, 13.87)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.12 (0.04, 0.39)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Kiesman 2013: Test threshold was not pre-specified.												

P.2.30 PPA versus non-PPA

P.2.30.1 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Panegyres 2009)	Prospective	102	0.50 (0.19, 0.81)	0.99 (0.92, 1.00)	**LR+**	97.00 (5.54, 1697.47)	Not serious	n/a	Serious	Not serious	-	MODERATE
					LR-	0.50 (0.24, 1.05)	Not serious	n/a	Serious	Serious		LOW

Notes on indirectness
Panegyres 2009: The study only recruited people with early onset dementia (<65 years old).

P.2.31 VaD and mixed dementias versus AD

P.2.31.1 Hachinski ischemic score, HIS (≥5)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Siritho 2006)	Prospective	214	0.86 (0.77, 0.92)	0.73 (0.65, 0.80)	**LR+**	3.17 (2.36, 4.25)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.19 (0.11, 0.33)	V. serious	n/a	Not serious	Not serious		LOW

Notes on risk of bias
Siritho 2006: Subgroup analysis excluded >45% study population; optimised test-threshold was used and it was unclear whether the index test results were interpreted without knowledge of the results of the reference standard or whether the reference standard was interpreted without knowledge of the results of the index test.

P.2.32 VaD versus AD and mixed dementia (AD plus VaD)

P.2.32.1 ADDTC (possible)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Gold 2002)	Retrospective	89	0.70 (0.47, 0.86)	0.78 (0.67, 0.86)	**LR+**	3.22 (1.89, 5.48)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.38 (0.19, 0.76)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.32.2 ADDTC (probable)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Gold 2002)	Retrospective	89	0.25 (0.11, 0.48)	0.91 (0.82, 0.96)	**LR+**	2.88 (0.98, 8.44)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.82 (0.63, 1.07)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.32.3 ADDTC criteria

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Bachetta 2007)	Retrospective	110	0.58 (0.42, 0.73)	0.74 (0.63, 0.83)	**LR+**	2.27 (1.41, 3.66)	Not serious	n/a	Serious	Serious	-	LOW
					LR-	0.56 (0.37, 0.84)	Not serious	n/a	Serious	Serious		LOW
Notes on indirectness Bachetta 2007: Participants were selected to be >90 years old												

P.2.32.4 Hachinski ischemic score, HIS (≥7)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Bachetta 2007)	Retrospective	110	0.56 (0.39, 0.71)	0.66 (0.55, 0.76)	**LR+**	1.64 (1.07, 2.53)	Not serious	n/a	Serious	Serious	-	LOW
					LR-	0.67 (0.45, 1.00)	Not serious	n/a	Serious	Serious		LOW
Notes on indirectness Bachetta 2007: Participants were selected to be >90 years old												

P.2.32.5 NINDS-AIREN (possible)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Gold 2002)	Retrospective	89	0.55 (0.34, 0.75)	0.84 (0.73, 0.91)	**LR+**	3.45 (1.76, 6.75)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.54 (0.33, 0.88)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.32.6 NINDS-AIREN (probable)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Gold 2002)	Retrospective	89	0.20 (0.08, 0.43)	0.93 (0.84, 0.97)	**LR+**	2.76 (0.82, 9.32)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.86 (0.69, 1.08)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.32.7 NINDS-AIREN criteria

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Bachetta 2007)	Retrospective	110	0.56 (0.39, 0.71)	0.73 (0.62, 0.82)	**LR+**	2.06 (1.28, 3.31)	Not serious	n/a	Serious	Serious	-	LOW
					LR-	0.61 (0.41, 0.90)	Not serious	n/a	Serious	Serious		LOW
Notes on indirectness Bachetta 2007: Participants were selected to be >90 years old												

P.2.33 VaD versus AD

P.2.33.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
2 studies (Launes 1991; McMurdo 1994)	2 × prospective	97	0.76 (0.60, 0.87)	0.77 (0.64, 0.86)	**LR+**	3.21 (1.90, 5.43)	Serious	Not serious	Not serious	Serious	-	LOW
					LR-	0.33 (0.18, 0.60)	Serious	Not serious	Not serious	Serious		LOW
Notes on risk of bias Launes 1991: Subgroup analysis used with >10% study population excluded. McMurdo 1994: Subgroup analysis used with >10% study population discarded.												

P.2.33.2 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	247	0.71 (0.50, 0.85)	0.97 (0.94, 0.98)	**LR+**	22.57 (10.42, 48.88)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.30 (0.16, 0.56)	Serious	n/a	Not serious	Serious		LOW

Notes on risk of bias
Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.

P.2.34 VaD versus DLB

P.2.34.1 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	71	0.71 (0.50, 0.85)	0.96 (0.85, 0.99)	**LR+**	16.65 (4.19, 66.18)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.30 (0.16, 0.57)	Serious	n/a	Not serious	Serious		LOW

Notes on risk of bias
Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.

P.2.35 VaD versus FTD

P.2.35.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
1 study (Launes 1991)	Prospective	38	0.76 (0.58, 0.87)	0.60 (0.20, 0.90)	**LR+**	1.89 (0.64, 5.64)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.40 (0.16, 1.03)	Serious	n/a	Not serious	Serious		LOW

Notes on risk of bias
Launes 1991: Subgroup analysis used with >10% study population excluded.

P.2.35.2 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	116	0.71 (0.50, 0.85)	0.96 (0.89, 0.98)	**LR+**	16.29 (6.04, 43.94)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.30 (0.16, 0.57)	Serious	n/a	Not serious	Serious		LOW

Notes on risk of bias
Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.

P.2.36 VaD versus non-VaD dementia plus unclassifiable

P.2.36.1 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Boutoleau-Bretonniere 2012)	Prospective	56	0.88 (0.46, 0.98)	0.75 (0.61, 0.85)	**LR+**	3.50 (2.01, 6.10)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.17 (0.03, 1.05)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases.												

P.2.37 VaD versus non-VaD

P.2.37.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
2 studies (Launes 1991; McMurdo 1994)	2 × prospective	204	0.76 (0.60, 0.87)	0.64 (0.40, 0.83)	**LR+**	2.16 (1.05, 4.45)	Not serious	Serious	Not serious	Serious	-	LOW
					LR-	0.44 (0.24, 0.81)	Not serious	Not serious	Not serious	Serious		MODERATE

P.2.38 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	504	0.71 (0.50, 0.85)	0.96 (0.94, 0.98)	**LR+**	18.89 (11.22, 31.80)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.30 (0.16, 0.57)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.39 VaD versus other dementias

P.2.39.1 HIS (≥7)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Gustafson 2010)	Prospective	190	0.69 (0.56, 0.80)	0.92 (0.86, 0.96)	**LR+**	8.69 (4.79, 15.75)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.33 (0.22, 0.50)	Not serious	n/a	Not serious	Serious		MODERATE

Notes on risk of bias
Gustafson 2010: The study was not downgraded for subgroup analysis as <10% population was excluded.

P.2.39.2 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	386	0.71 (0.50, 0.85)	0.96 (0.94, 0.98)	**LR+**	19.72 (10.91, 35.66)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.30 (0.16, 0.56)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.												

P.3 Meta-analyses

P.3.1 Dementia versus no dementia

P.3.1.1 ACE (<83)

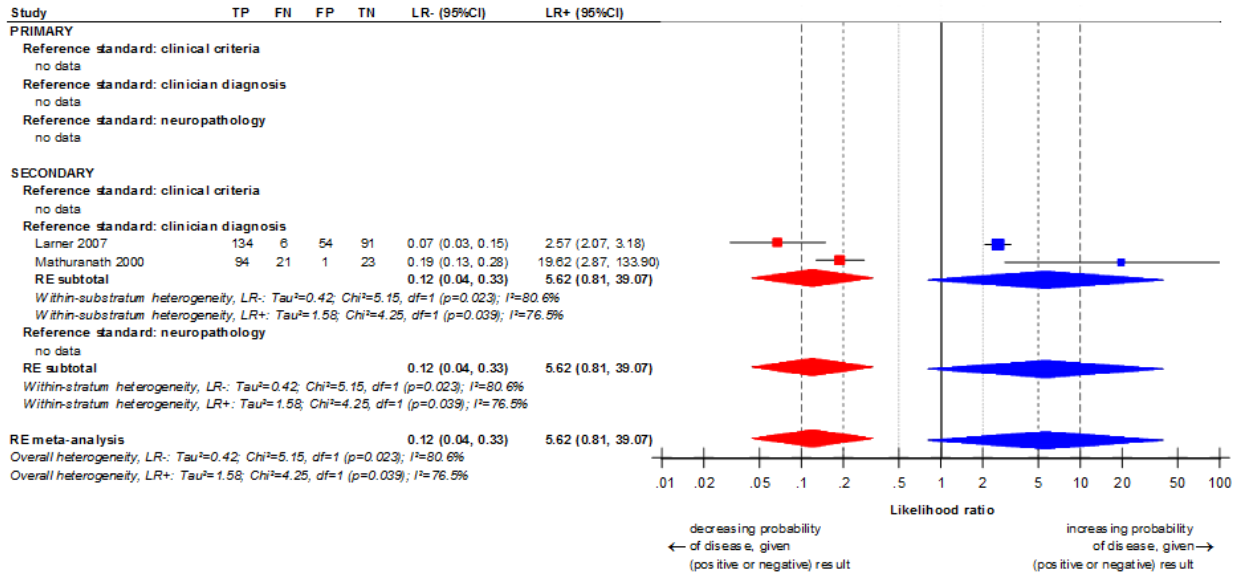


Figure 1 Dementia versus no dementia: ACE (<83) – forest plot: likelihood ratios

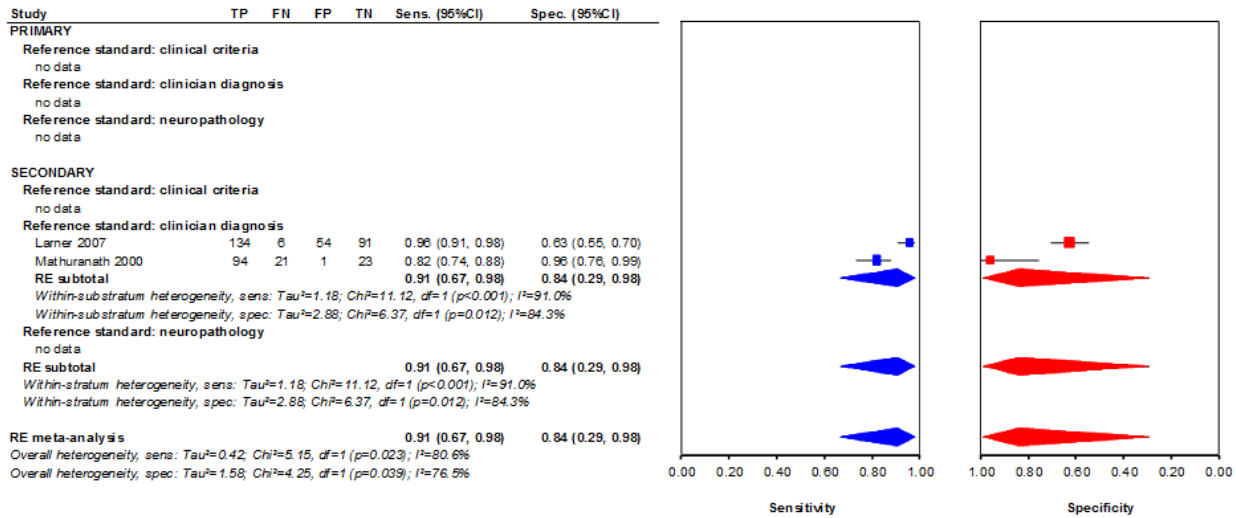


Figure 2 Dementia versus no dementia: ACE (<83) – forest plot: sensitivity and specificity

P.3.1.2 ACE (<88)

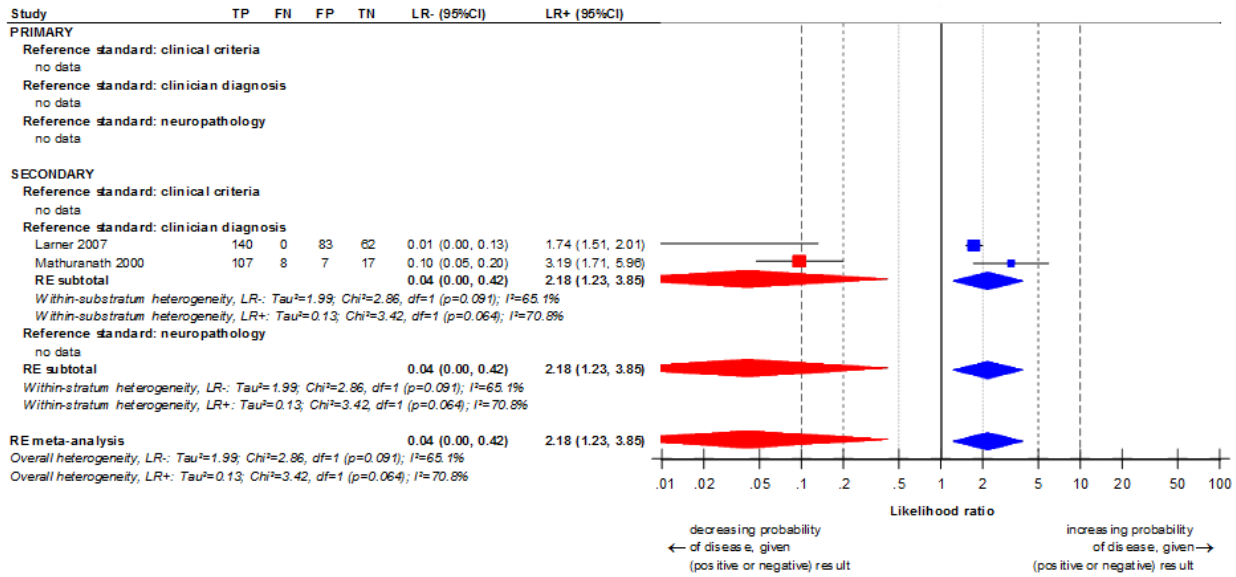


Figure 3 Dementia versus no dementia: ACE (<88) – forest plot: likelihood ratios

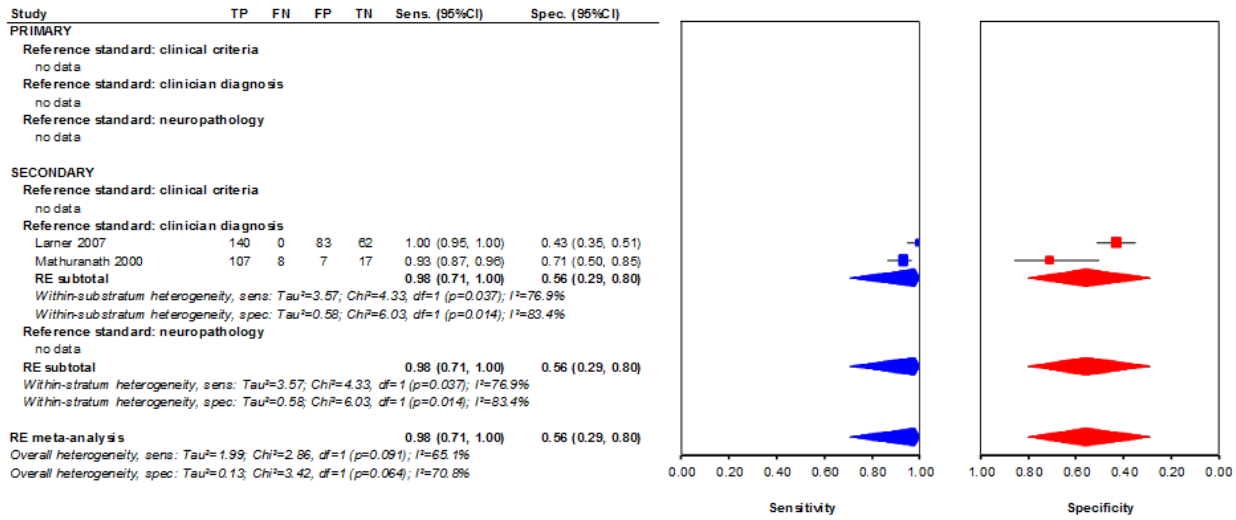


Figure 4 Dementia versus no dementia: ACE (<88) – forest plot: sensitivity and specificity

P.3.1.3 ACE-R (<83)

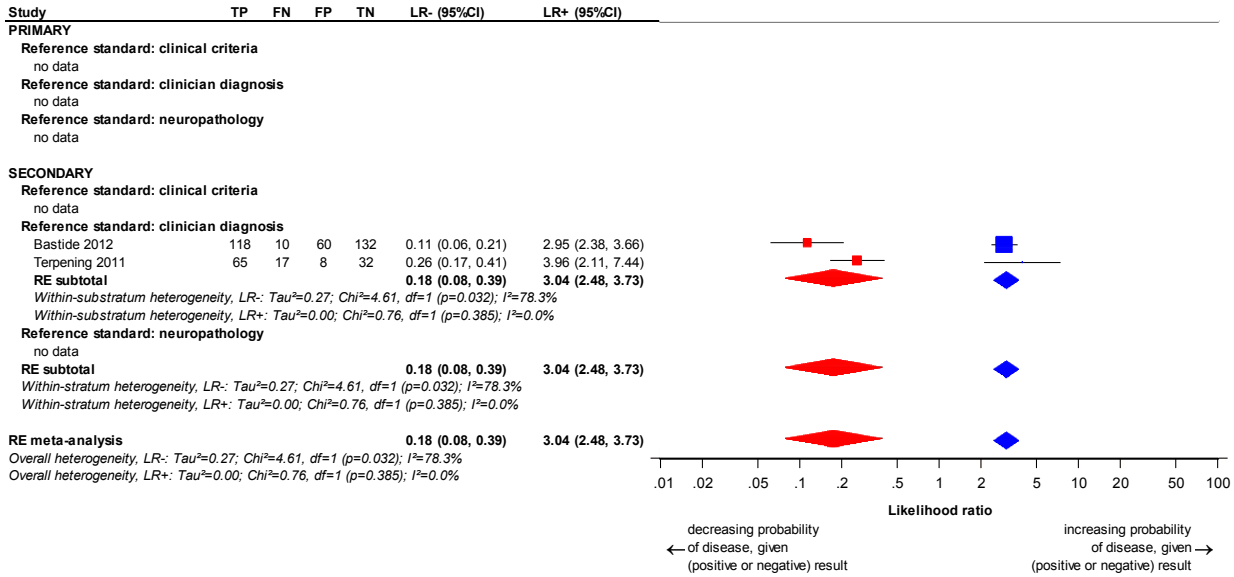


Figure 5 Dementia versus no dementia: ACE-R (<83) – forest plot: likelihood ratios

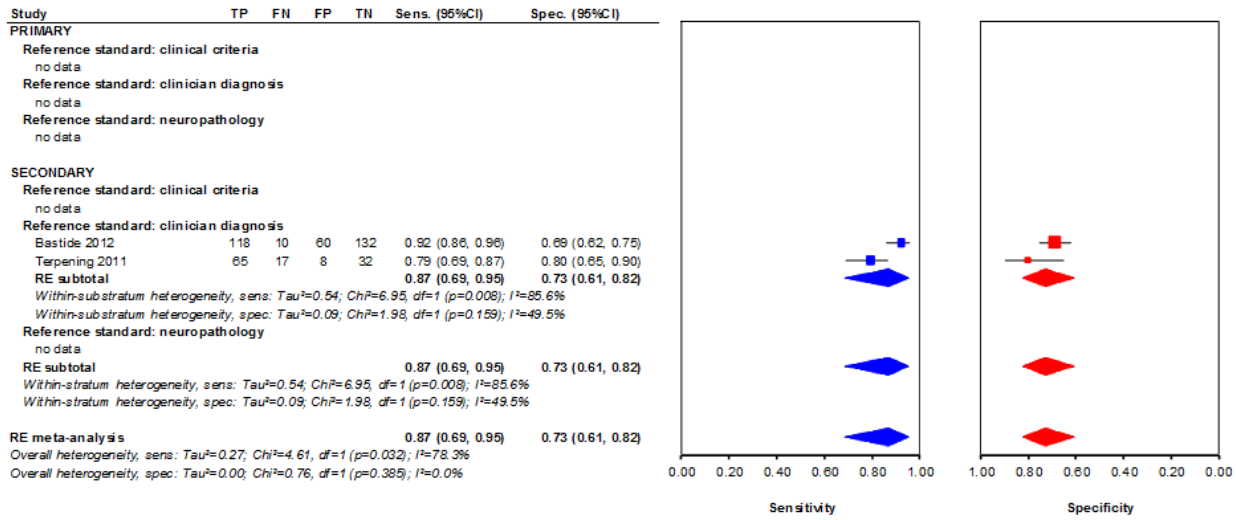


Figure 6 Dementia versus no dementia: ACE-R (<83) – forest plot: sensitivity and specificity

P.3.1.4 Clock Drawing Test, CDT, Shulman scoring method (>2)

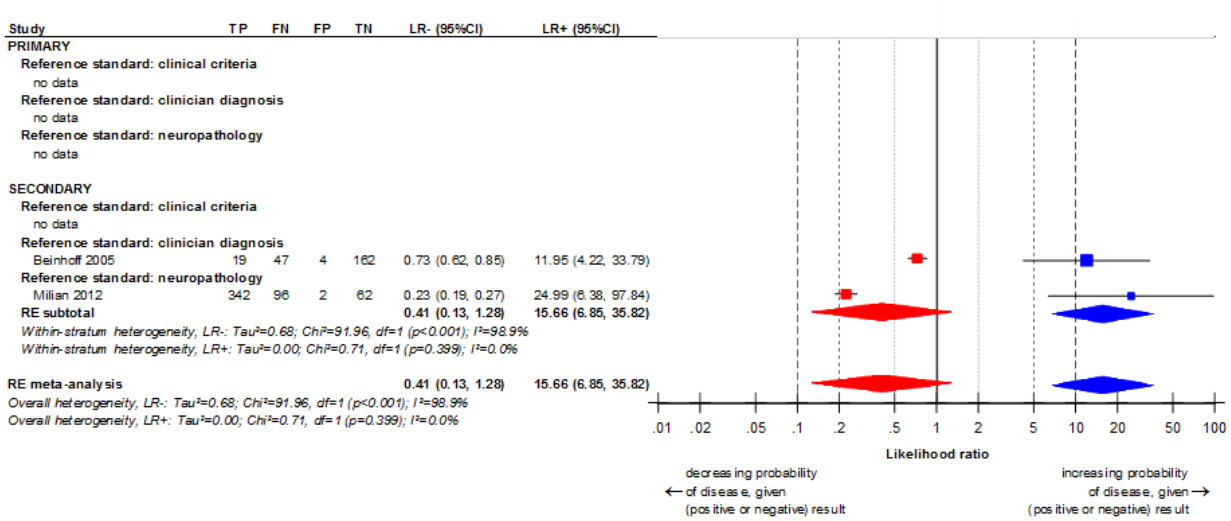


Figure 7 Dementia versus no dementia: CDT (>2) – forest plot: likelihood ratios

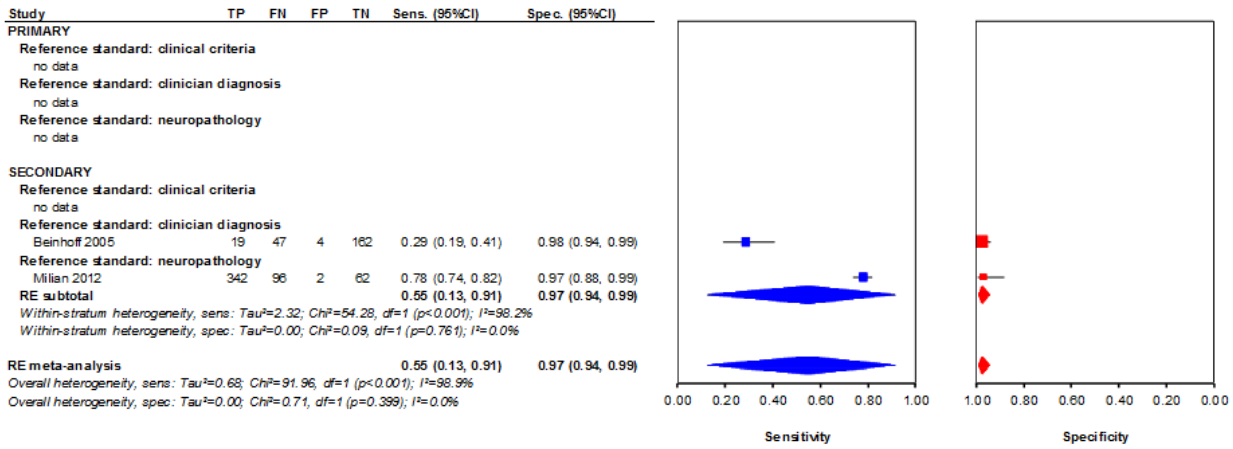


Figure 8 Dementia versus no dementia: CDT (>2) – forest plot: sensitivity and specificity

P.3.1.5 FDG-PET

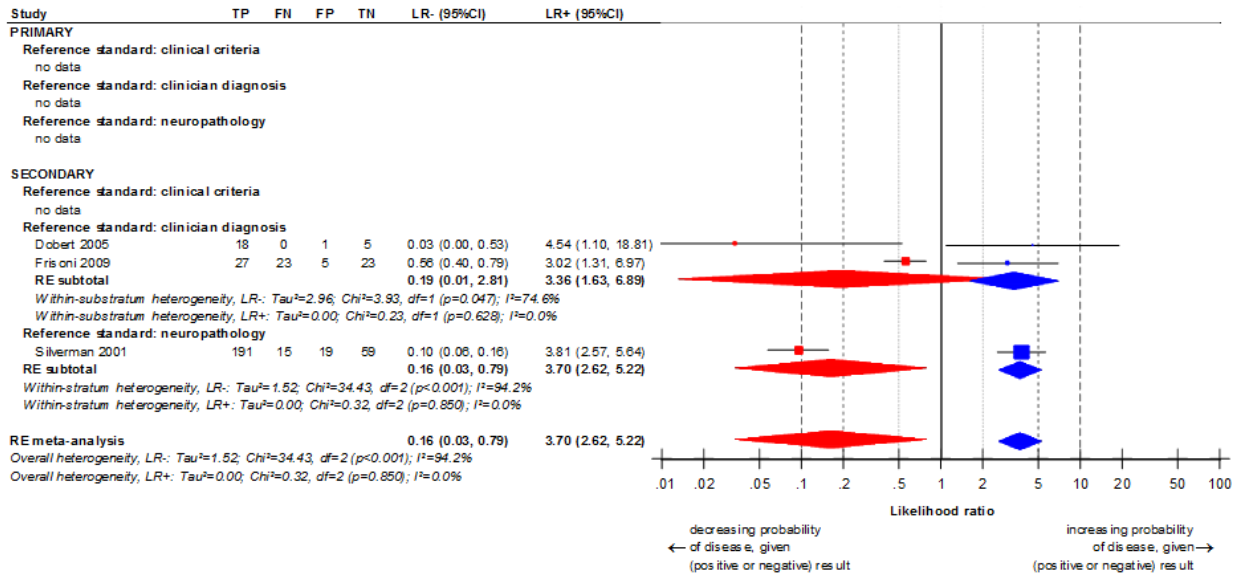


Figure 9 Dementia versus no dementia: FDG-PET – forest plot: likelihood ratios

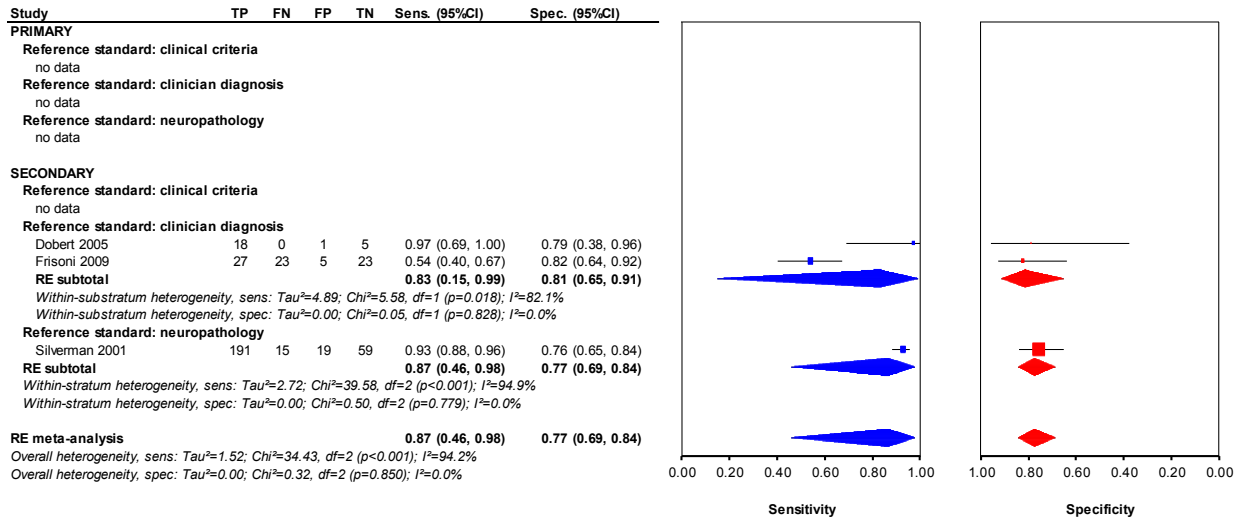


Figure 10 Dementia versus no dementia: FDG-PET – forest plot: sensitivity and specificity

P.3.1.6 IQCODE (16 item, >3.5)

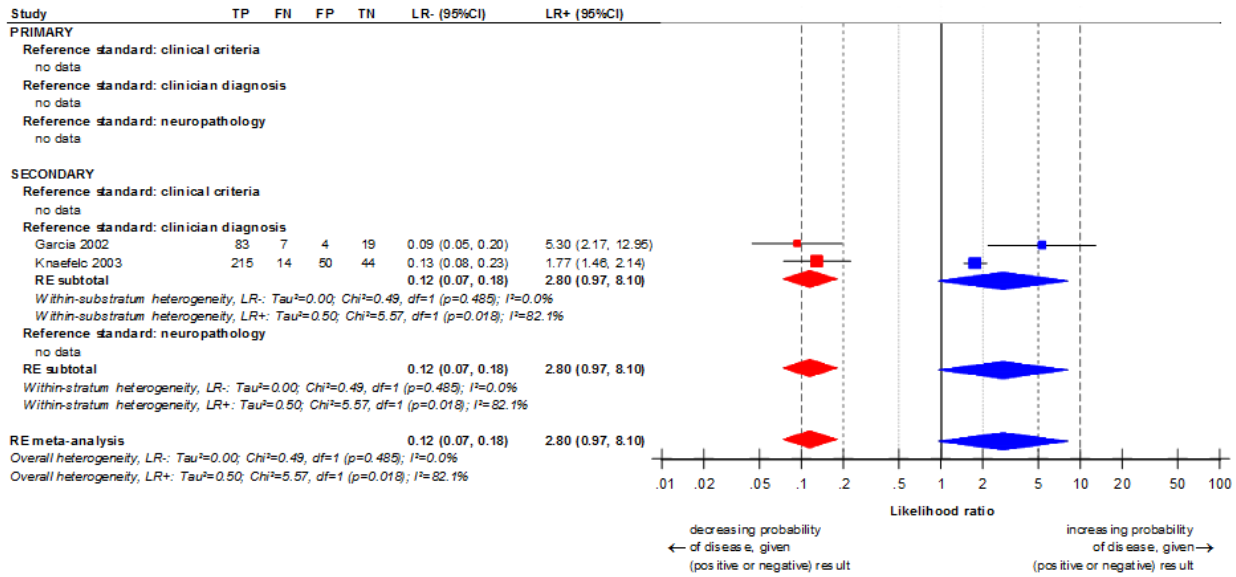


Figure 11 Dementia versus no dementia: IQCODE (16 item, >3.5) – forest plot: likelihood ratios

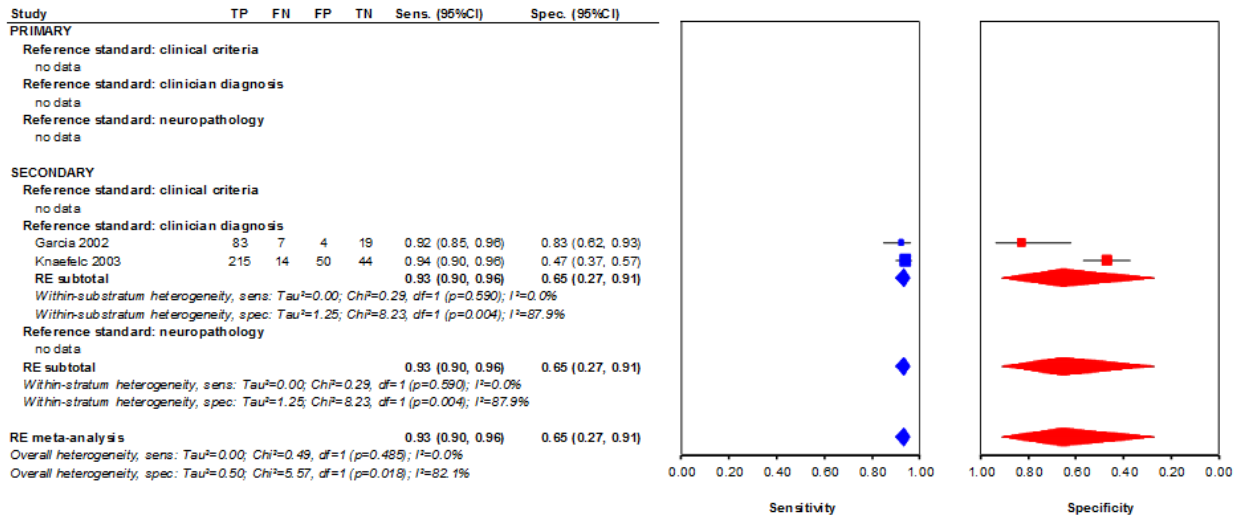


Figure 12Dementia versus no dementia: IQCODE (16 item, >3.5) – forest plot: sensitivity and specificity

P.3.1.7 IQCODE (26 item, >3.5)

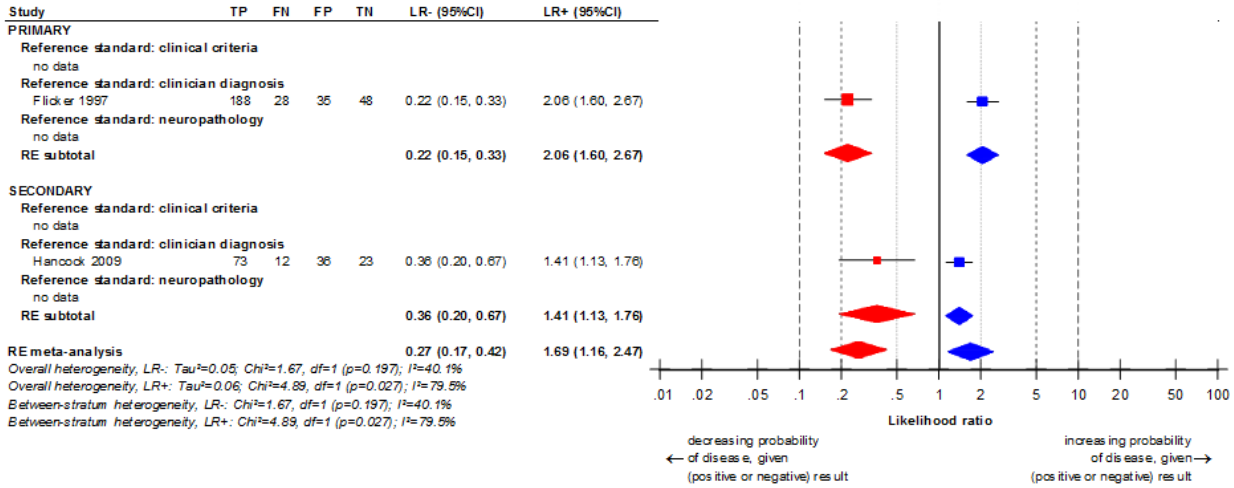


Figure 13Dementia versus no dementia: IQCODE (26 item, >3.5) – forest plot: likelihood ratios

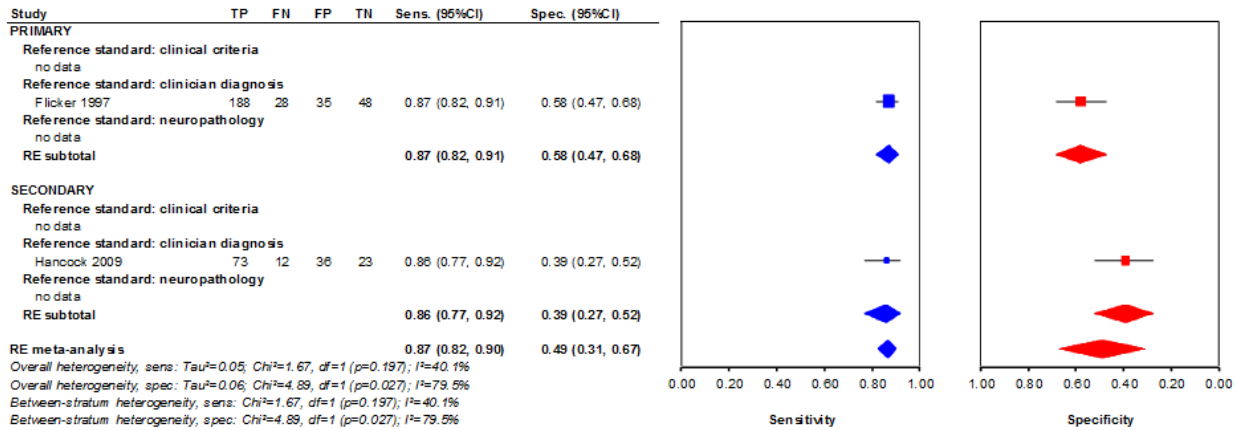


Figure 14Dementia versus no dementia: IQCODE (26 item, >3.5) – forest plot: sensitivity and specificity

P.3.1.8 IQCODE (26 item, >3.6)

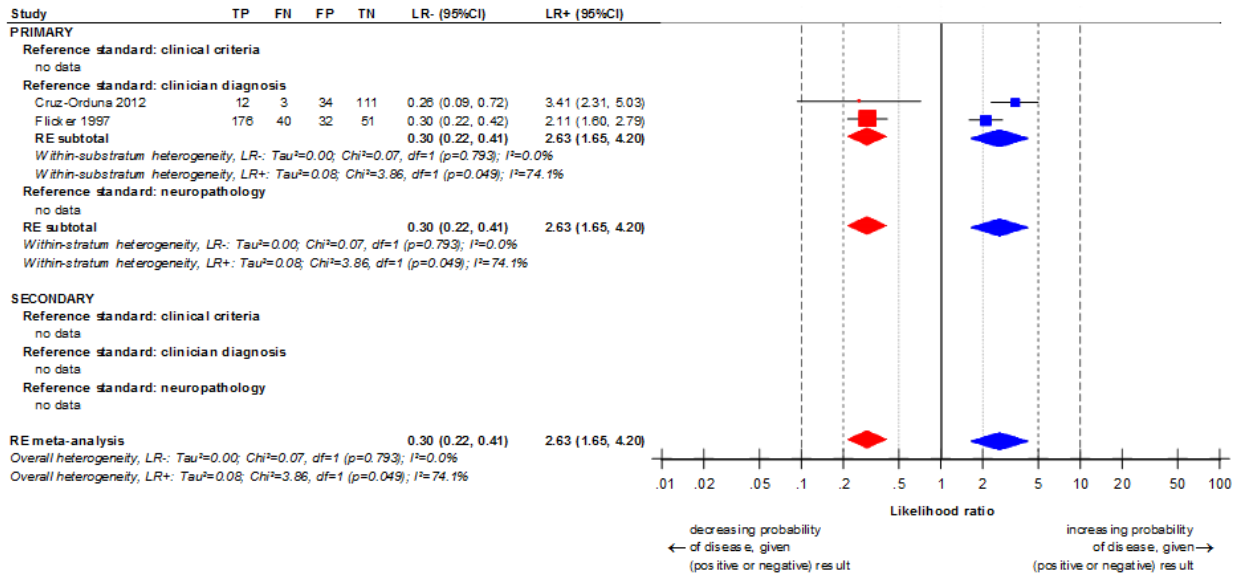


Figure 15Dementia versus no dementia: IQCODE (26 item, >3.6) – forest plot: likelihood ratios

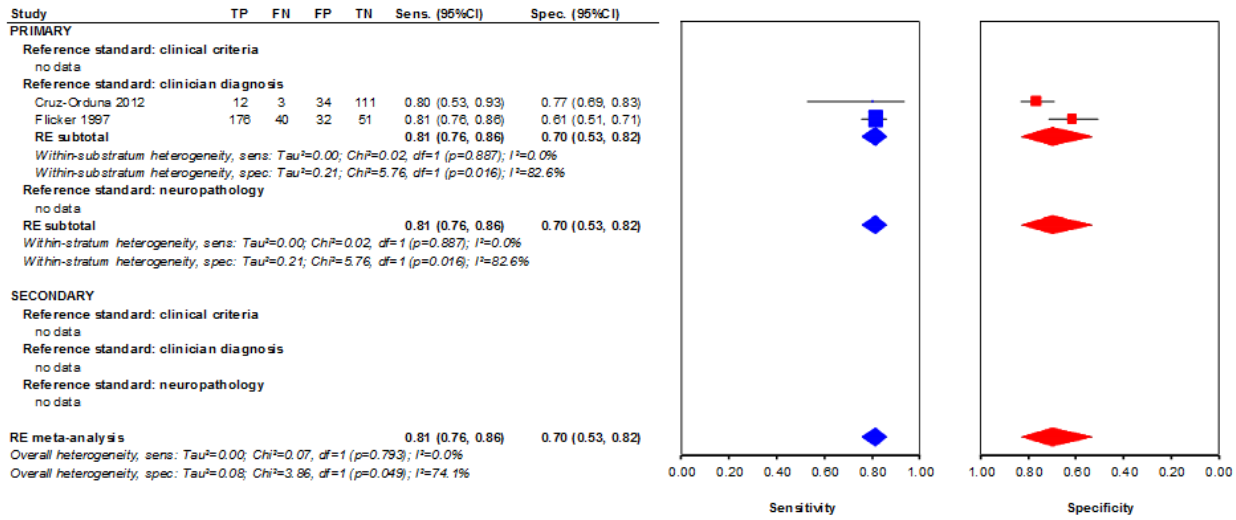


Figure 16Dementia versus no dementia: IQCODE (26 item, >3.6) – forest plot: sensitivity and specificity

P.3.1.9 MIS (<5)

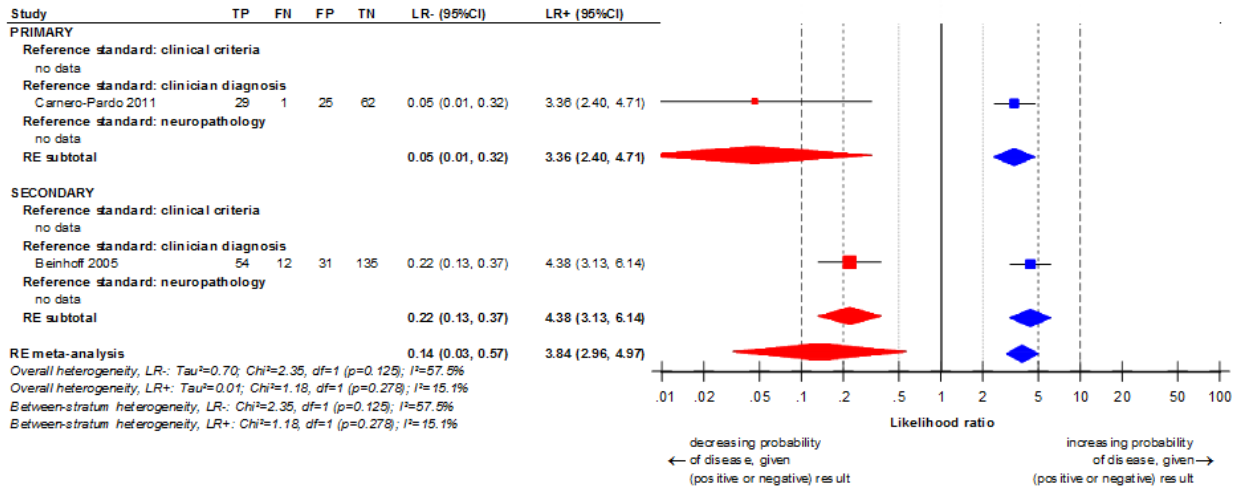


Figure 17Dementia versus no dementia: MIS (<5) – forest plot: likelihood ratios

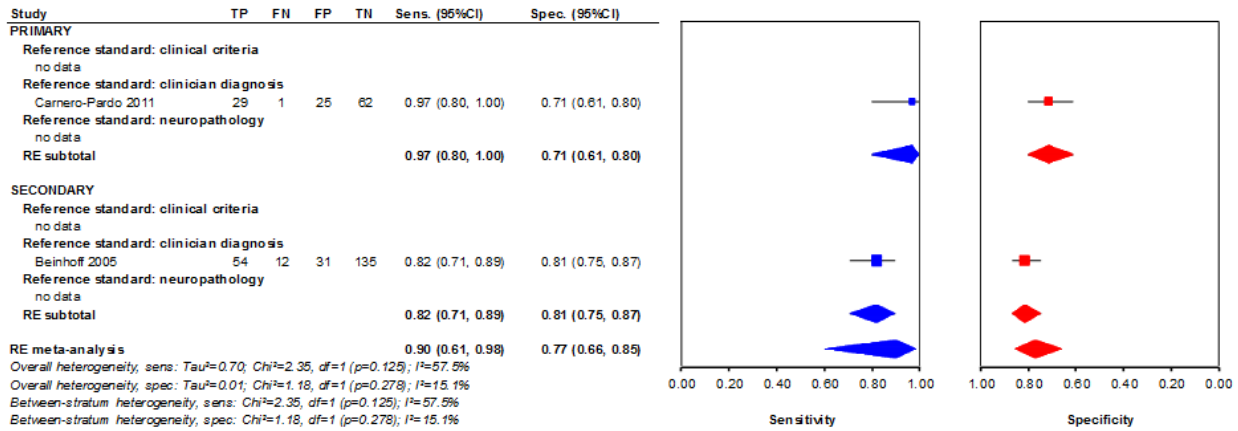


Figure 18Dementia versus no dementia: MIS (<5) – forest plot: sensitivity and specificity

P.3.1.10 MMSE (<18)

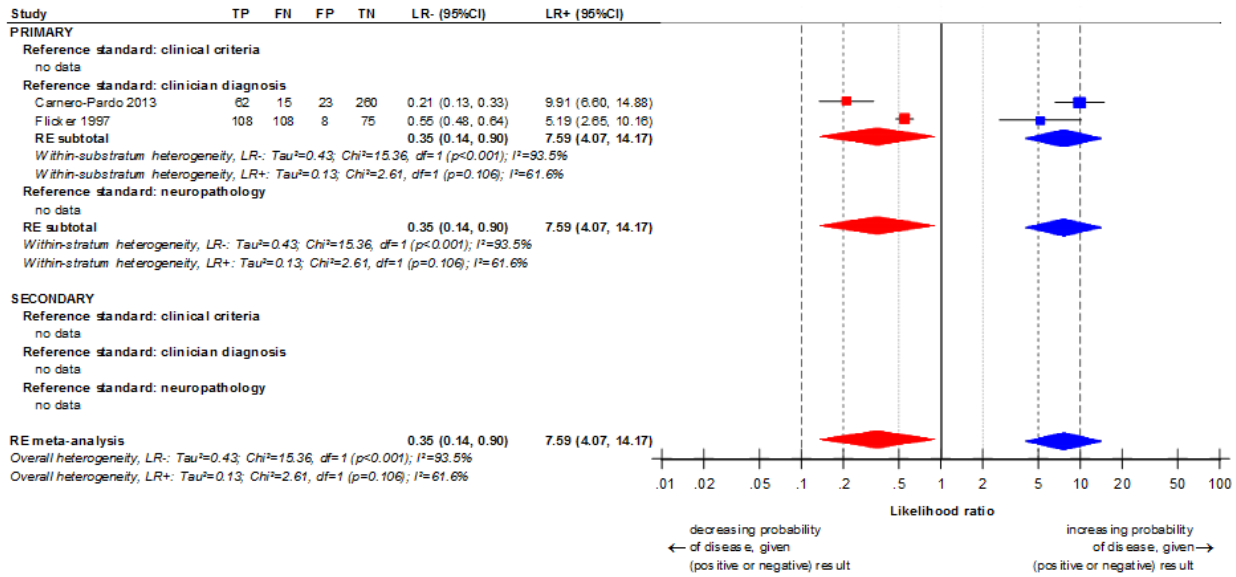


Figure 19Dementia versus no dementia: MMSE (<18) – forest plot: likelihood ratios

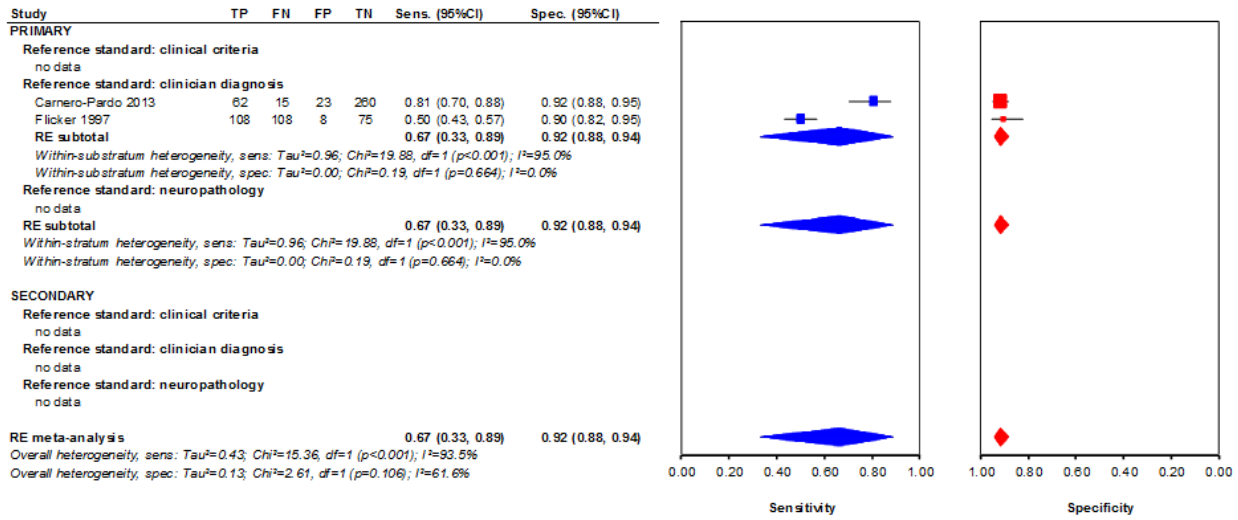


Figure 20 Dementia versus no dementia: MMSE (<18) – forest plot: sensitivity and specificity

P.3.1.11 MMSE (<19)

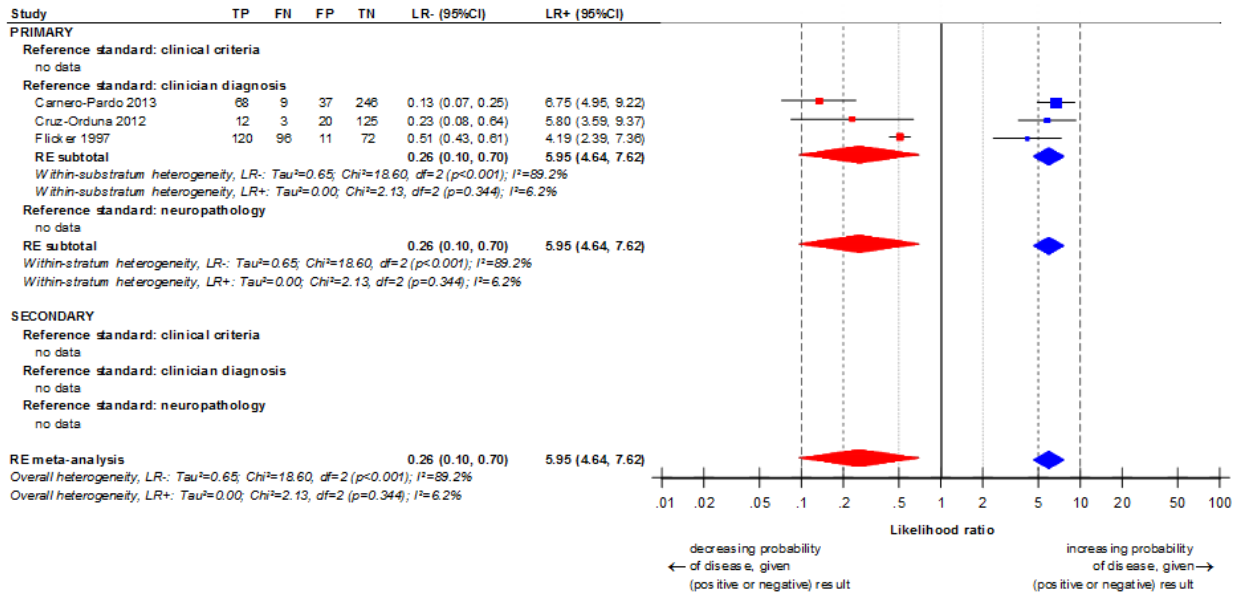


Figure 21 Dementia versus no dementia: MMSE (<19) – forest plot: likelihood ratios

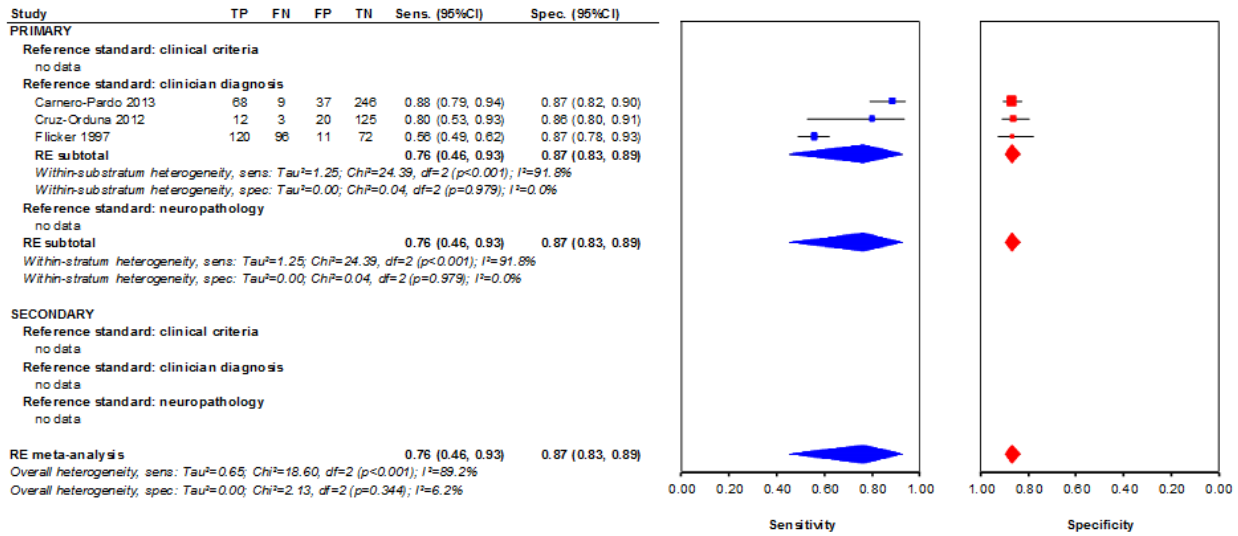


Figure 22Dementia versus no dementia: MMSE (<19) – forest plot: sensitivity and specificity

P.3.1.12 MMSE (<20)

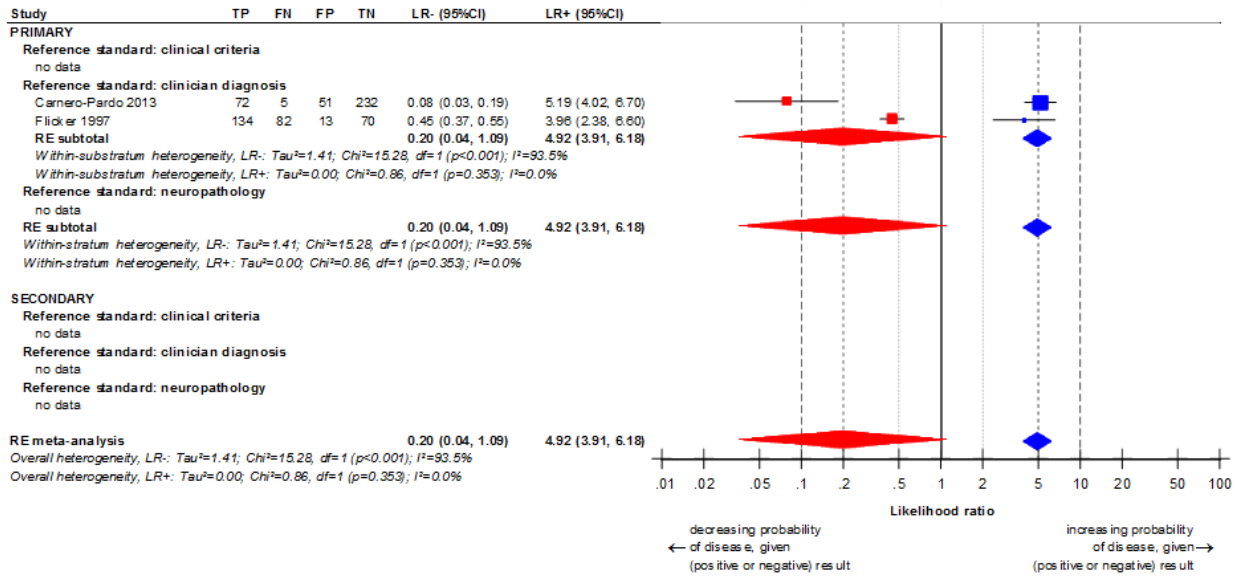


Figure 23Dementia versus no dementia: MMSE (<20) – forest plot: likelihood ratios

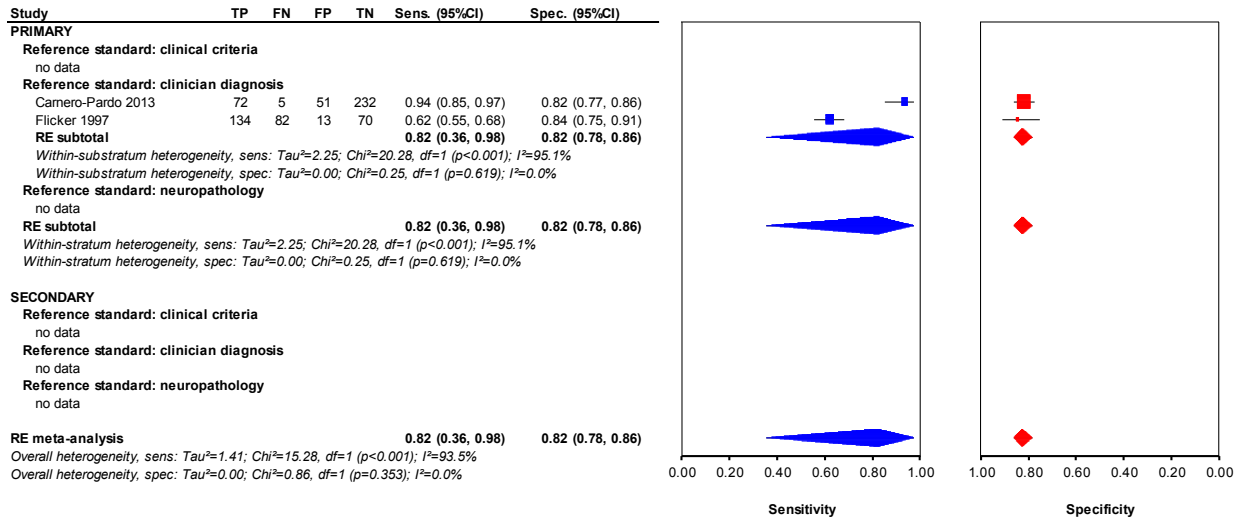


Figure 24Dementia versus no dementia: MMSE (<20) – forest plot: sensitivity and specificity

P.3.1.13 MMSE (<21)

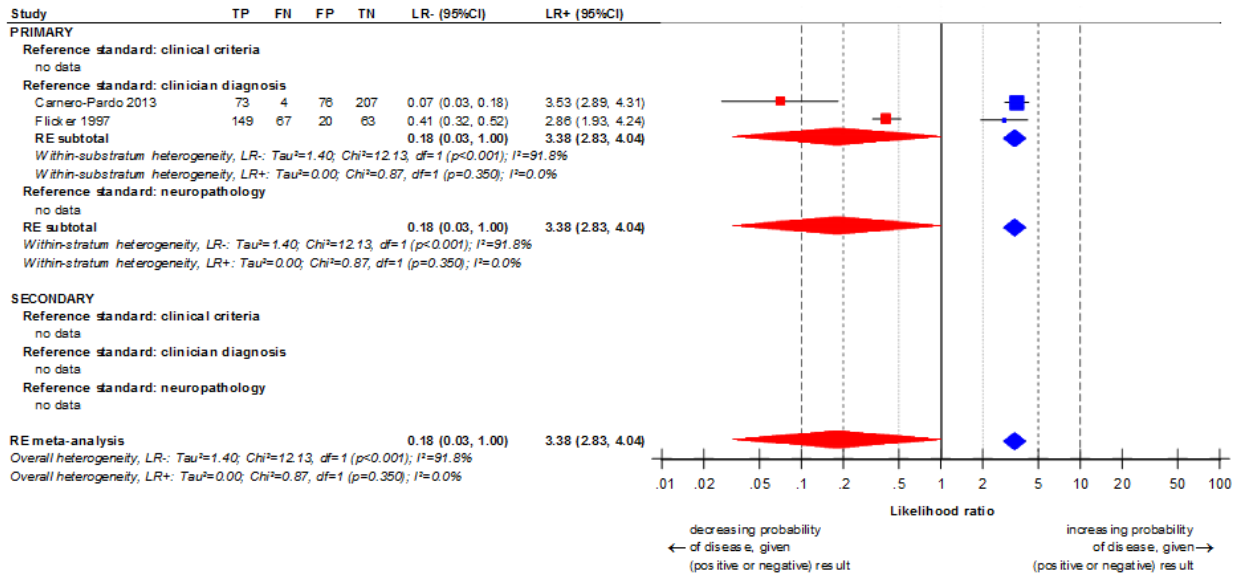


Figure 25Dementia versus no dementia: MMSE (<21) – forest plot: likelihood ratios

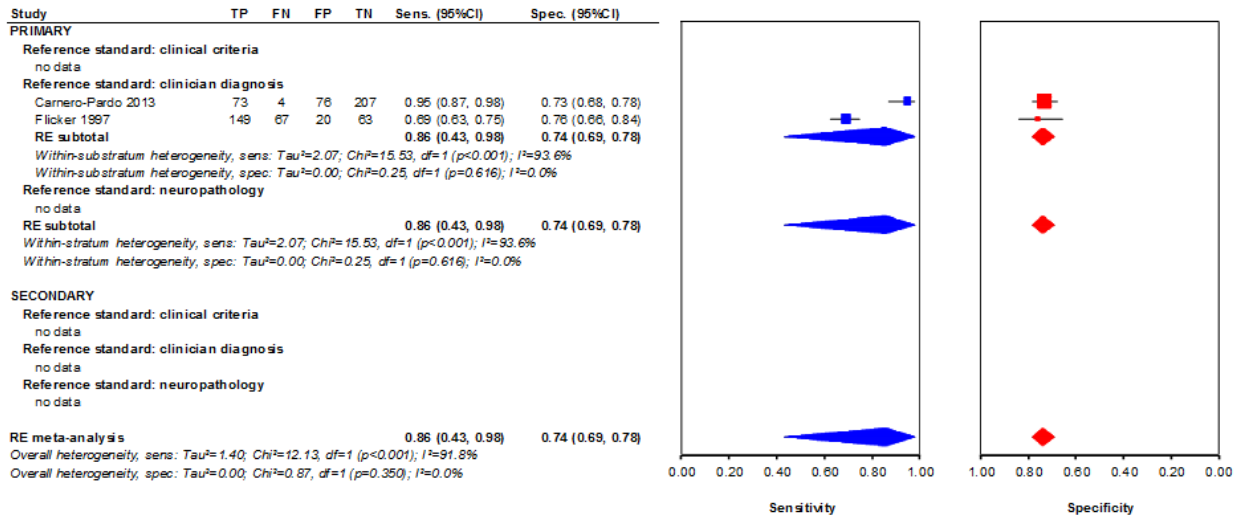


Figure 26Dementia versus no dementia: MMSE (<21) – forest plot: sensitivity and specificity

P.3.1.14 MMSE (<22)

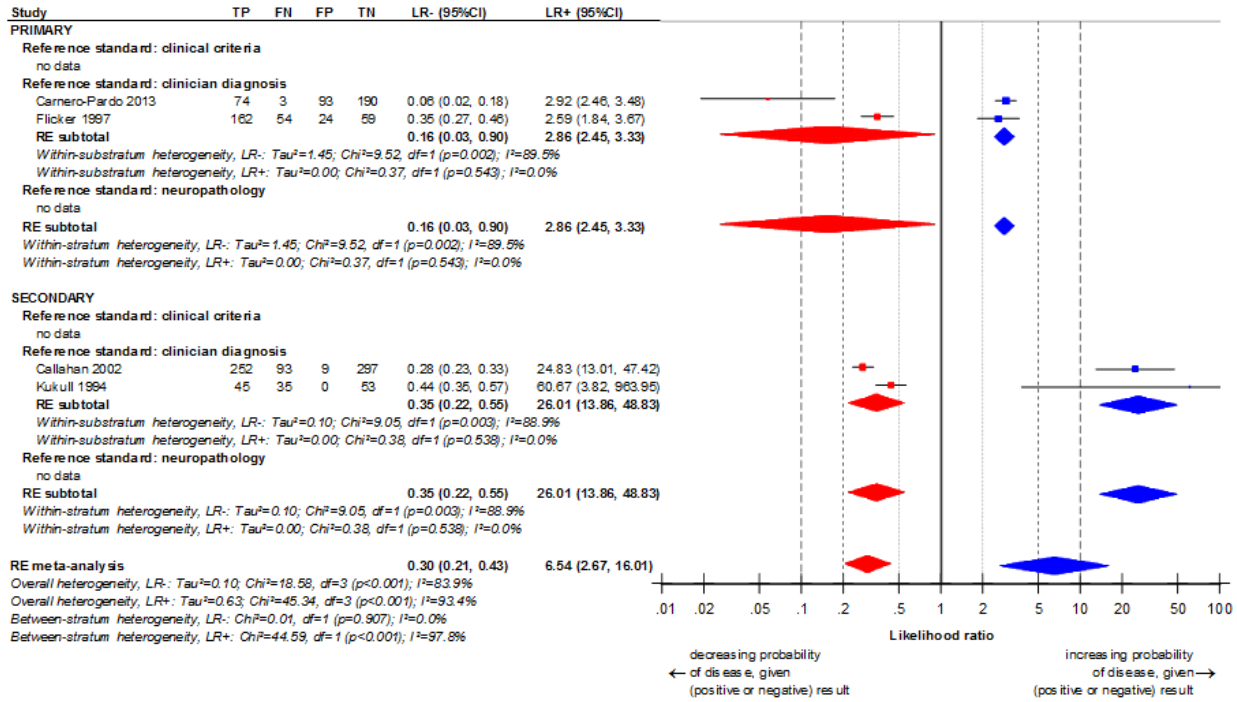


Figure 27 Dementia versus no dementia: MMSE (<22) – forest plot: likelihood ratios

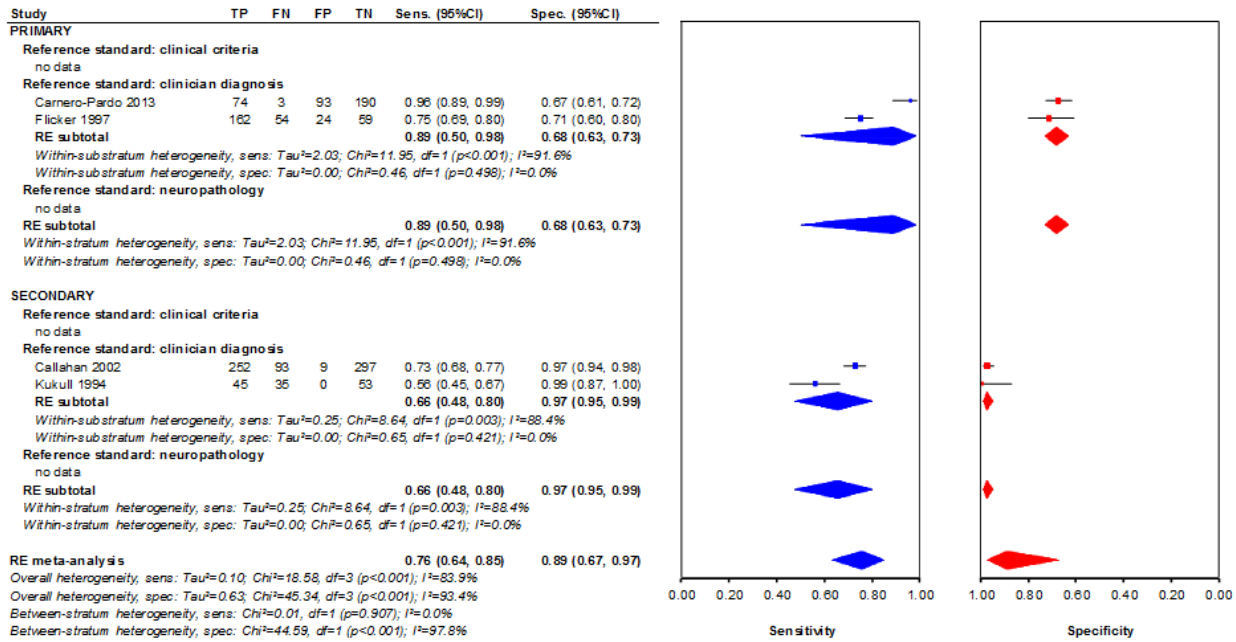


Figure 28 Dementia versus no dementia: MMSE (<22) – forest plot: sensitivity and specificity

P.3.1.15 MMSE (<23)

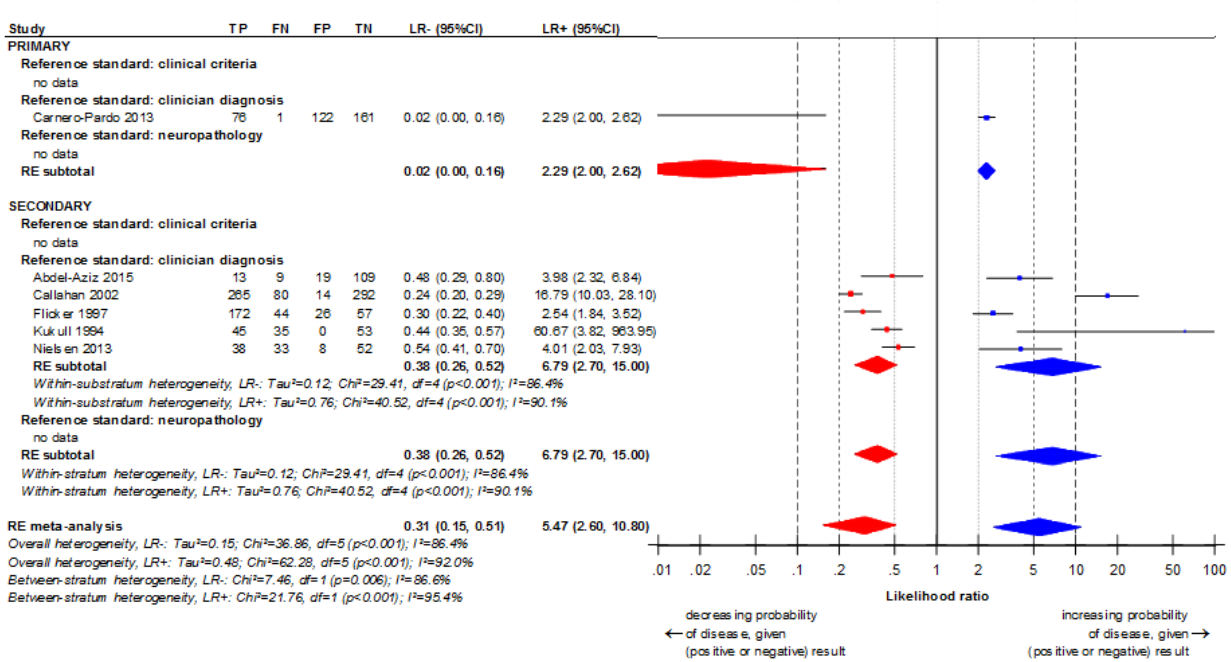


Figure 29 Dementia versus no dementia: MMSE (<23) – forest plot: likelihood ratios

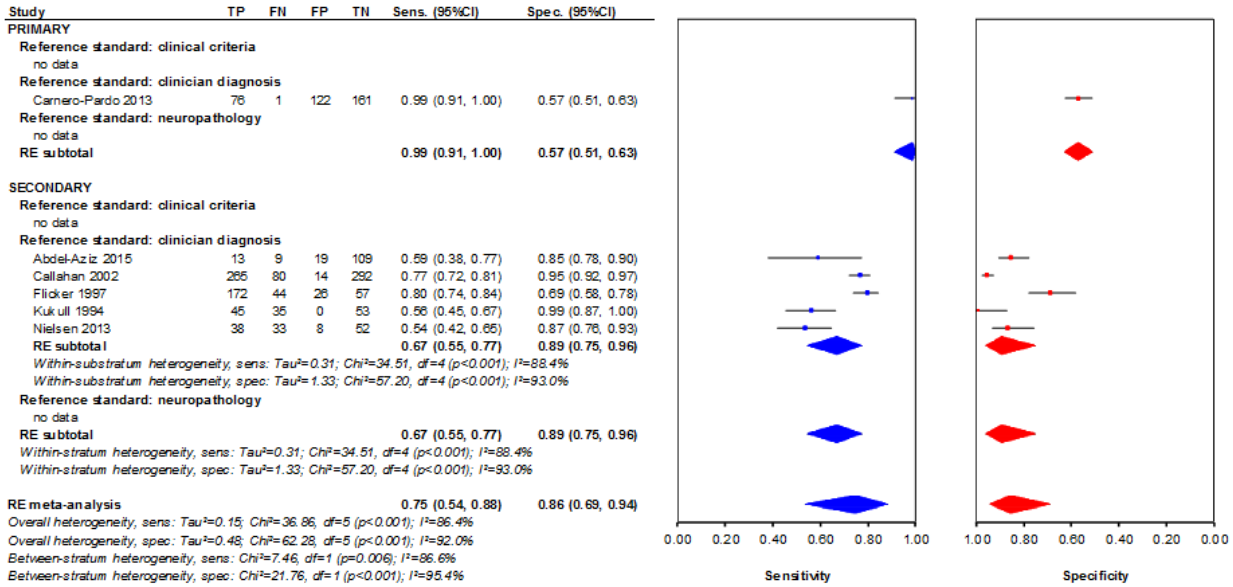


Figure 30 Dementia versus no dementia: MMSE (<23) – forest plot: sensitivity and specificity

P.3.1.16 MMSE (<24)

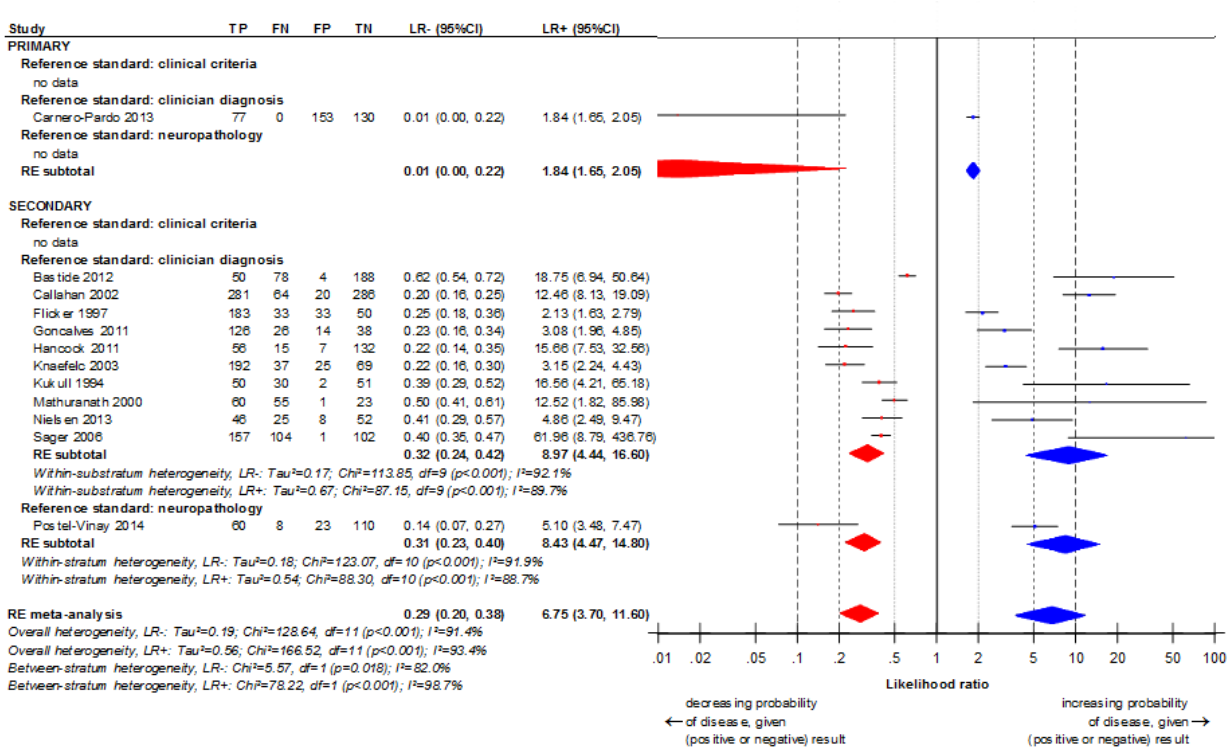


Figure 31 Dementia versus no dementia: MMSE (<24) – forest plot: likelihood ratios

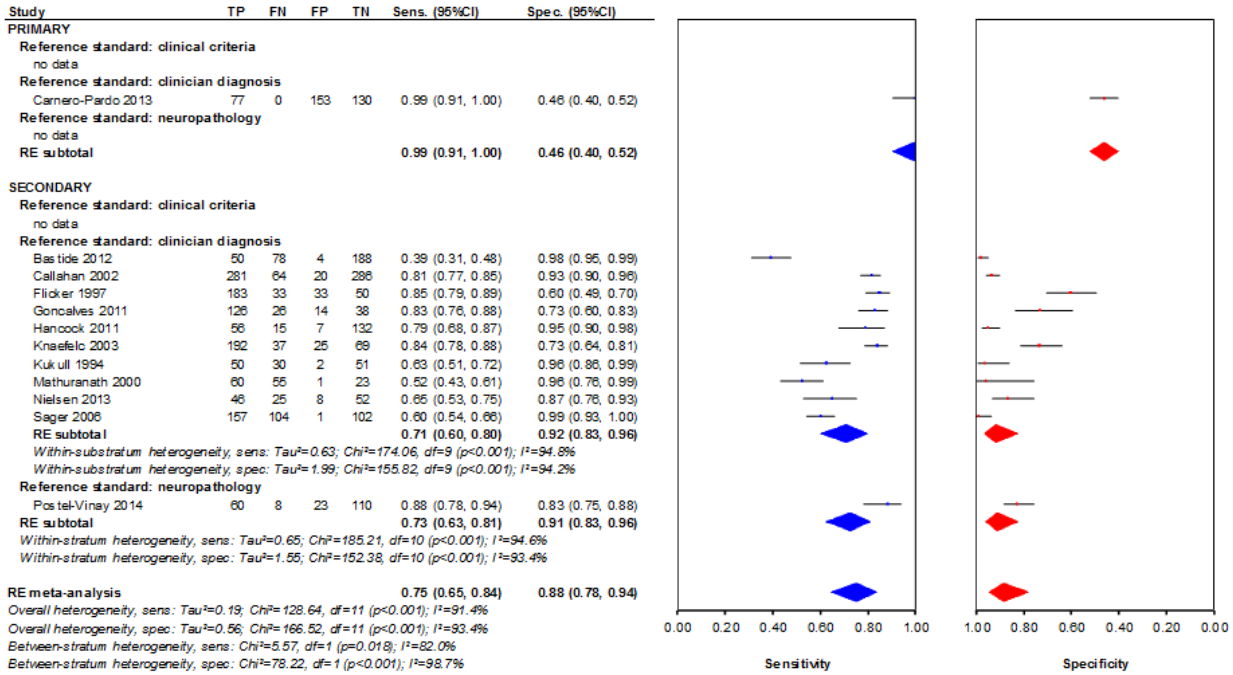


Figure 32Dementia versus no dementia: MMSE (<24) – forest plot: sensitivity and specificity

P.3.1.17 MMSE (<25)

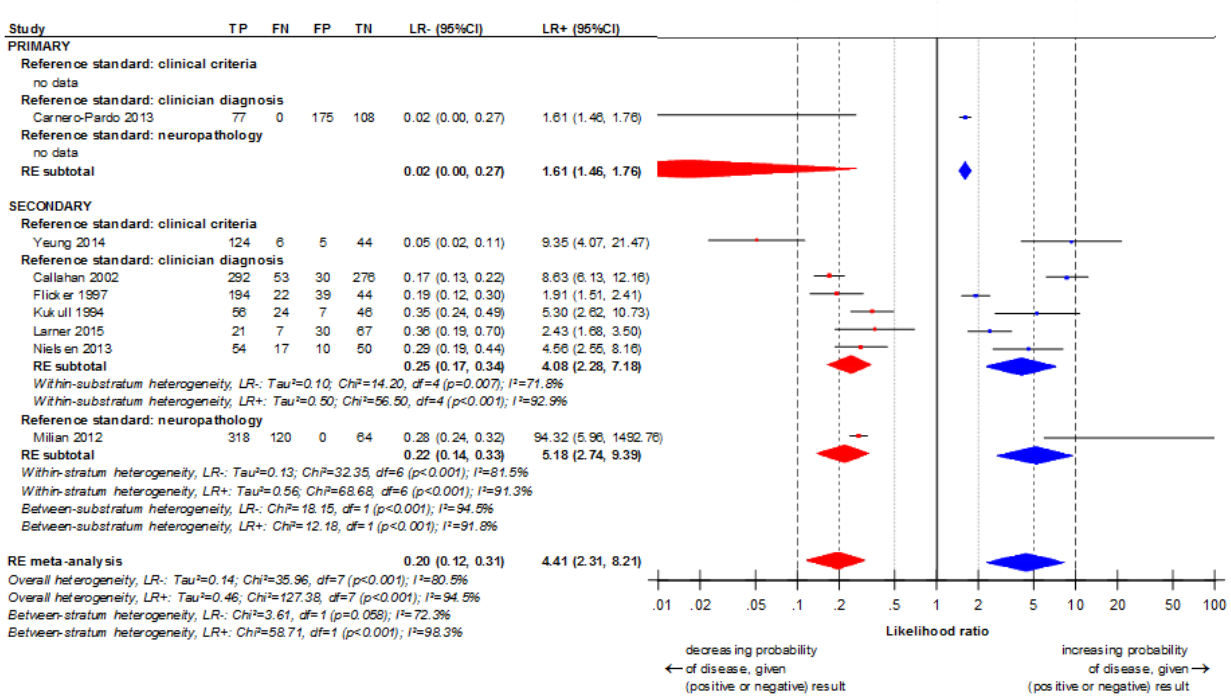


Figure 33Dementia versus no dementia: MMSE (<25) – forest plot: likelihood ratios

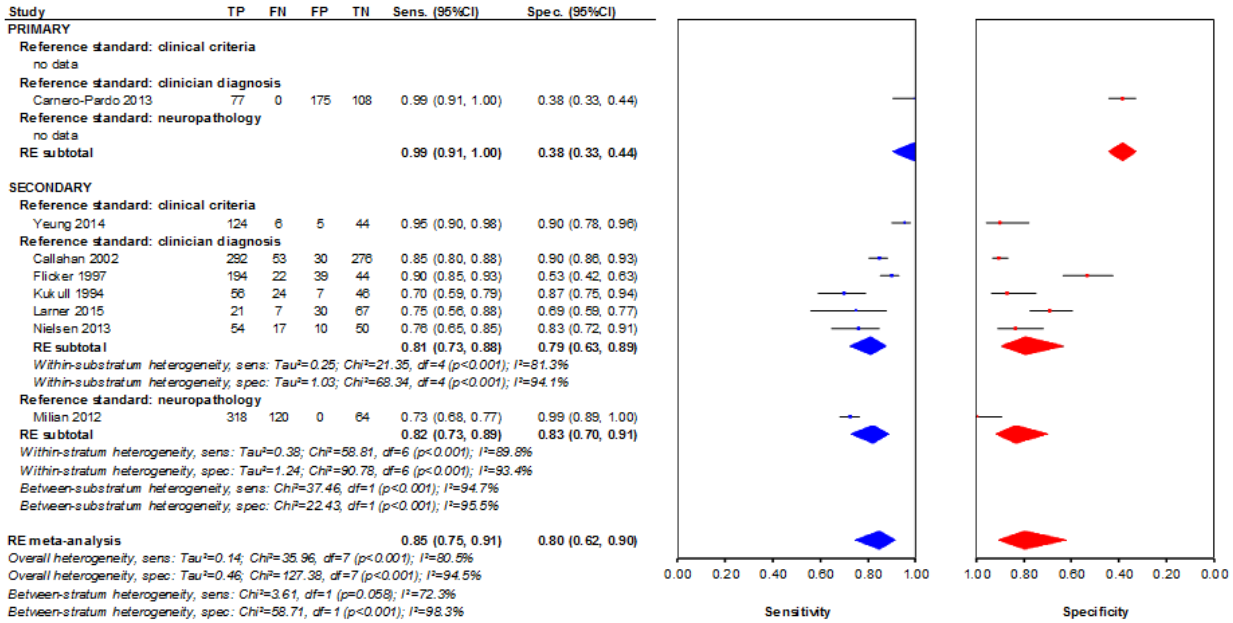


Figure 34Dementia versus no dementia: MMSE (<25) – forest plot: sensitivity and specificity

P.3.1.18 MMSE (<26)

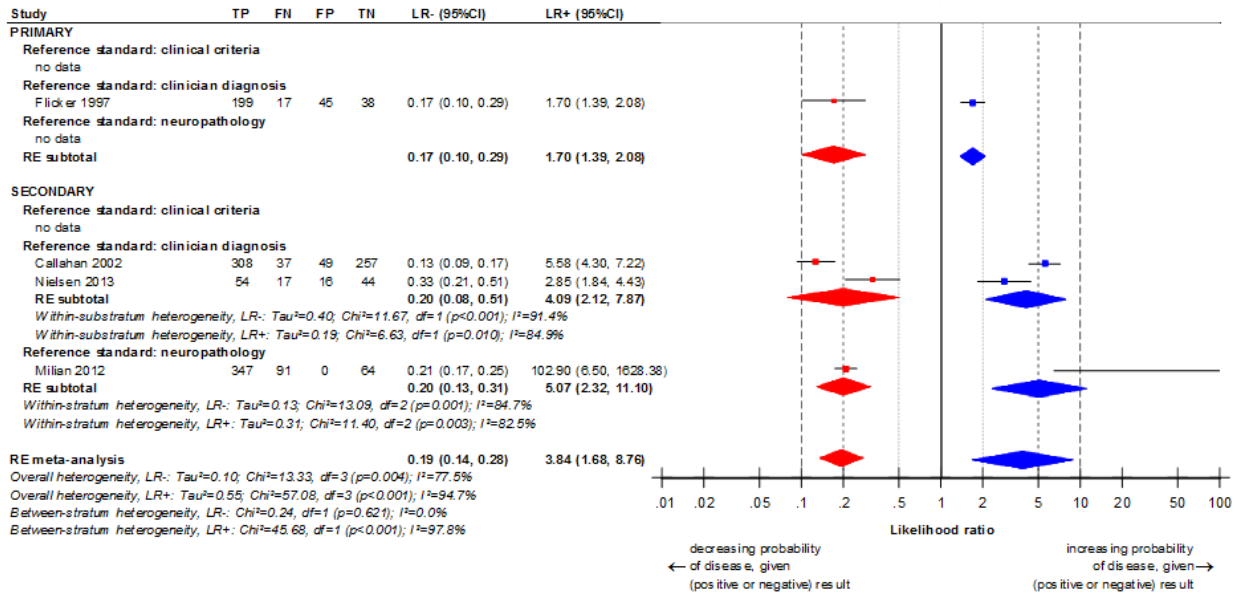


Figure 35Dementia versus no dementia: MMSE (<26) – forest plot: likelihood ratios

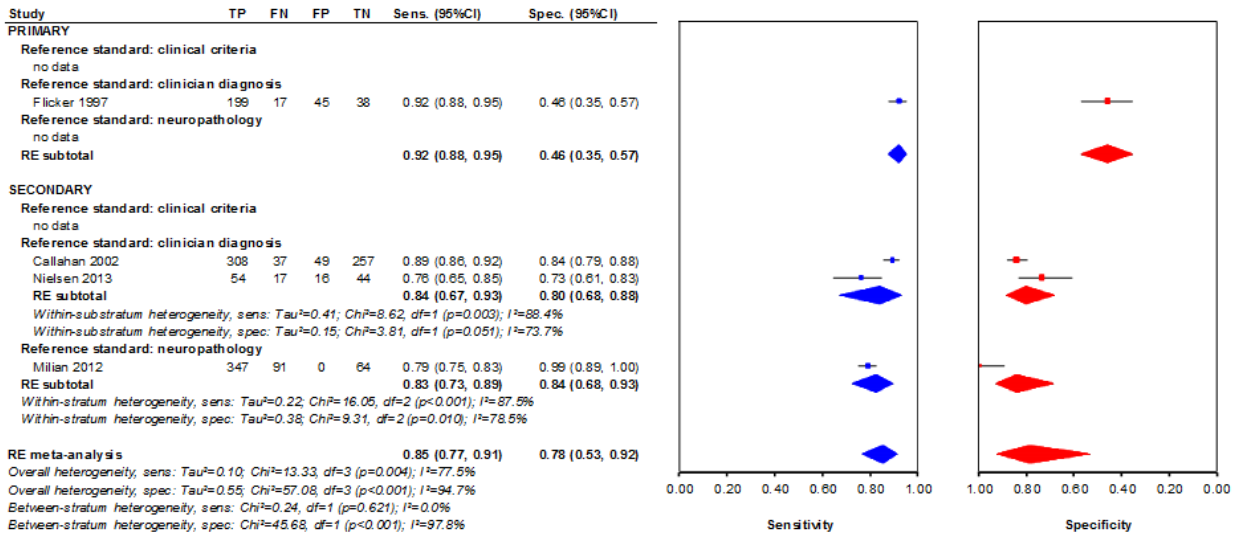


Figure 36Dementia versus no dementia: MMSE (<26) – forest plot: sensitivity and specificity

P.3.1.19 MMSE (<27)

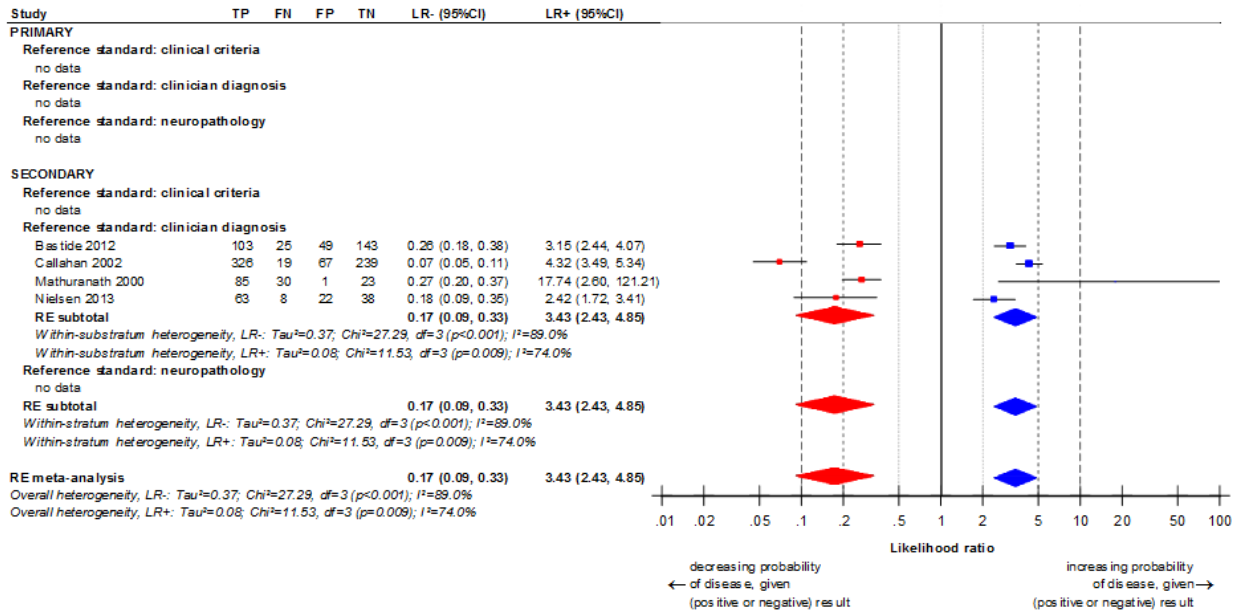


Figure 37 Dementia versus no dementia: MMSE (<27) – forest plot: likelihood ratios

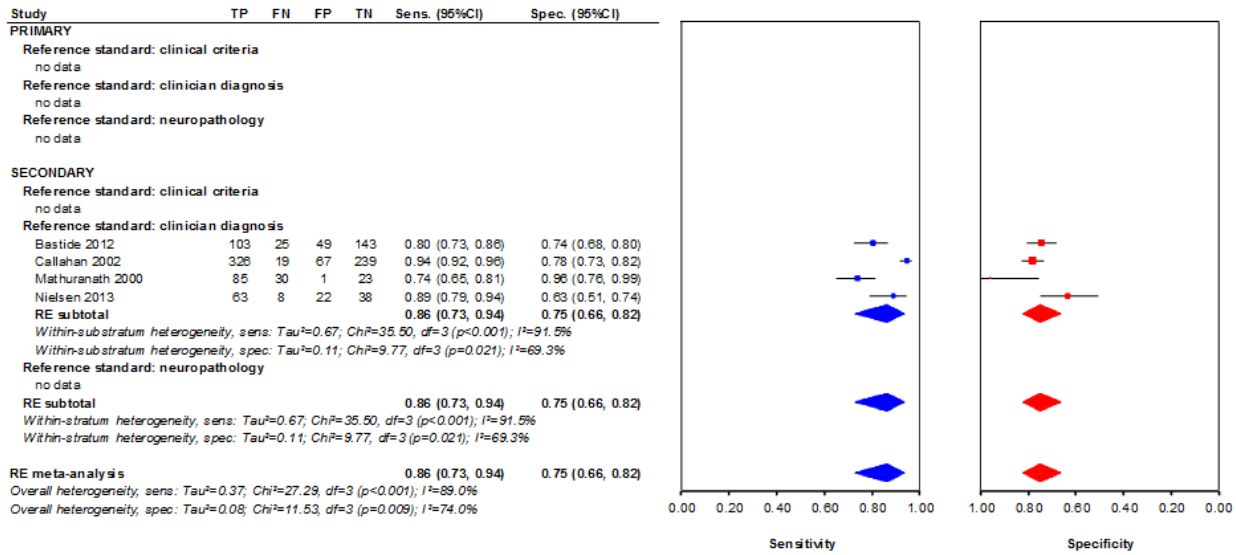


Figure 38 Dementia versus no dementia: MMSE (<27) – forest plot: sensitivity and specificity

P.3.1.20 MMSE (<28)

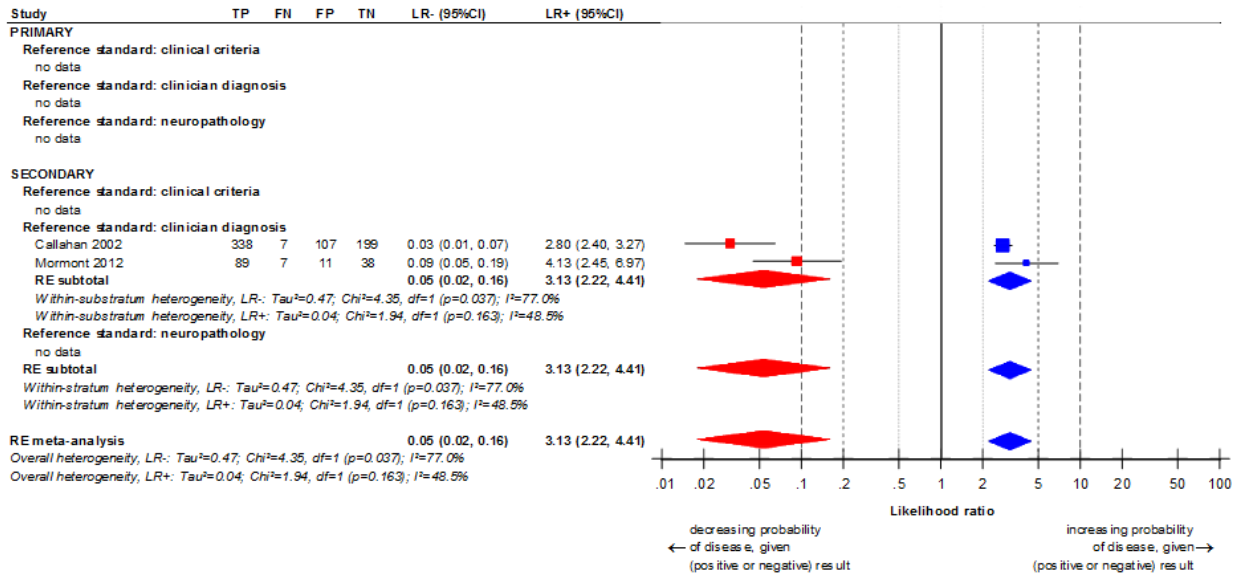


Figure 39 Dementia versus no dementia: MMSE (<28) – forest plot: likelihood ratios

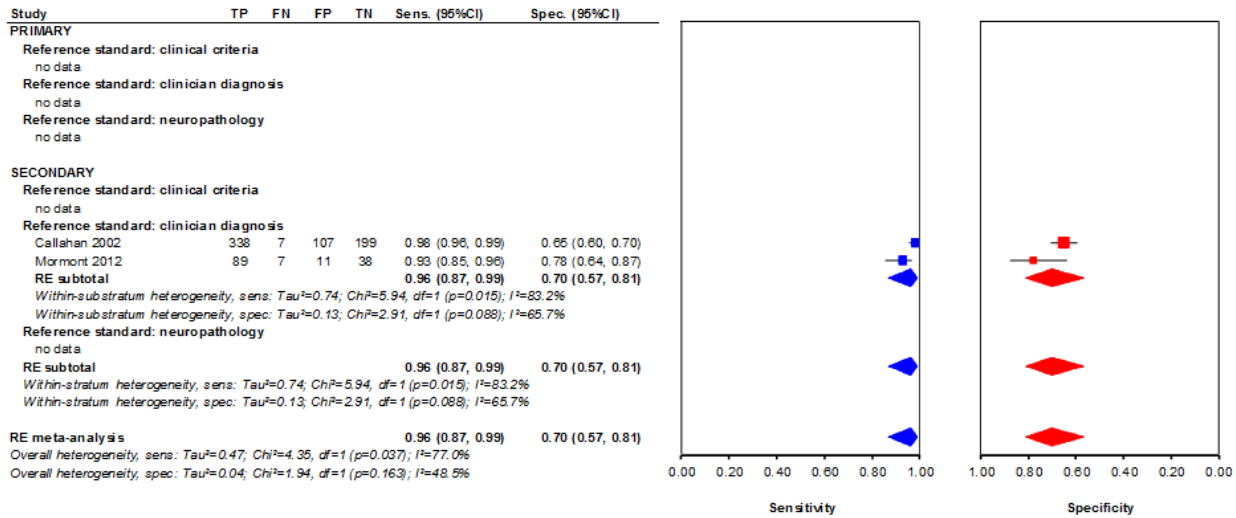


Figure 40 Dementia versus no dementia: MMSE (<28) – forest plot: sensitivity and specificity

P.3.1.21 MoCA (<19)

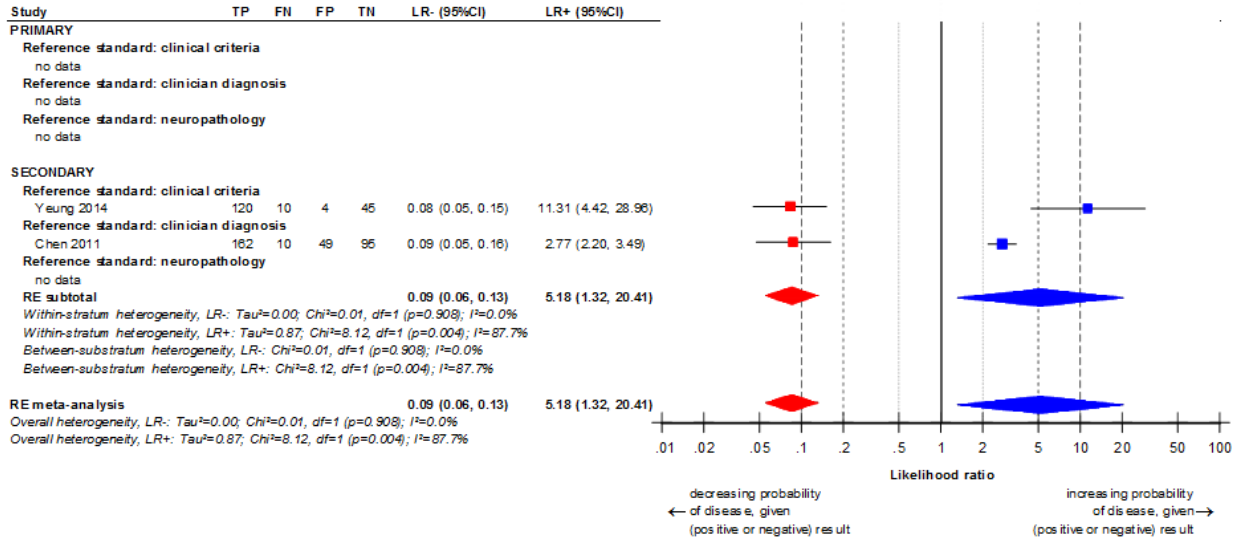


Figure 41 Dementia versus no dementia: MoCA (<19) – forest plot: likelihood ratios

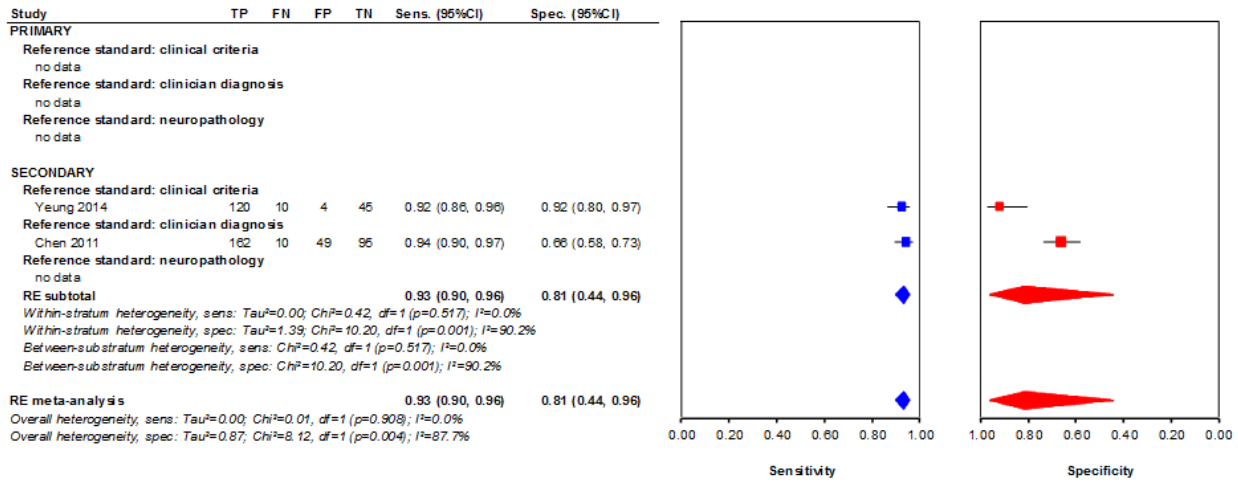


Figure 42Dementia versus no dementia: MoCA (<19) – forest plot: sensitivity and specificity

P.3.1.22 MRI

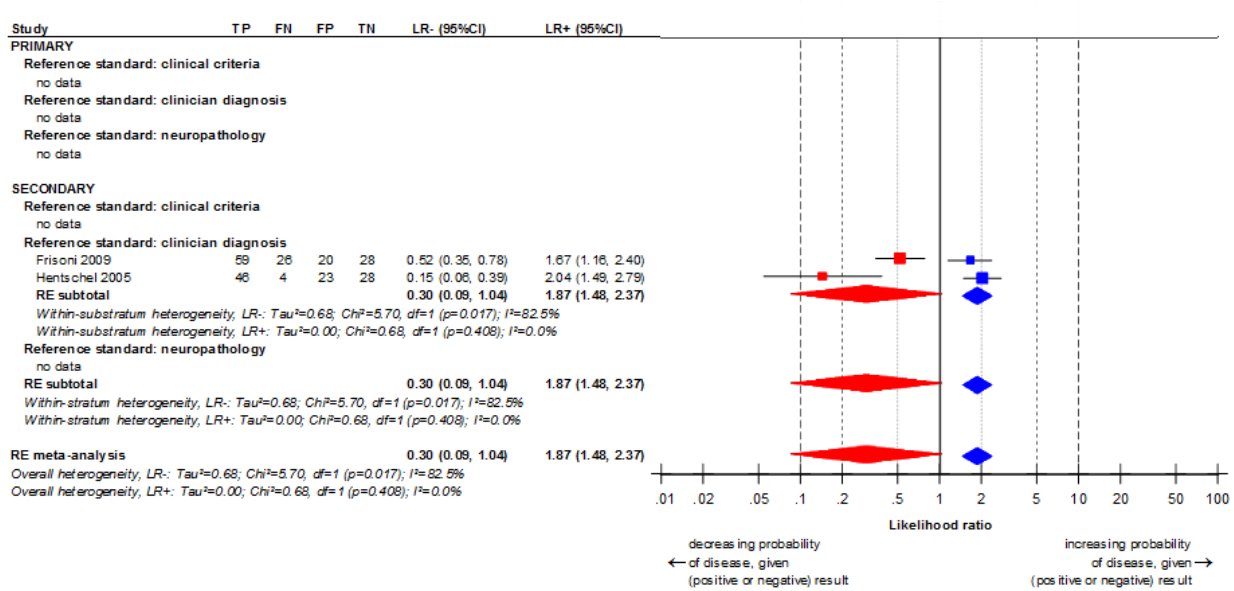


Figure 43 Dementia versus no dementia: MRI – forest plot: likelihood ratios

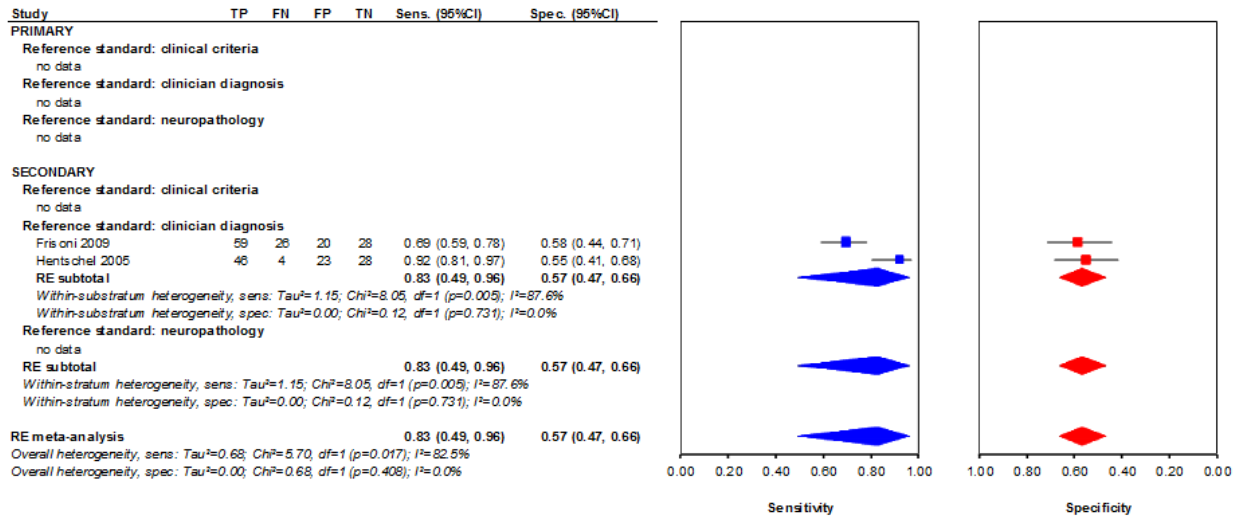


Figure 44 Dementia versus no dementia: MRI – forest plot: sensitivity and specificity

P.3.2 AD versus FTD

P.3.2.1 99mTc-HMPAO SPECT

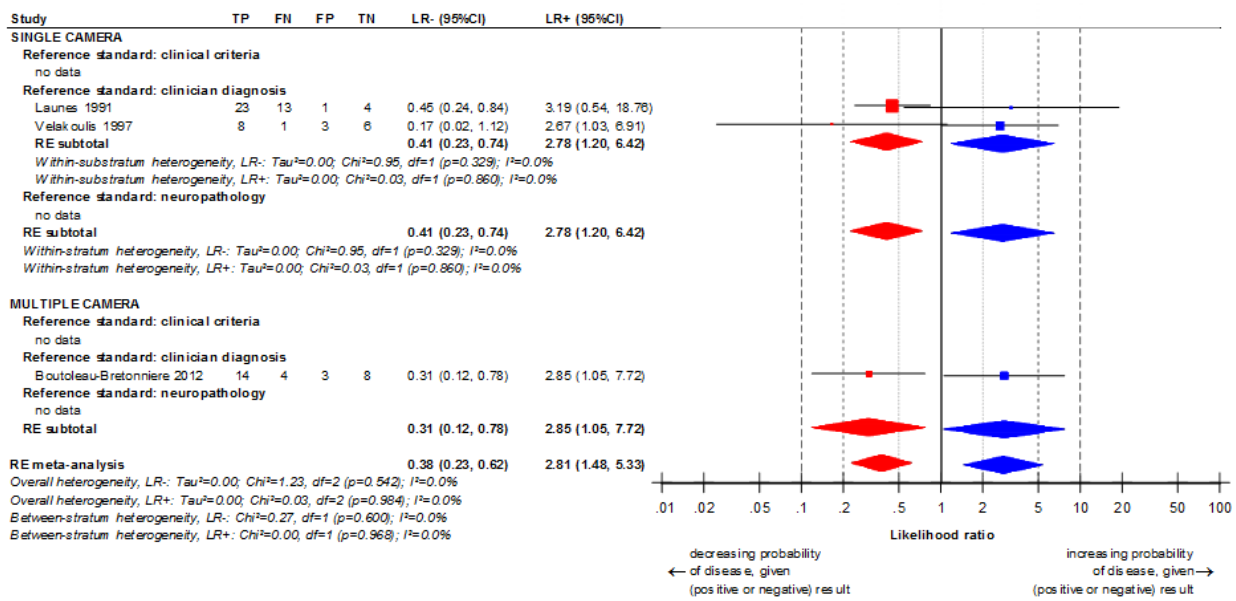


Figure 45AD versus FTD: 99mTc-HMPAO SPECT – forest plot: likelihood ratios

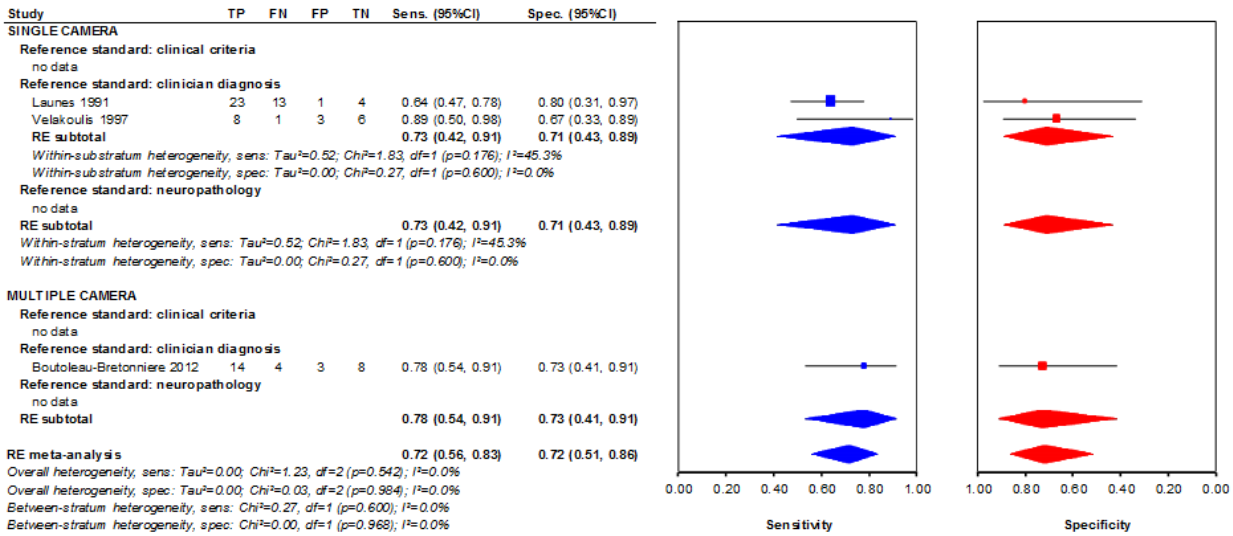


Figure 46AD versus FTD: 99mTc-HMPAO SPECT – forest plot: sensitivity and specificity

P.3.3 AD versus non-AD

P.3.3.1 99mTc-ECD SPECT, visual assessment method

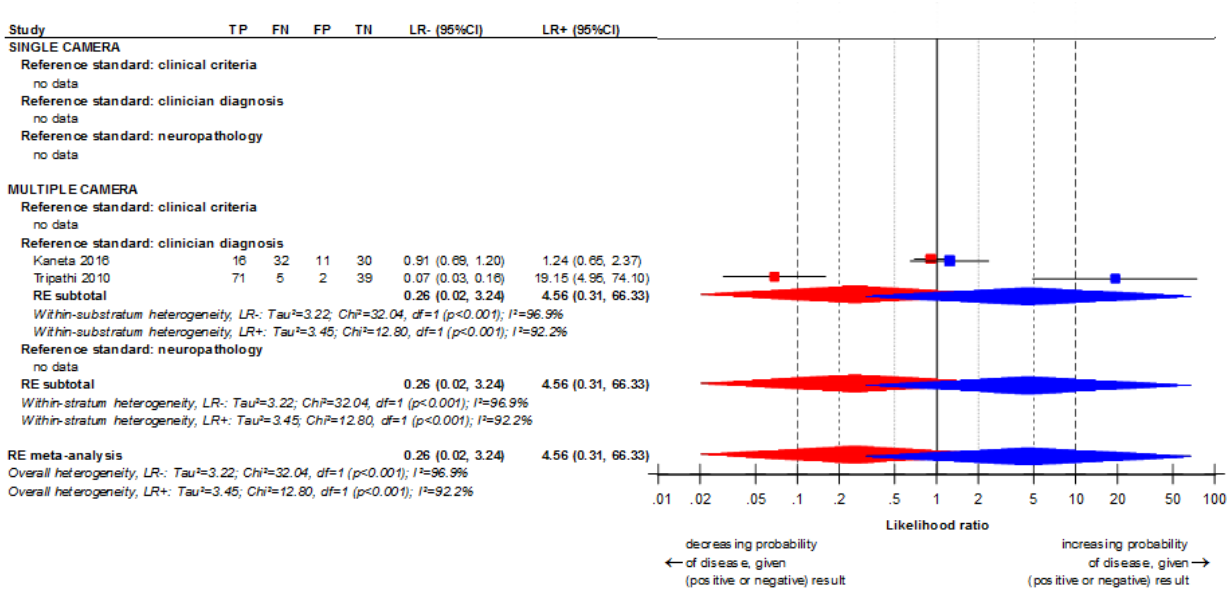


Figure 47 AD versus non-AD: 99mTc-ECD SPECT, visual assessment method – forest plot: likelihood ratios

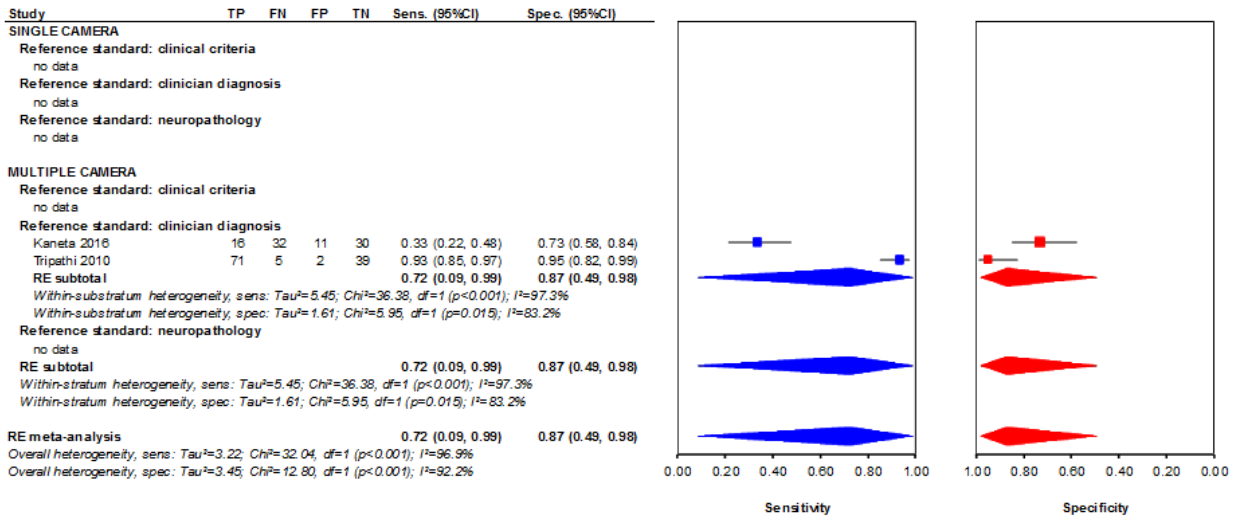


Figure 48AD versus non-AD: 99mTc-ECD SPECT, visual assessment method – forest plot: sensitivity and specificity

P.3.3.2 99mTc-HMPAO SPECT

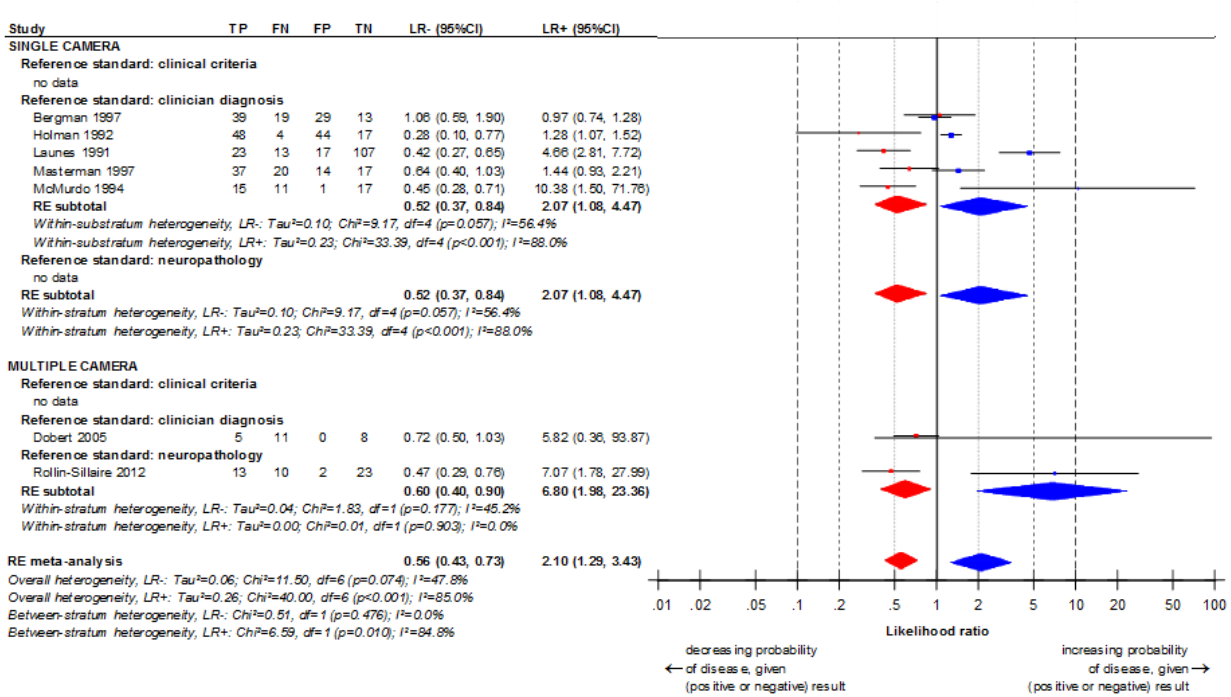


Figure 49AD versus non-AD: 99mTc-HMPAO SPECT – forest plot: likelihood ratios

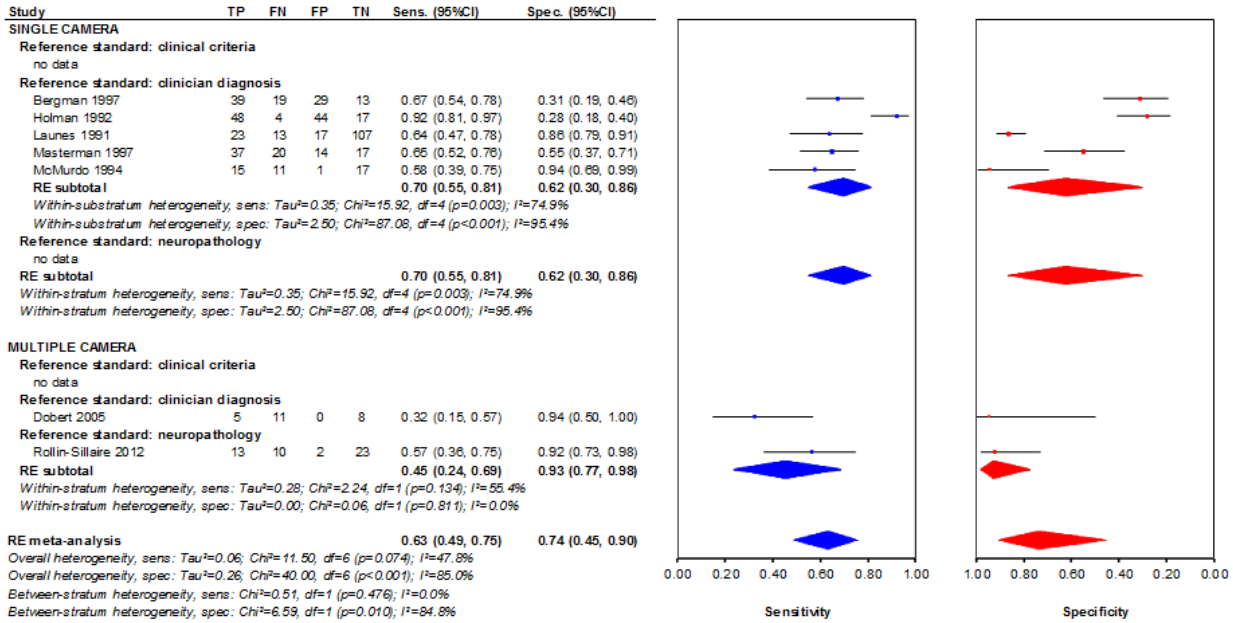


Figure 50AD versus non-AD: 99mTc-HMPAO SPECT – forest plot: sensitivity and specificity

P.3.3.3 Amyloid Beta 1-42

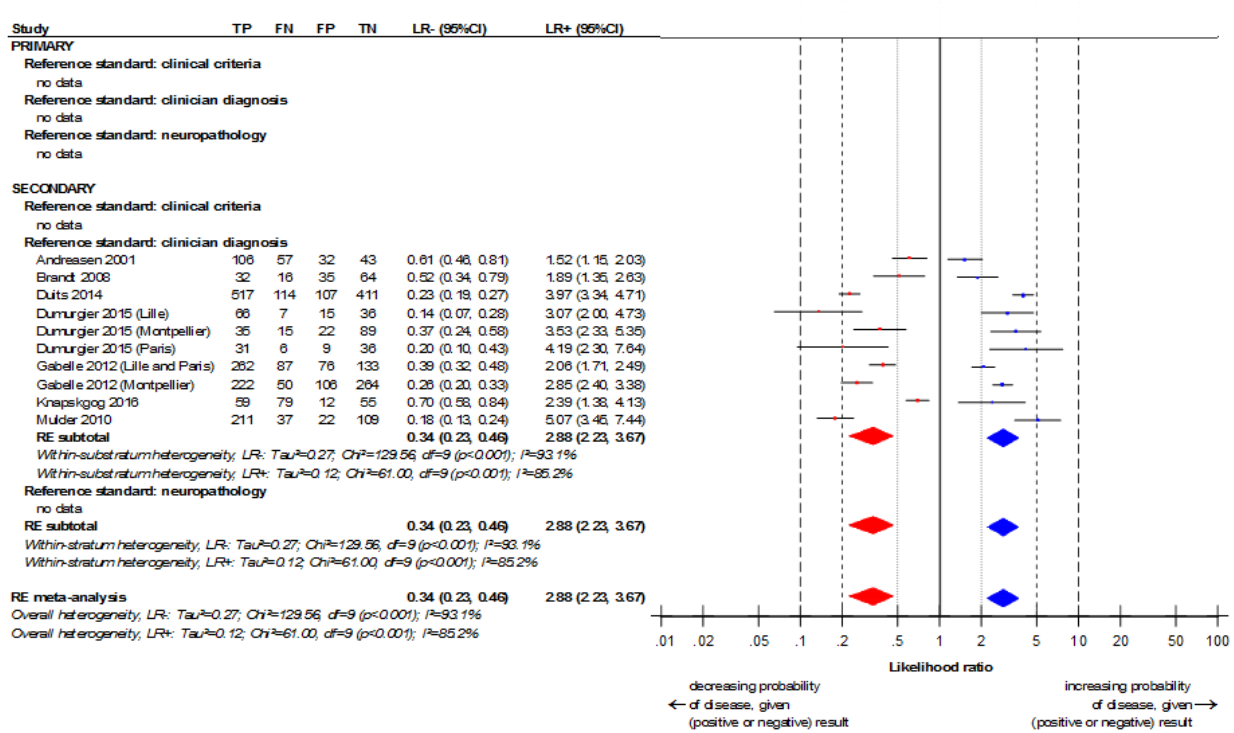


Figure 51AD versus non-AD: Amyloid Beta 1-42 – forest plot: likelihood ratios

Study	TP	FN	FP	TN	Sens. (95%CI)	Spec. (95%CI)
PRIMARY						
Reference standard: clinical criteria						
no data						
Reference standard: clinician diagnosis						
no data						
Reference standard: neuropathology						
no data						
SECONDARY						
Reference standard: clinical criteria						
no data						
Reference standard: clinician diagnosis						
Andreasen 2001	106	57	32	43	0.65 (0.57, 0.72)	0.57 (0.46, 0.68)
Brandt 2008	32	16	35	64	0.67 (0.52, 0.78)	0.65 (0.55, 0.73)
Duits 2014	517	114	107	411	0.82 (0.79, 0.85)	0.79 (0.76, 0.83)
Dumurgier 2015 (Lille)	66	7	15	36	0.90 (0.81, 0.95)	0.71 (0.57, 0.81)
Dumurgier 2015 (Montpellier)	35	15	22	89	0.70 (0.56, 0.81)	0.80 (0.72, 0.87)
Dumurgier 2015 (Paris)	31	6	9	36	0.84 (0.68, 0.93)	0.80 (0.66, 0.89)
Gabelle 2012 (Lille and Paris)	262	87	76	133	0.75 (0.70, 0.79)	0.64 (0.57, 0.70)
Gabelle 2012 (Montpellier)	222	50	106	264	0.82 (0.77, 0.86)	0.71 (0.67, 0.76)
Knapskgog 2016	59	79	12	55	0.43 (0.35, 0.51)	0.82 (0.71, 0.90)
Mulder 2010	211	37	22	109	0.85 (0.80, 0.89)	0.83 (0.76, 0.89)
RE subtotal					**0.76 (0.67, 0.83)**	**0.74 (0.68, 0.79)**
Within-substratum heterogeneity, sens: Tau^2=0.46; Chi^2=137.72, df=9 (p<0.001); I^2=93.5%						
Within-substratum heterogeneity, spec: Tau^2=0.15; Chi^2=47.42, df=9 (p<0.001); I^2=80.1%						
Reference standard: neuropathology						
no data						
RE subtotal					**0.76 (0.67, 0.83)**	**0.74 (0.68, 0.79)**
Within-stratum heterogeneity, sens: Tau^2=0.46; Chi^2=137.72, df=9 (p<0.001); I^2=93.5%						
Within-stratum heterogeneity, spec: Tau^2=0.15; Chi^2=47.42, df=9 (p<0.001); I^2=80.1%						
RE meta-analysis					**0.76 (0.67, 0.83)**	**0.74 (0.68, 0.79)**
Overall heterogeneity, sens: Tau^2=0.27; Chi^2=129.56, df=9 (p<0.001); I^2=93.1%						
Overall heterogeneity, spec: Tau^2=0.12; Chi^2=61.00, df=9 (p<0.001); I^2=85.2%						

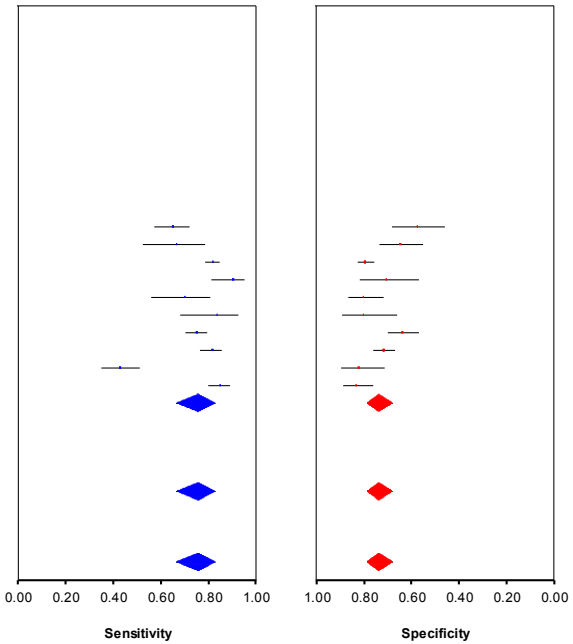


Figure 52 AD versus non-AD: Amyloid Beta 1-42 – forest plot: sensitivity and specificity

P.3.3.4 Amyloid Beta 1-42/p-tau

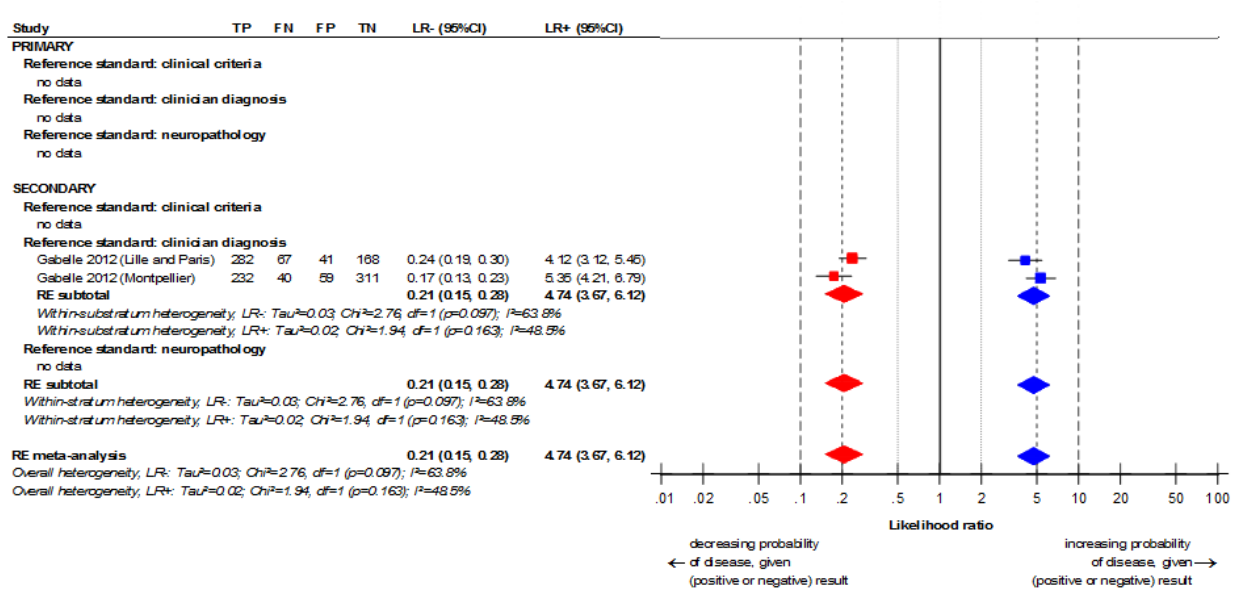


Figure 53AD versus non-AD: Amyloid Beta 1-42/p-tau – forest plot: likelihood ratios

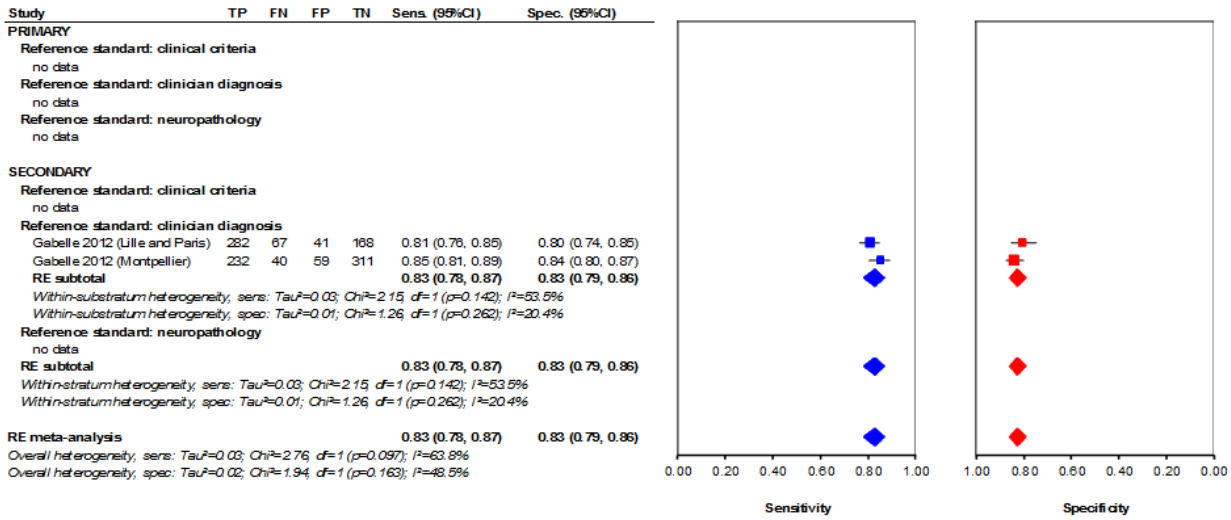


Figure 54AD versus non-AD: Amyloid Beta 1-42/p-tau – forest plot: sensitivity and specificity

P.3.3.5 Amyloid Beta 1-42/Total Tau

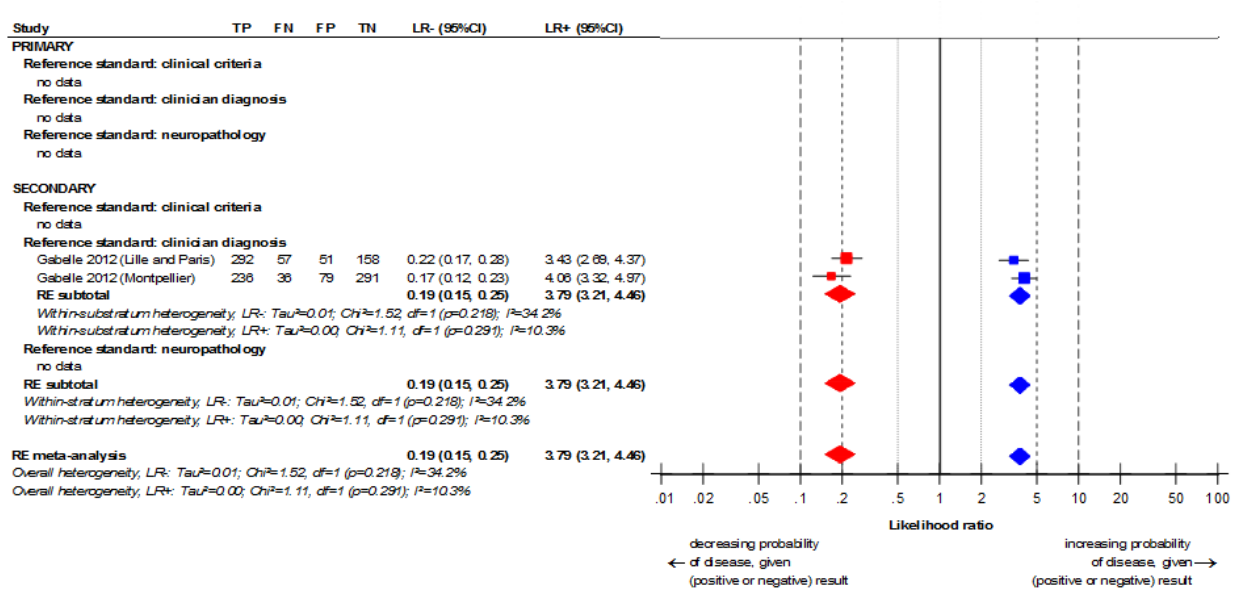


Figure 55AD versus non-AD: Amyloid Beta 1-42/Total Tau – forest plot: likelihood ratios

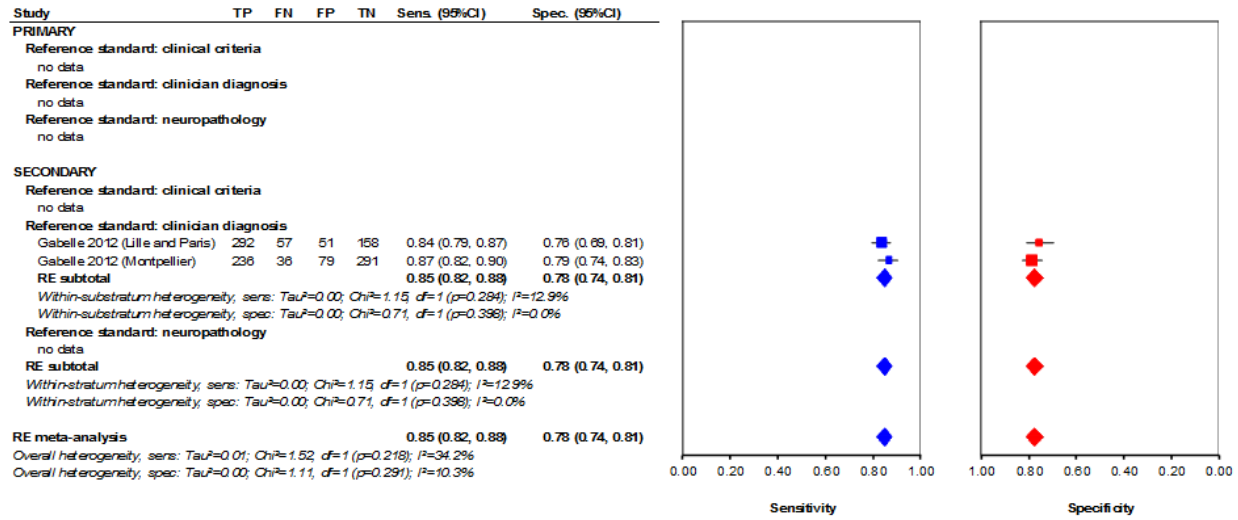


Figure 56AD versus non-AD: Amyloid Beta 1-42/Total Tau – forest plot: sensitivity and specificity

P.3.3.6 Amyloid Beta 42/40

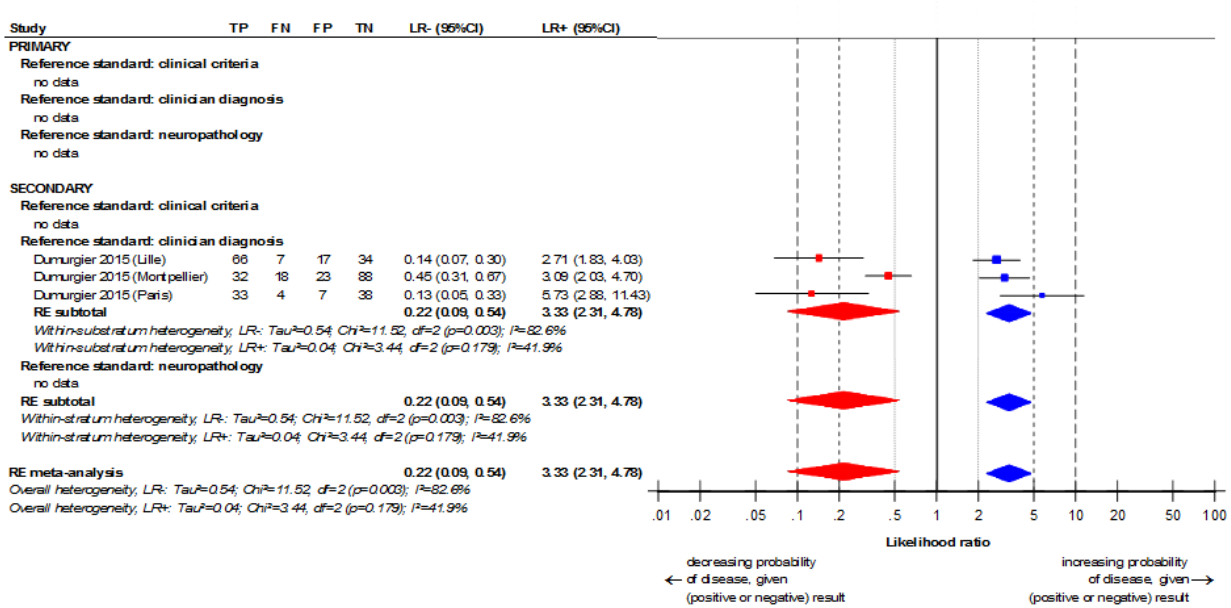


Figure 57AD versus non-AD: Amyloid Beta 42/40 – forest plot: likelihood ratios

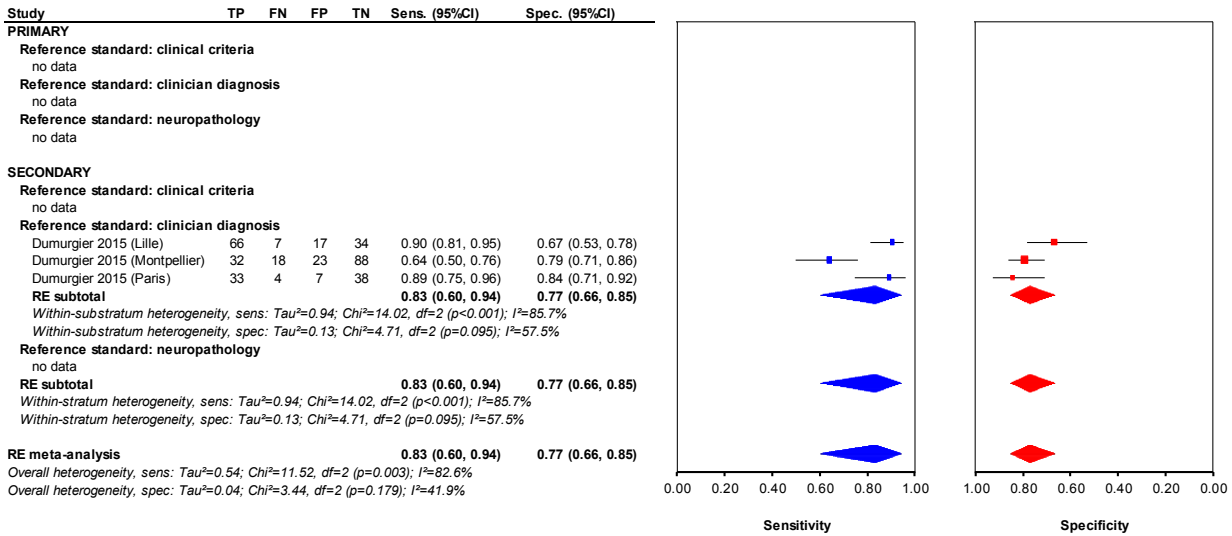


Figure 58AD versus non-AD: Amyloid Beta 42/40 – forest plot: sensitivity and specificity

P.3.3.7 Amyloid Beta 1-42, Total tau and p-tau 181 abnormal

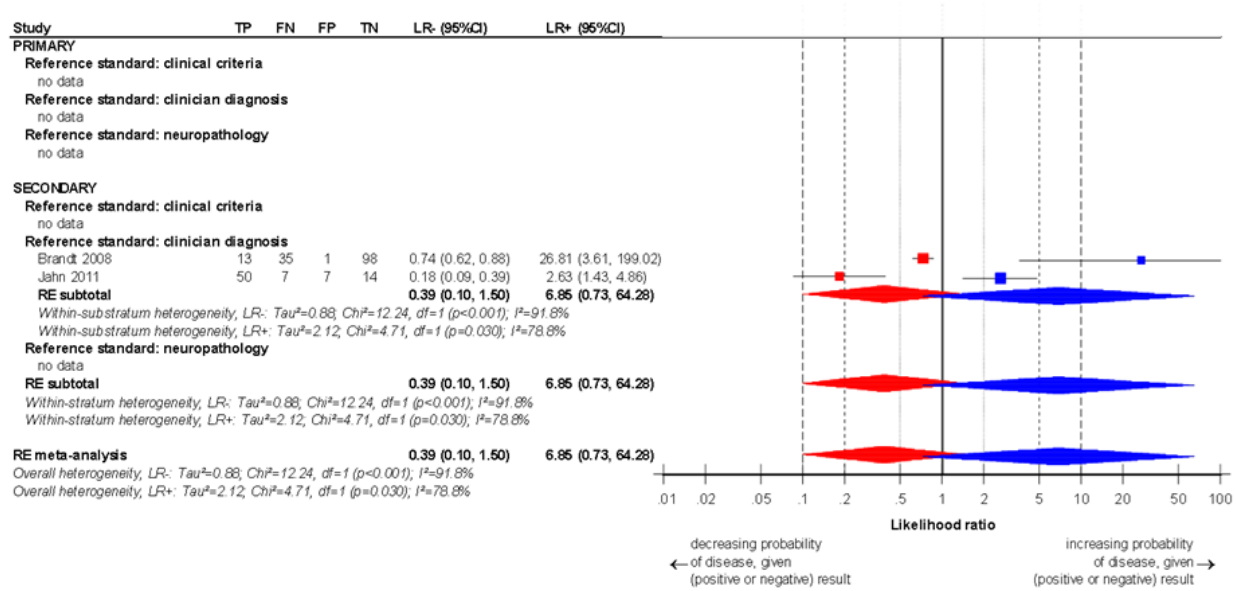


Figure 59: AD versus non-AD: Amyloid Beta 1-42, total tau and p-tau 181- forest plot- likelihood ratios

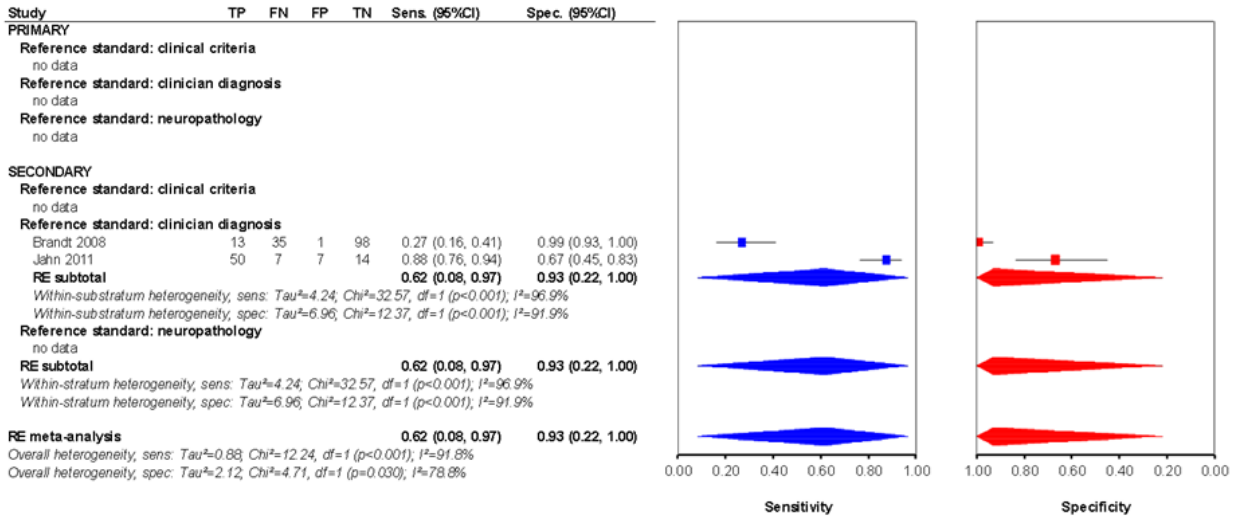


Figure 60 AD versus non-AD: Amyloid Beta 1-42, total tau and p-tau 181- forest plot- sensitivity and specificity

P.3.3.8 FDG-PET

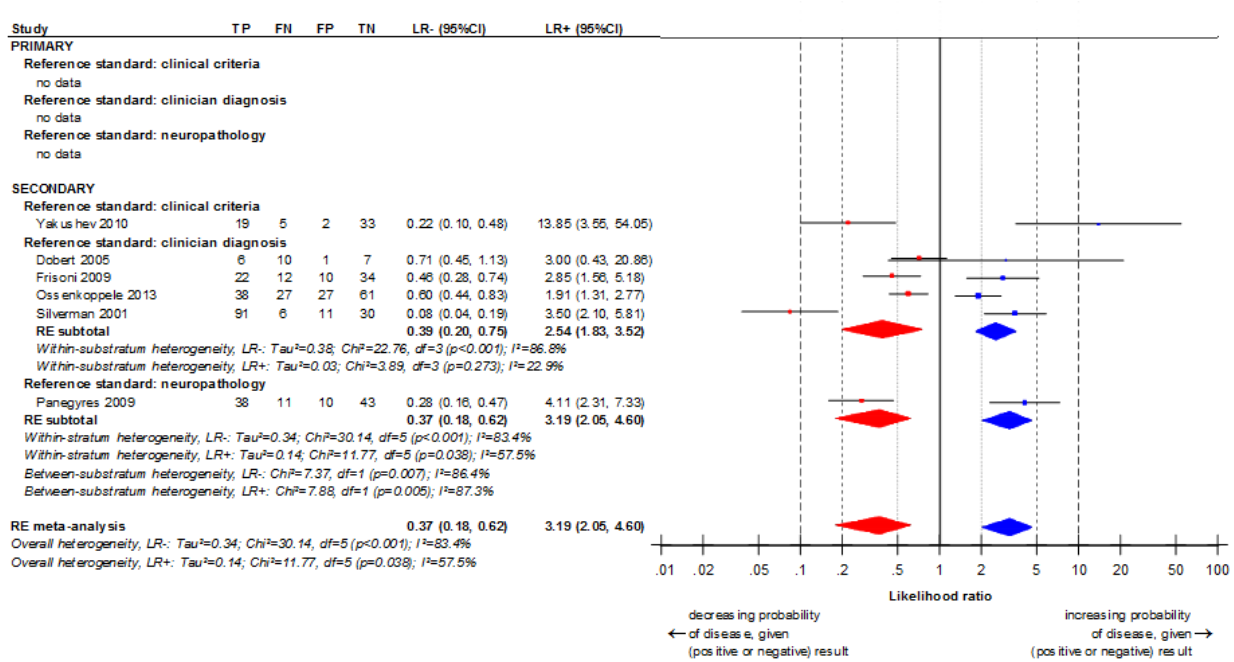


Figure 61AD versus non-AD: FDG-PET – forest plot: likelihood ratios

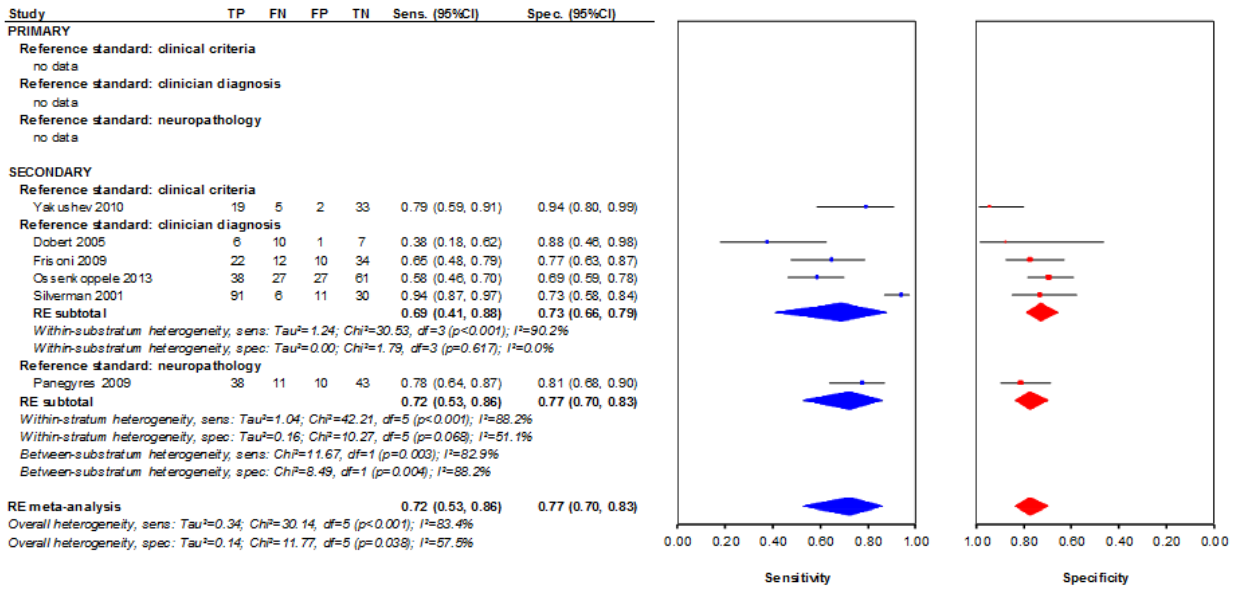


Figure 62AD versus non-AD: FDG-PET – forest plot: sensitivity and specificity

P.3.3.9 MRI

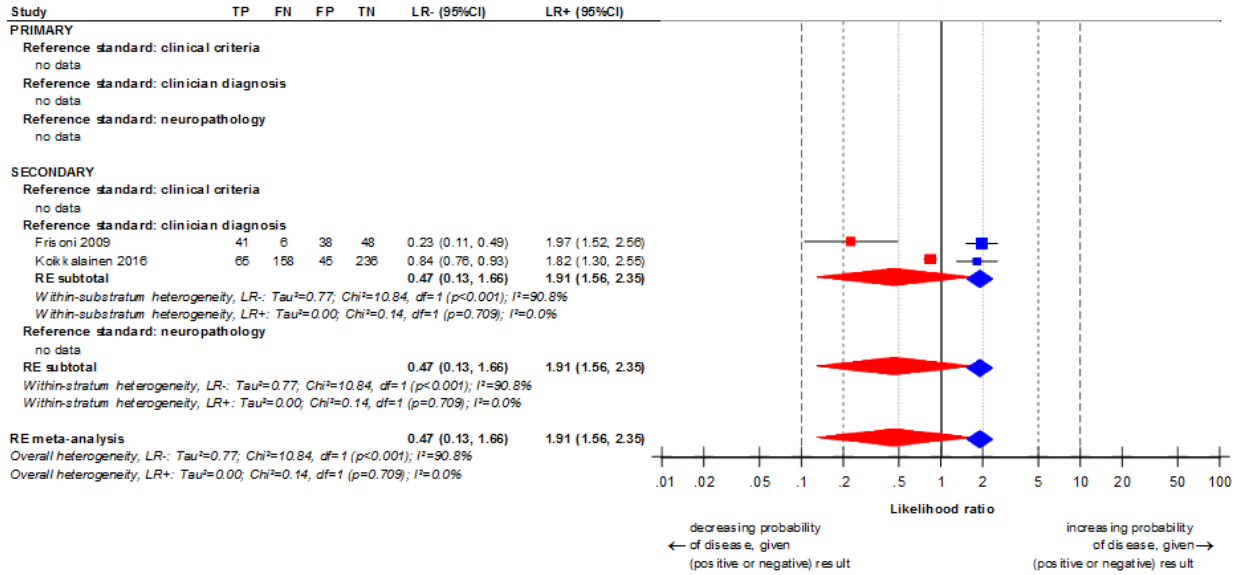


Figure 63AD versus non-AD: MRI – forest plot: likelihood ratios

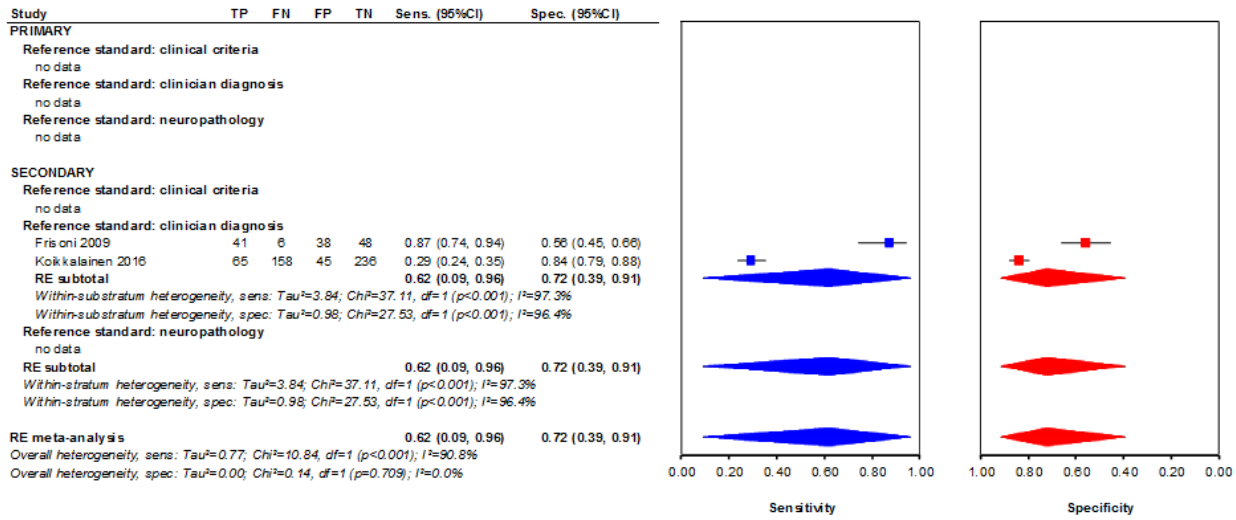


Figure 64AD versus non-AD: MRI – forest plot: sensitivity and specificity

P.3.3.10 p-tau 181

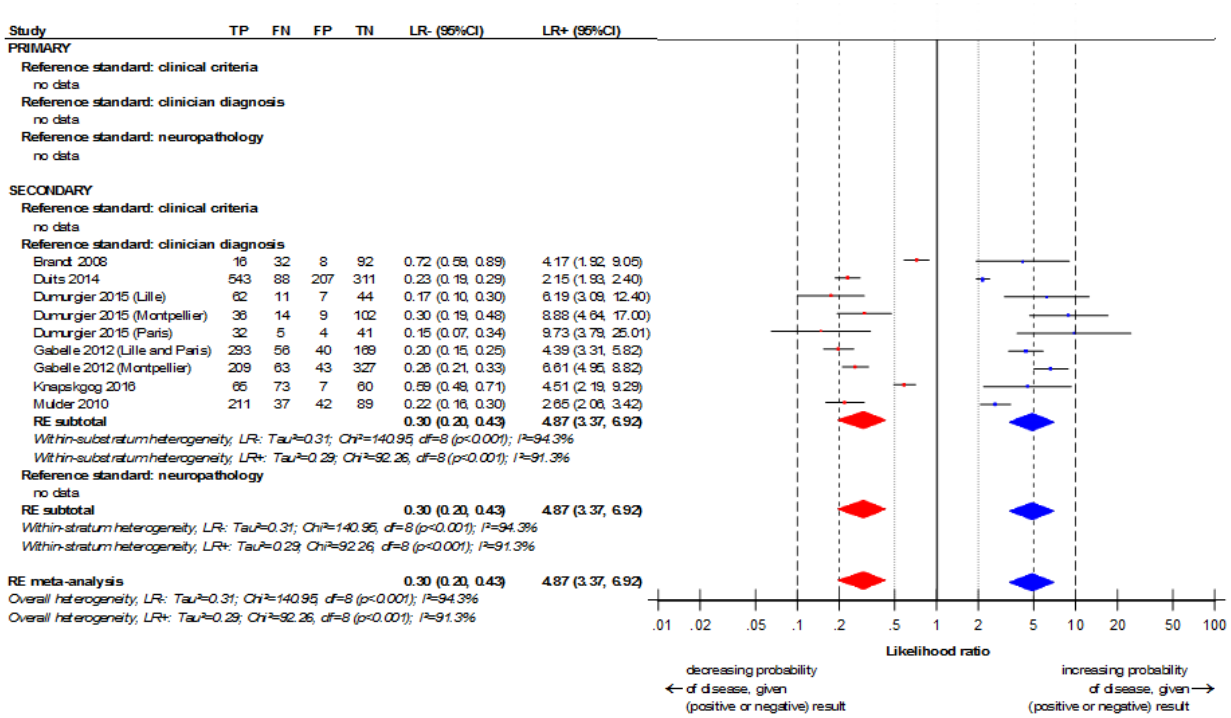


Figure 65AD versus non-AD: p-tau 181 – forest plot: likelihood ratios

P.3.3.11 p-tau/Amyloid Beta 1-42

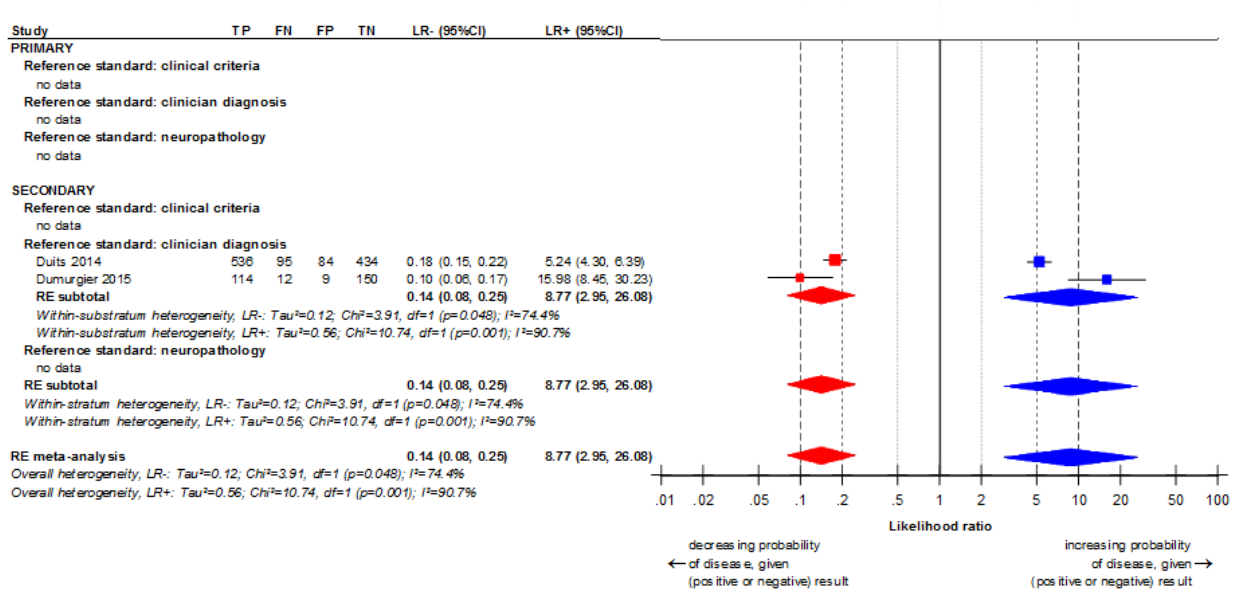


Figure 66AD versus non-AD: p-tau/Amyloid Beta 1-42 – forest plot: likelihood ratios

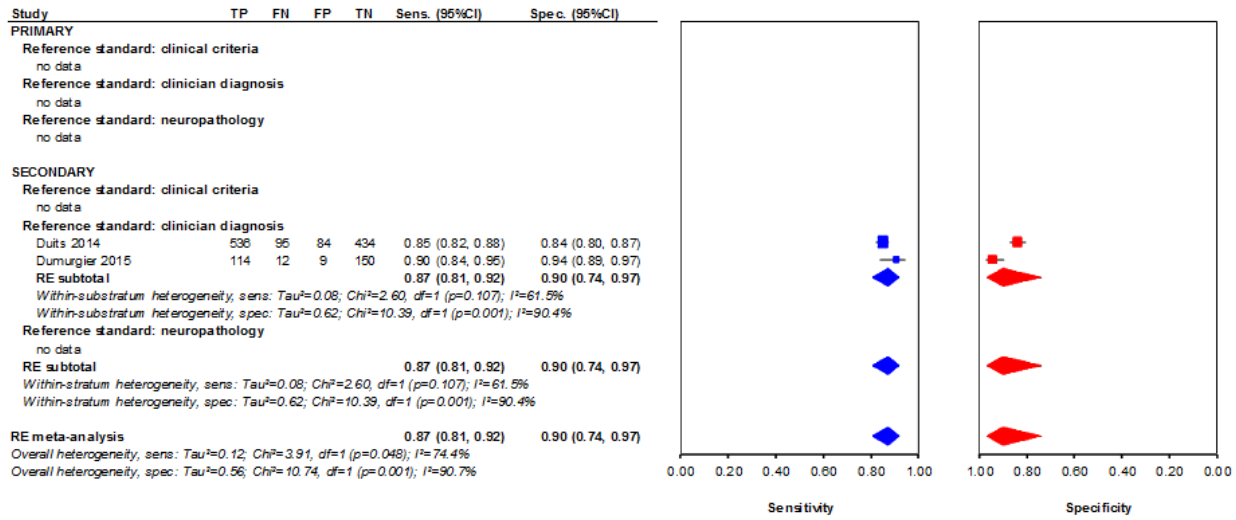
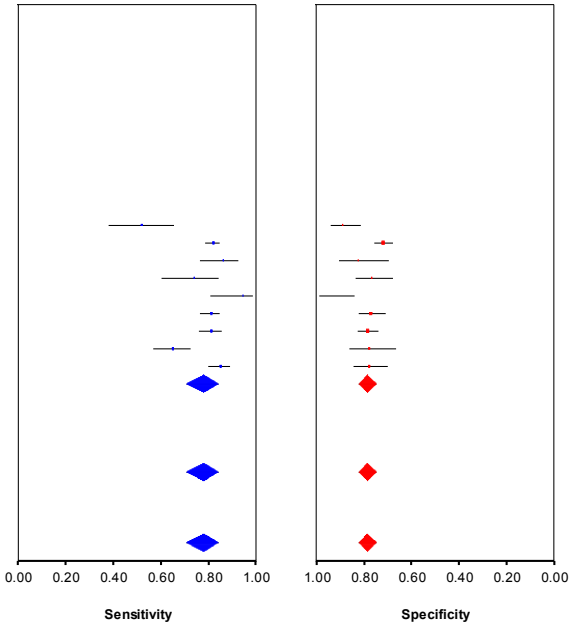


Figure 67AD versus non-AD: p-tau/Amyloid Beta 1-42 – forest plot: sensitivity and specificity

P.3.3.12 Total Tau

Study	TP	FN	FP	TN	Sens. (95%CI)	Spec. (95%CI)
PRIMARY						
Reference standard: clinical criteria						
no data						
Reference standard: clinician diagnosis						
no data						
Reference standard: neuropathology						
no data						
SECONDARY						
Reference standard: clinical criteria						
no data						
Reference standard: clinician diagnosis						
Brandt 2008	25	23	11	88	0.52 (0.38, 0.66)	0.89 (0.81, 0.94)
Duits 2014	517	114	146	372	0.82 (0.79, 0.85)	0.72 (0.68, 0.76)
Dumurgier 2015 (Lille)	63	10	9	42	0.86 (0.76, 0.92)	0.82 (0.69, 0.91)
Dumurgier 2015 (Montpellier)	37	13	26	85	0.74 (0.60, 0.84)	0.77 (0.68, 0.84)
Dumurgier 2015 (Paris)	35	2	2	43	0.95 (0.81, 0.99)	0.96 (0.84, 0.99)
Gabelle 2012 (Lille and Paris)	283	66	48	161	0.81 (0.77, 0.85)	0.77 (0.71, 0.82)
Gabelle 2012 (Montpellier)	221	51	80	290	0.81 (0.76, 0.85)	0.78 (0.74, 0.82)
Knapskgog 2016	90	48	15	52	0.65 (0.57, 0.73)	0.78 (0.66, 0.86)
Mulder 2010	211	37	29	102	0.85 (0.80, 0.89)	0.78 (0.70, 0.84)
RE subtotal					**0.78 (0.71, 0.84)**	**0.78 (0.75, 0.82)**
Within-substratum heterogeneity, sens: Tau^2=0.21; Chi^2=56.60, df=8 (p<0.001); I^2=85.9%						
Within-substratum heterogeneity, spec: Tau^2=0.08; Chi^2=25.91, df=8 (p=0.001); I^2=69.1%						
Reference standard: neuropathology						
no data						
RE subtotal					**0.78 (0.71, 0.84)**	**0.78 (0.75, 0.82)**
Within-stratum heterogeneity, sens: Tau^2=0.21; Chi^2=56.60, df=8 (p<0.001); I^2=85.9%						
Within-stratum heterogeneity, spec: Tau^2=0.08; Chi^2=25.91, df=8 (p=0.001); I^2=69.1%						
RE meta-analysis					**0.78 (0.71, 0.84)**	**0.78 (0.75, 0.82)**
Overall heterogeneity, sens: Tau^2=0.12; Chi^2=49.23, df=8 (p<0.001); I^2=83.8%						
Overall heterogeneity, spec: Tau^2=0.02; Chi^2=16.14, df=8 (p=0.040); I^2=50.4%						



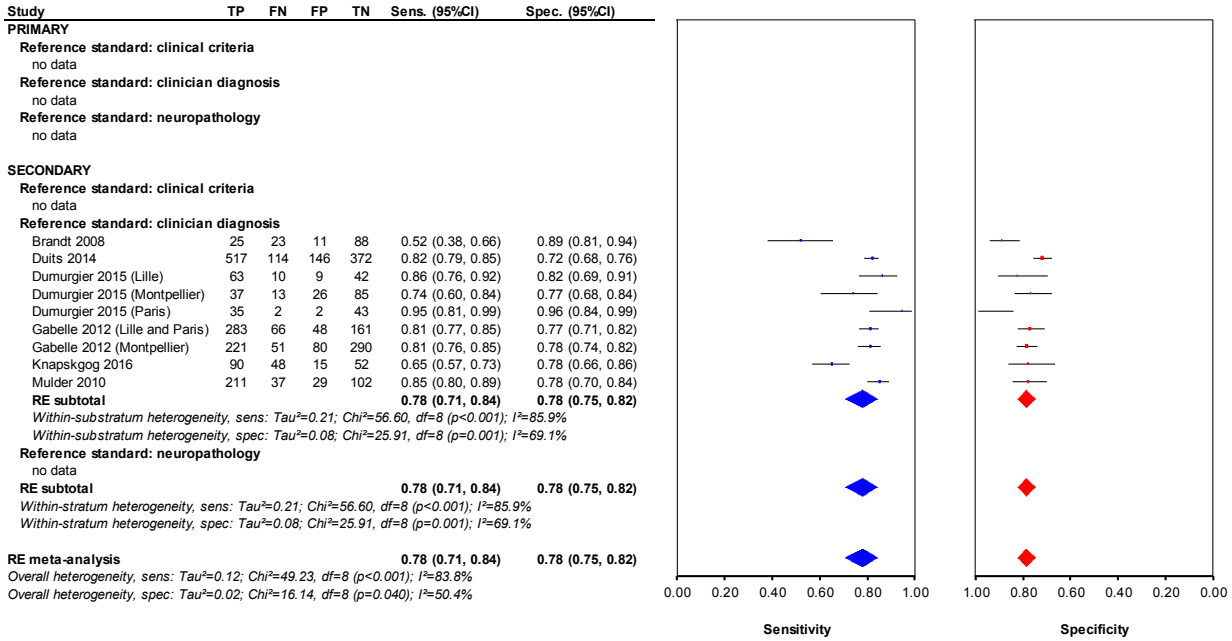


Figure 68AD versus non-AD: Total Tau – forest plot: sensitivity and specificity

P.3.4 AD versus other dementias

P.3.4.1 Amyloid Beta 1-42

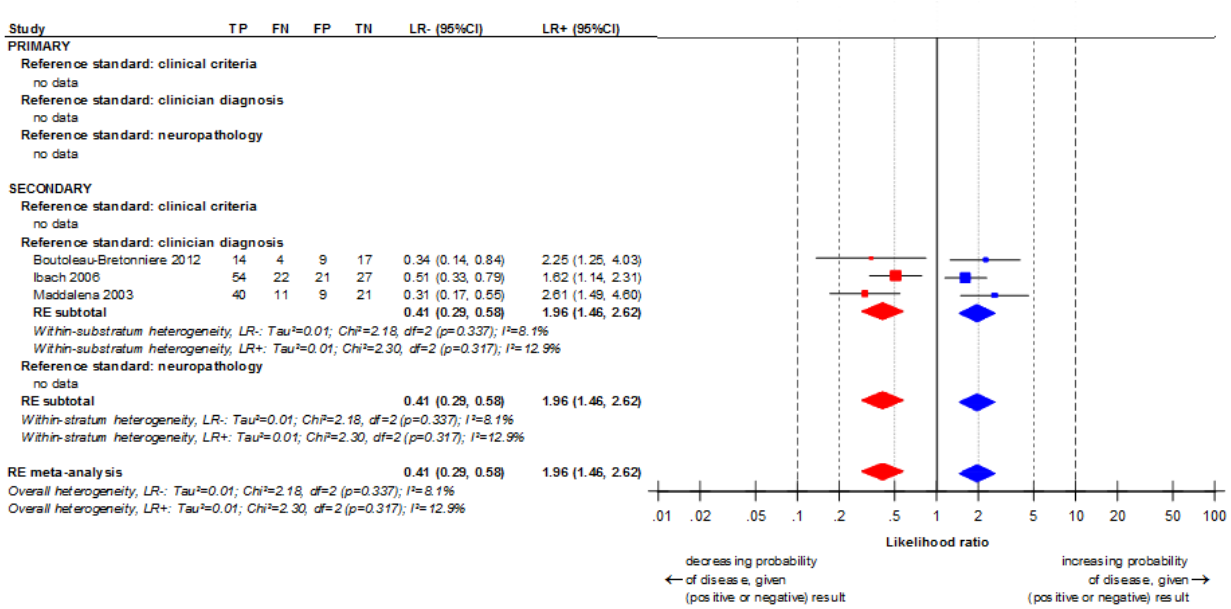


Figure 69AD versus other dementias: Amyloid Beta 1-42 – forest plot: likelihood ratios

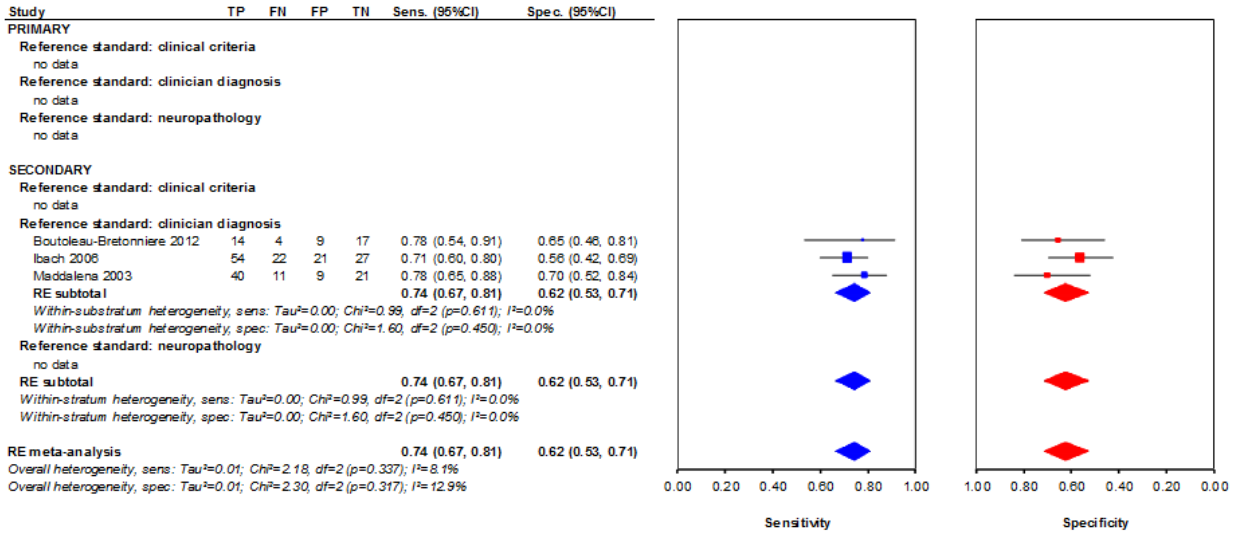


Figure 70AD versus other dementias: Amyloid Beta 1-42 – forest plot: sensitivity and specificity

P.3.4.2 FDG-PET

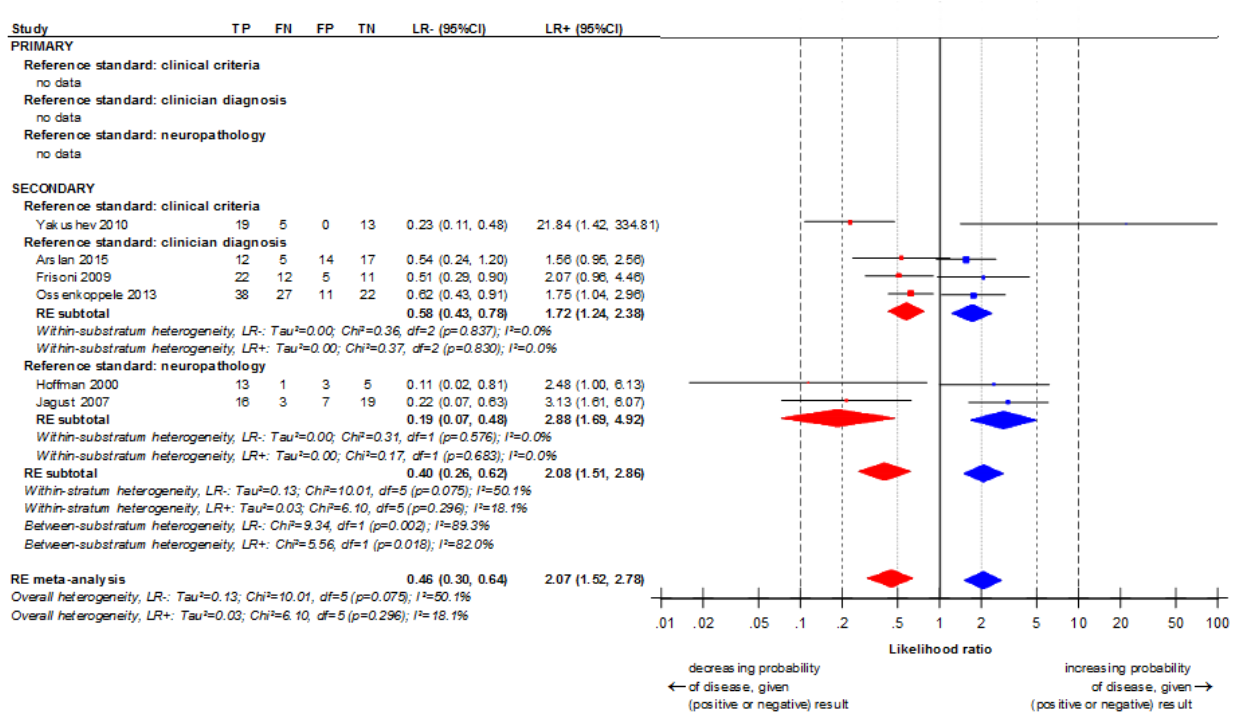


Figure 71AD versus other dementias: FDG-PET – forest plot: likelihood ratios

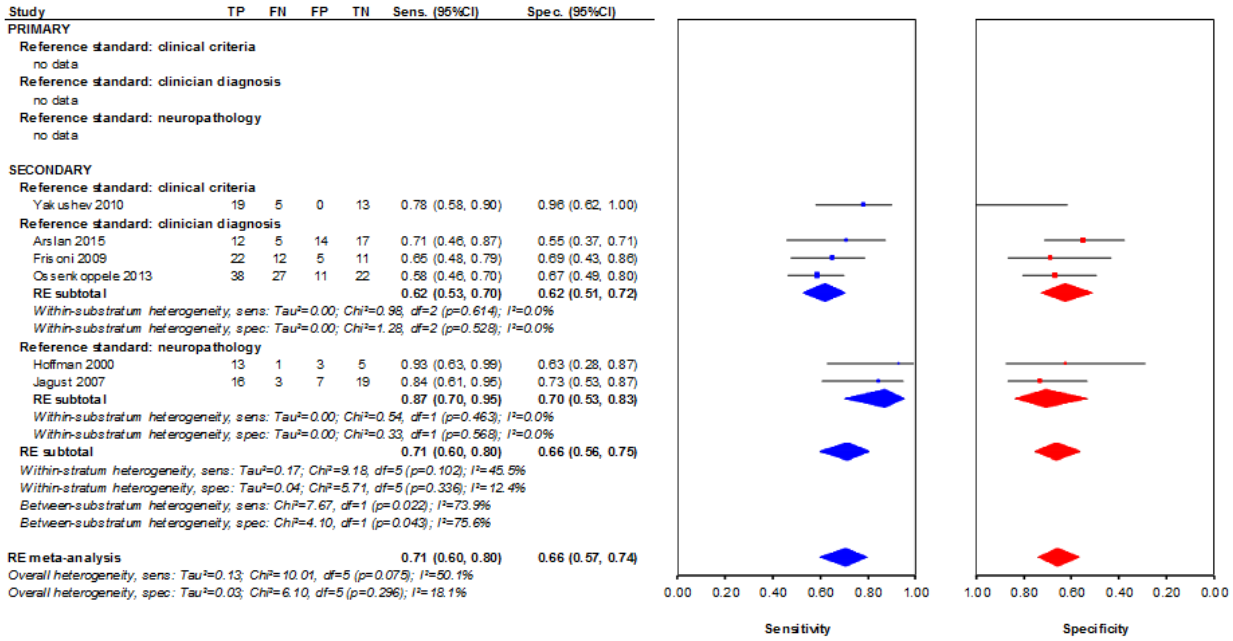


Figure 72AD versus other dementias: FDG-PET – forest plot: sensitivity and specificity

P.3.4.3 MRI

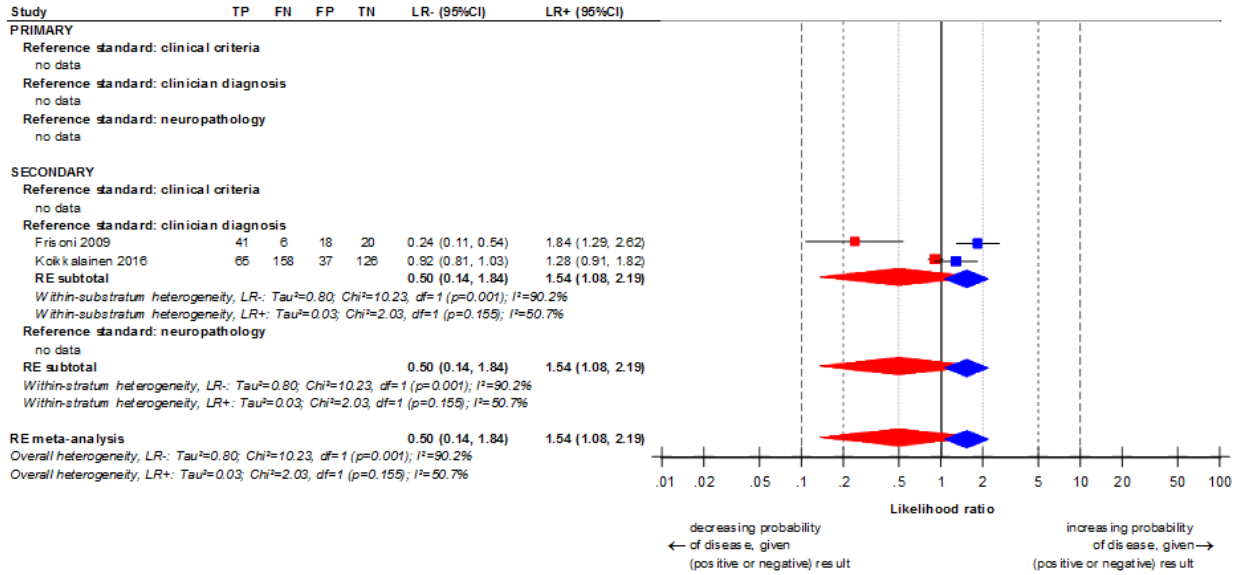


Figure 73AD versus other dementias: MRI – forest plot: likelihood ratios

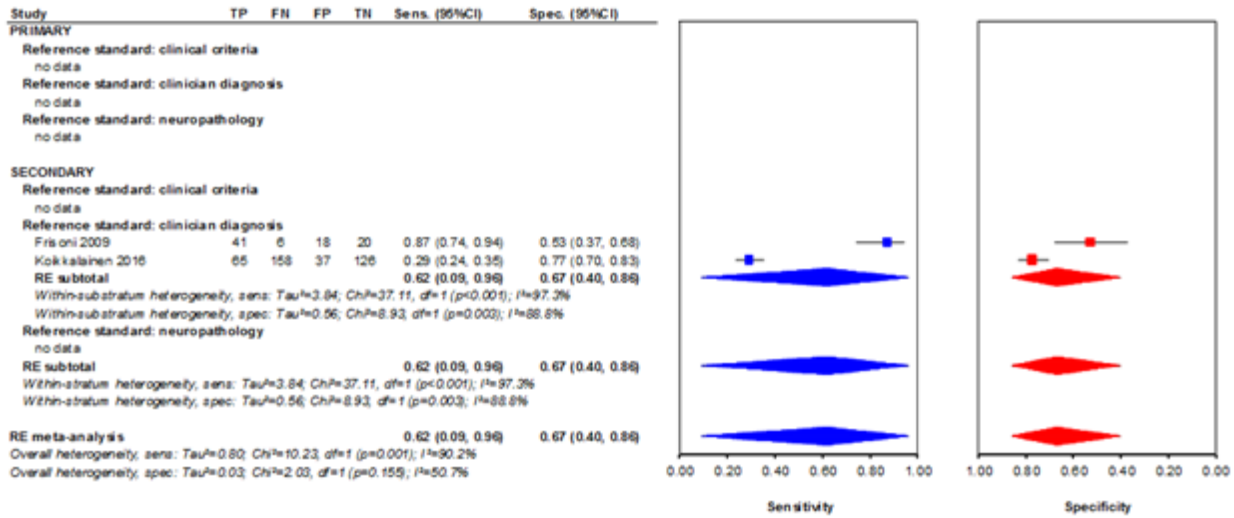


Figure 74AD versus other dementias: MRI – forest plot: sensitivity and specificity

P.3.4.4 p-tau 181

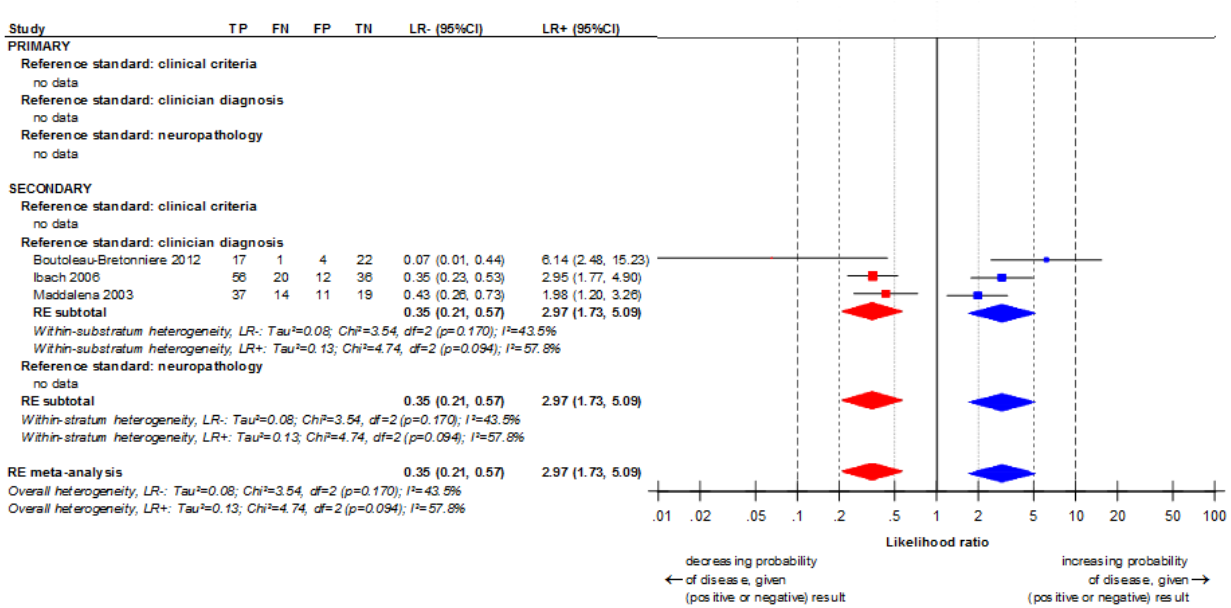


Figure 75AD versus other dementias: p-tau 181 – forest plot: likelihood ratios

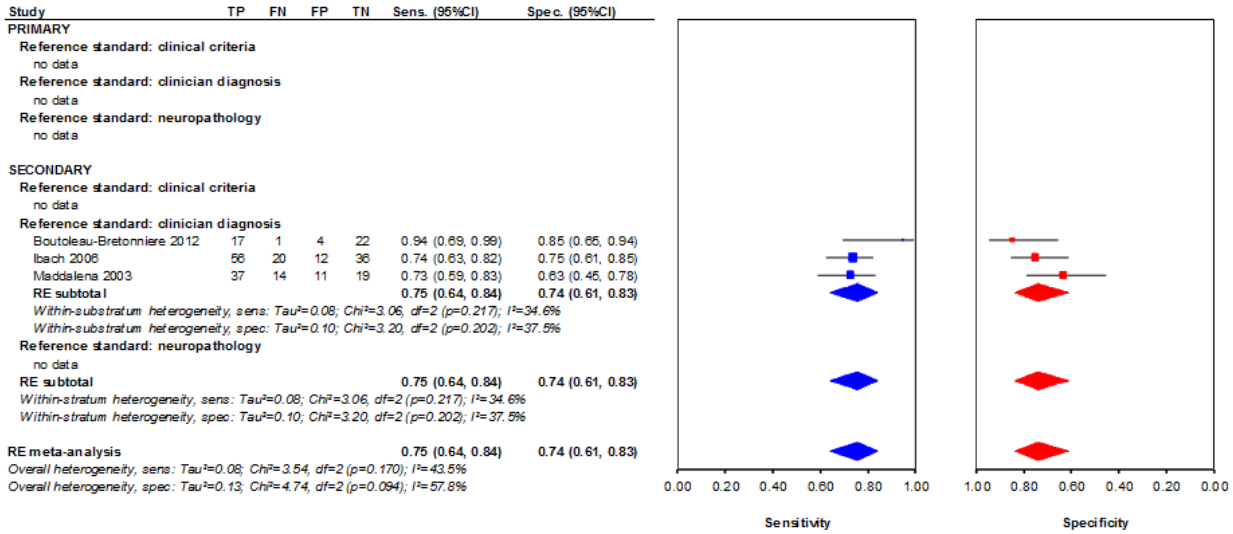
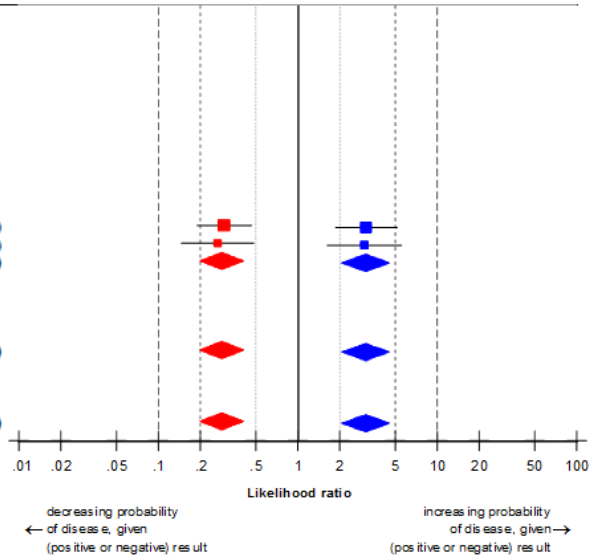


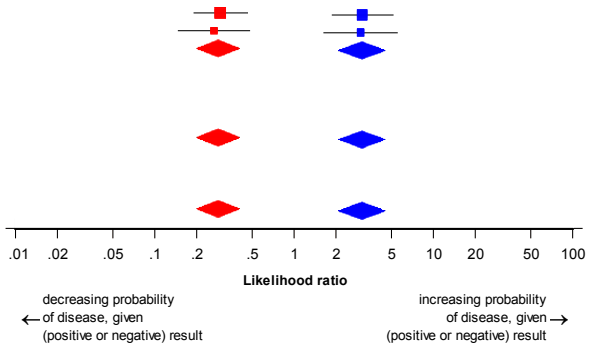
Figure 76AD versus other dementias: p-tau 181 – forest plot: sensitivity and specificity

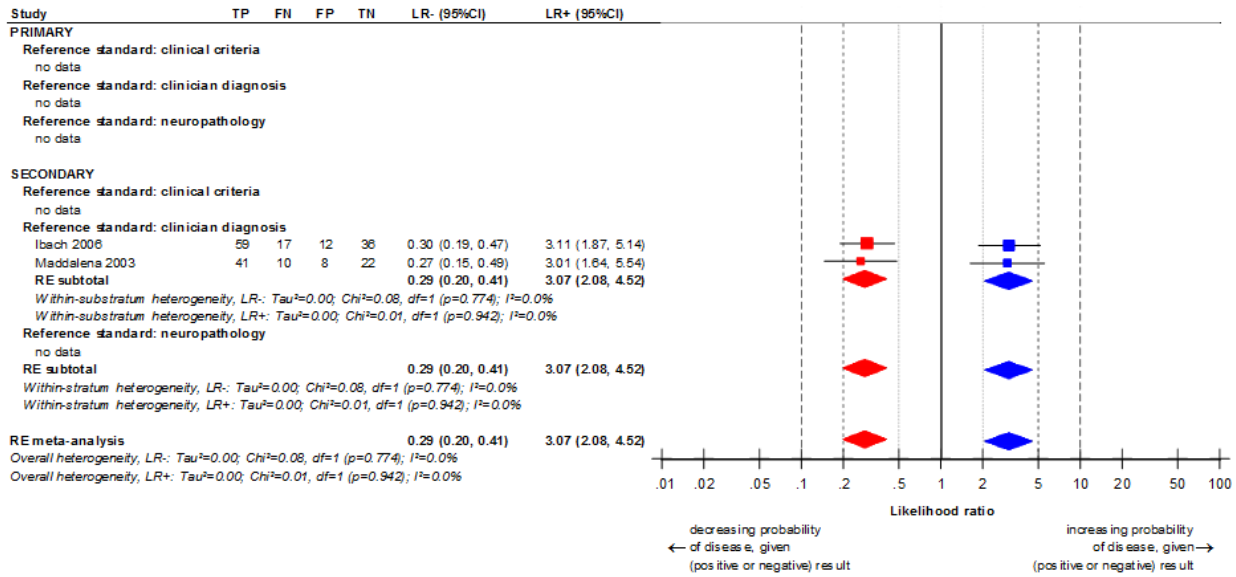
P.3.4.5 p-tau/Amyloid Beta 1-42

Study	TP	FN	FP	TN	LR- (95%CI)	LR+ (95%CI)
PRIMARY						
Reference standard: clinical criteria						
no data						
Reference standard: clinician diagnosis						
no data						
Reference standard: neuropathology						
no data						
SECONDARY						
Reference standard: clinical criteria						
no data						
Reference standard: clinician diagnosis						
Ibach 2006	59	17	12	36	0.30 (0.19, 0.47)	3.11 (1.87, 5.14)
Maddalena 2003	41	10	8	22	0.27 (0.15, 0.49)	3.01 (1.64, 5.54)
RE subtotal					**0.29 (0.20, 0.41)**	**3.07 (2.08, 4.52)**
Within-substratum heterogeneity, LR-: Tau²=0.00; Chi²=0.08, df=1 (p=0.774); I²=0.0%						
Within-substratum heterogeneity, LR+: Tau²=0.00; Chi²=0.01, df=1 (p=0.942); I²=0.0%						
Reference standard: neuropathology						
no data						
RE subtotal					**0.29 (0.20, 0.41)**	**3.07 (2.08, 4.52)**
Within-stratum heterogeneity, LR-: Tau²=0.00; Chi²=0.08, df=1 (p=0.774); I²=0.0%						
Within-stratum heterogeneity, LR+: Tau²=0.00; Chi²=0.01, df=1 (p=0.942); I²=0.0%						
RE meta-analysis					**0.29 (0.20, 0.41)**	**3.07 (2.08, 4.52)**
Overall heterogeneity, LR-: Tau²=0.00; Chi²=0.08, df=1 (p=0.774); I²=0.0%						
Overall heterogeneity, LR+: Tau²=0.00; Chi²=0.01, df=1 (p=0.942); I²=0.0%						



Study	TP	FN	FP	TN	LR- (95%CI)	LR+ (95%CI)
PRIMARY						
Reference standard: clinical criteria						
no data						
Reference standard: clinician diagnosis						
no data						
Reference standard: neuropathology						
no data						
SECONDARY						
Reference standard: clinical criteria						
no data						
Reference standard: clinician diagnosis						
Ibach 2006	59	17	12	36	0.30 (0.19, 0.47)	3.11 (1.87, 5.14)
Maddalena 2003	41	10	8	22	0.27 (0.15, 0.49)	3.01 (1.64, 5.54)
RE subtotal					**0.29 (0.20, 0.41)**	**3.07 (2.08, 4.52)**
Within-substratum heterogeneity, LR-: Tau²=0.00; Chi²=0.08, df=1 (p=0.774); I²=0.0%						
Within-substratum heterogeneity, LR+: Tau²=0.00; Chi²=0.01, df=1 (p=0.942); I²=0.0%						
Reference standard: neuropathology						
no data						
RE subtotal					**0.29 (0.20, 0.41)**	**3.07 (2.08, 4.52)**
Within-stratum heterogeneity, LR-: Tau²=0.00; Chi²=0.08, df=1 (p=0.774); I²=0.0%						
Within-stratum heterogeneity, LR+: Tau²=0.00; Chi²=0.01, df=1 (p=0.942); I²=0.0%						
RE meta-analysis					**0.29 (0.20, 0.41)**	**3.07 (2.08, 4.52)**
Overall heterogeneity, LR-: Tau²=0.00; Chi²=0.08, df=1 (p=0.774); I²=0.0%						
Overall heterogeneity, LR+: Tau²=0.00; Chi²=0.01, df=1 (p=0.942); I²=0.0%						





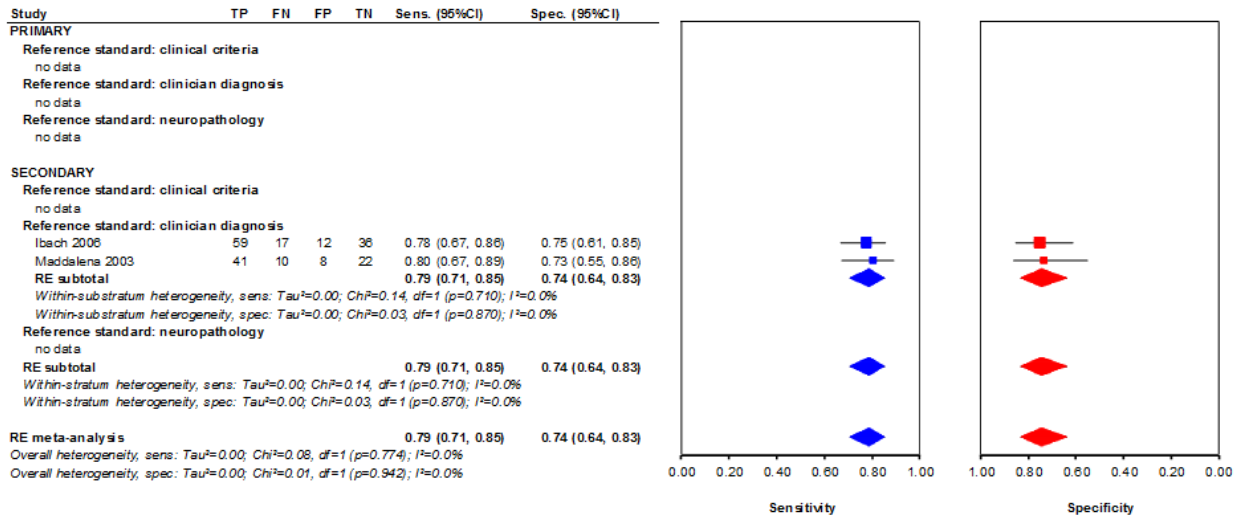


Figure 77 AD versus other dementias: p-tau/Amyloid Beta 1-42 – forest plot: sensitivity and specificity

P.3.4.6 Total tau

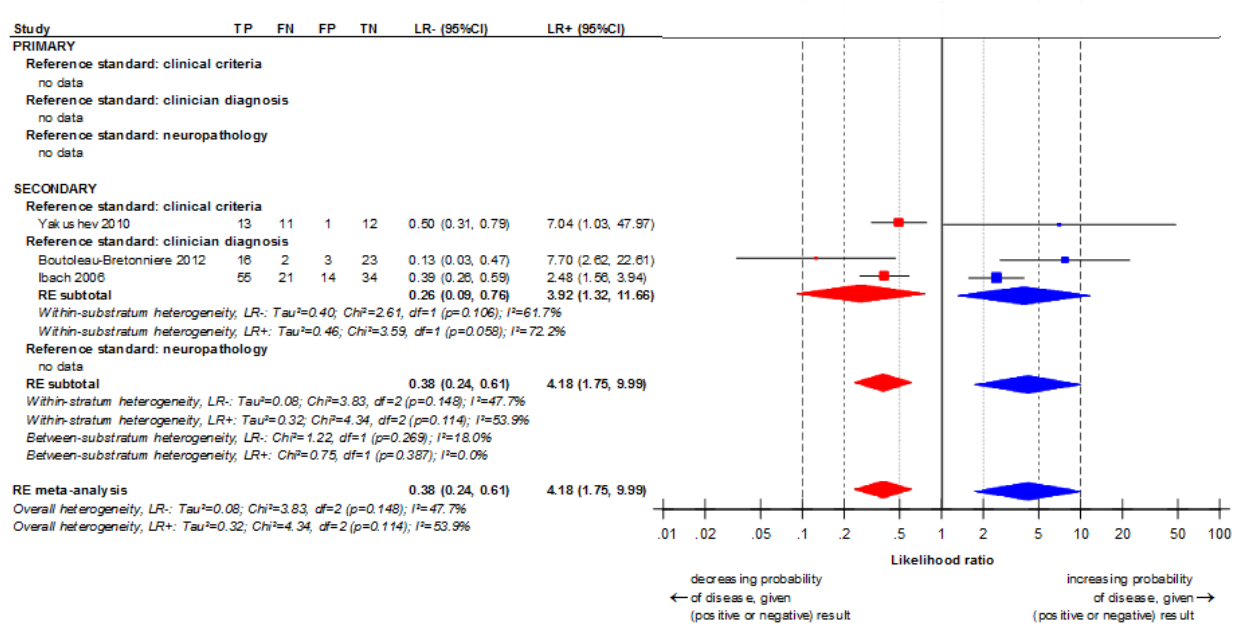


Figure 78AD versus other dementias: Total tau – forest plot: likelihood ratios

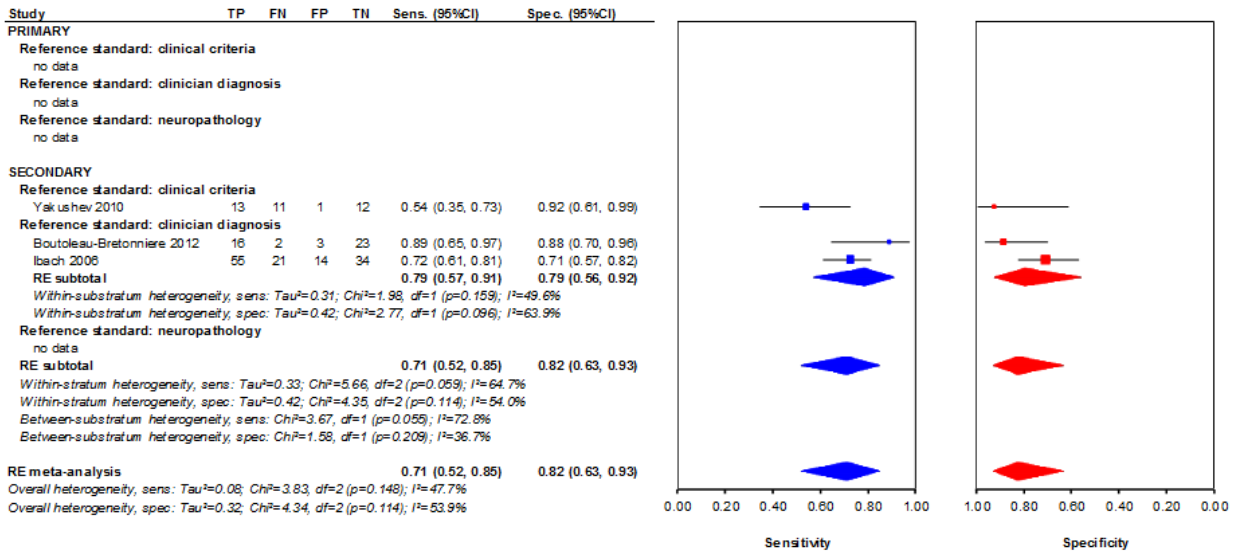


Figure 79AD versus other dementias: Total tau – forest plot: sensitivity and specificity

P.3.5 AD versus VaD

P.3.5.1 99mTc-HMPAO SPECT

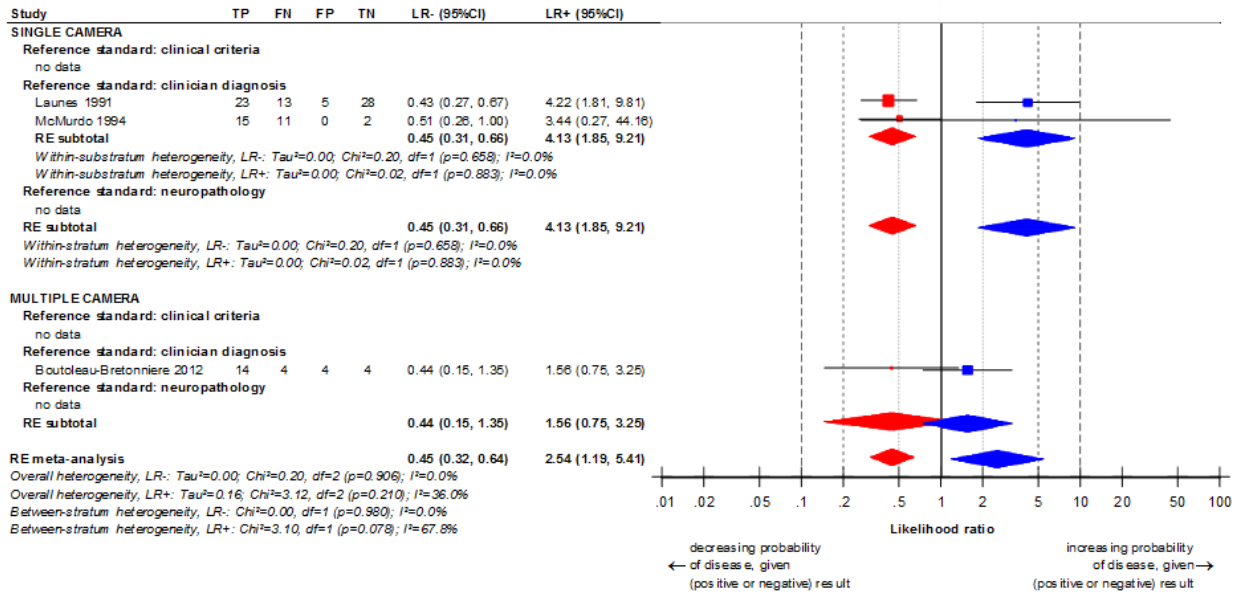


Figure 80AD versus VaD: 99mTc-HMPAO SPECT – forest plot: likelihood ratios

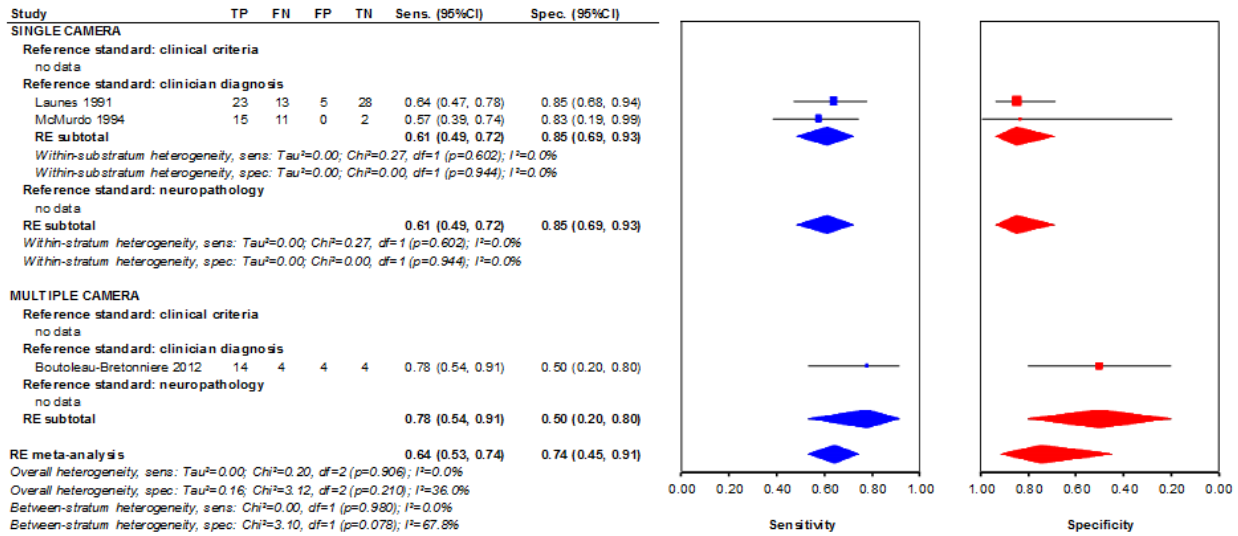


Figure 81AD versus VaD: 99mTc-HMPAO SPECT – forest plot: sensitivity and specificity

P.3.6 CJD versus non-CJD

P.3.6.1 CSF 14-3-3 ELISA

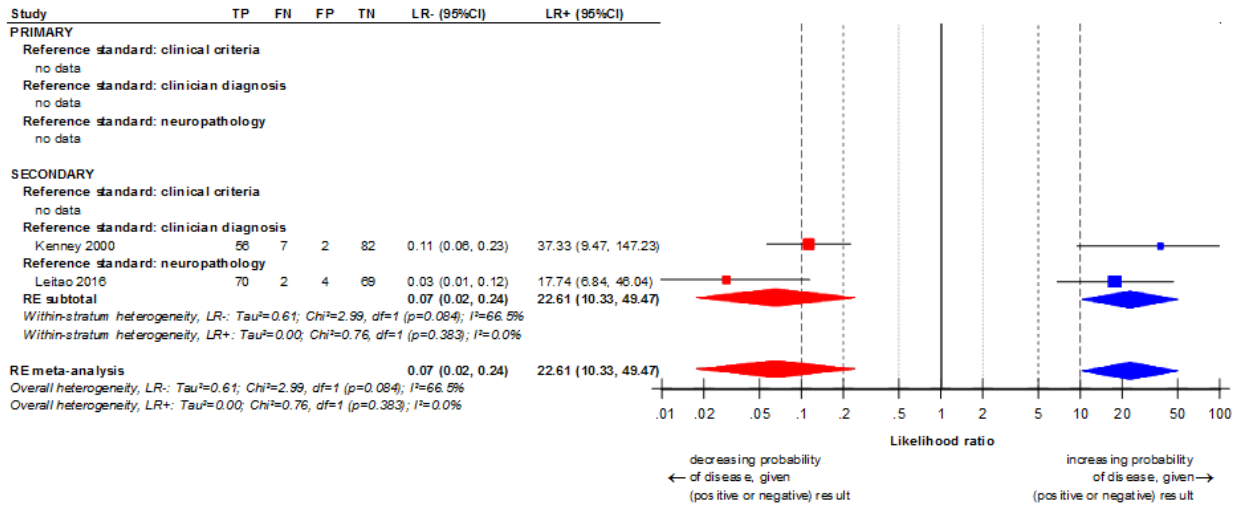


Figure 82CJD versus non-CJD: CSF 14-3-3 ELISA – forest plot: likelihood ratios

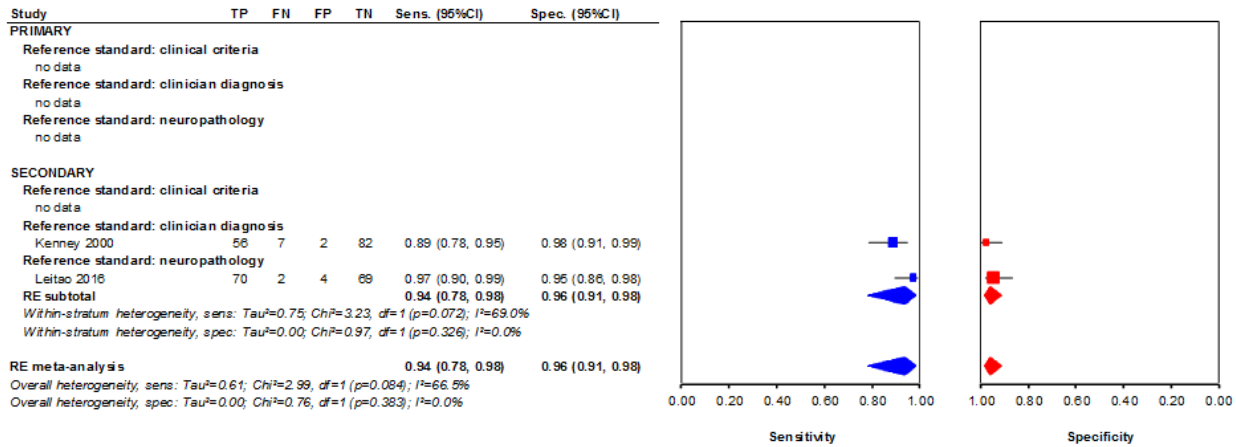


Figure 83CJD versus non-CJD: CSF 14-3-3 ELISA – forest plot: sensitivity and specificity

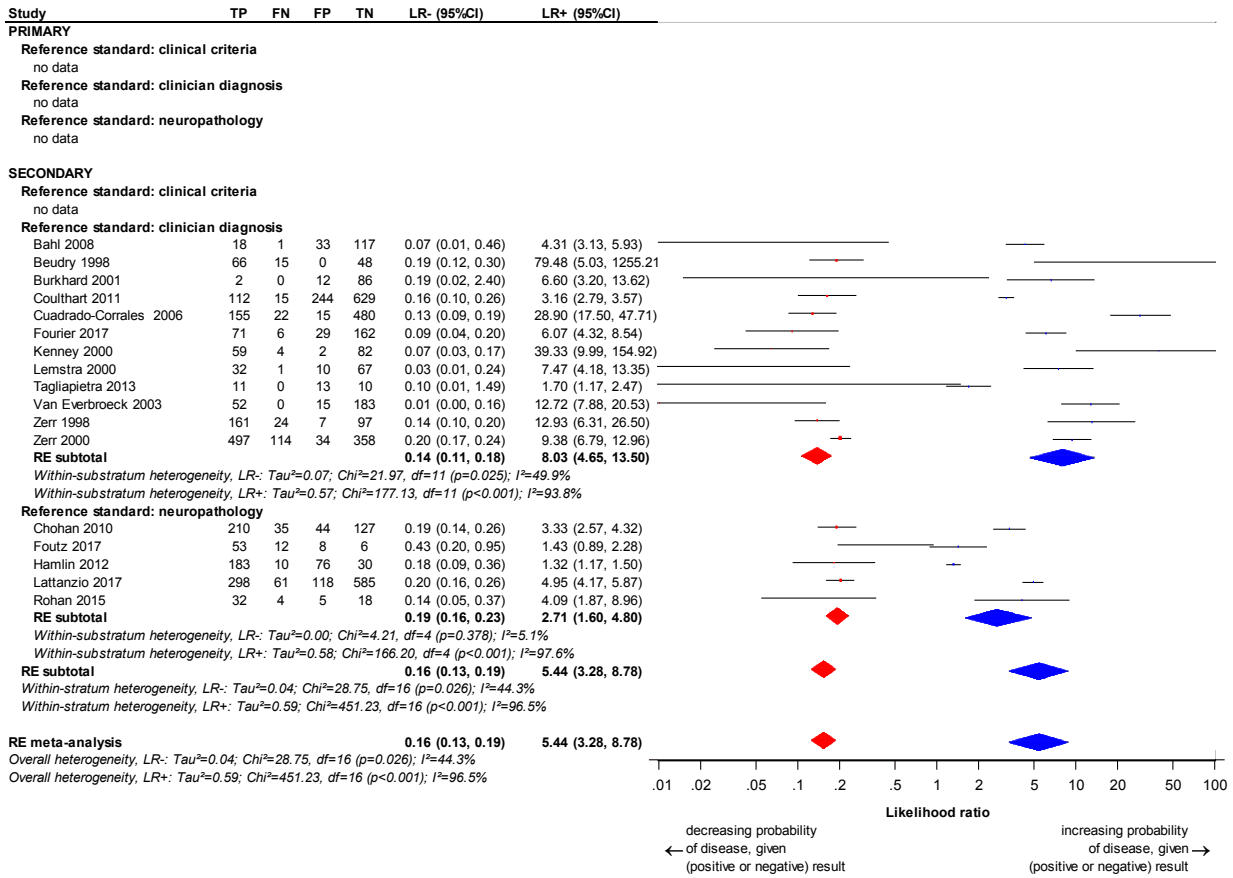


Figure 84CJD versus non-CJD: CSF 14-3-3 ELISA – forest plot: sensitivity and specificity

P.3.6.2 CSF 14-3-3 immunoblotting

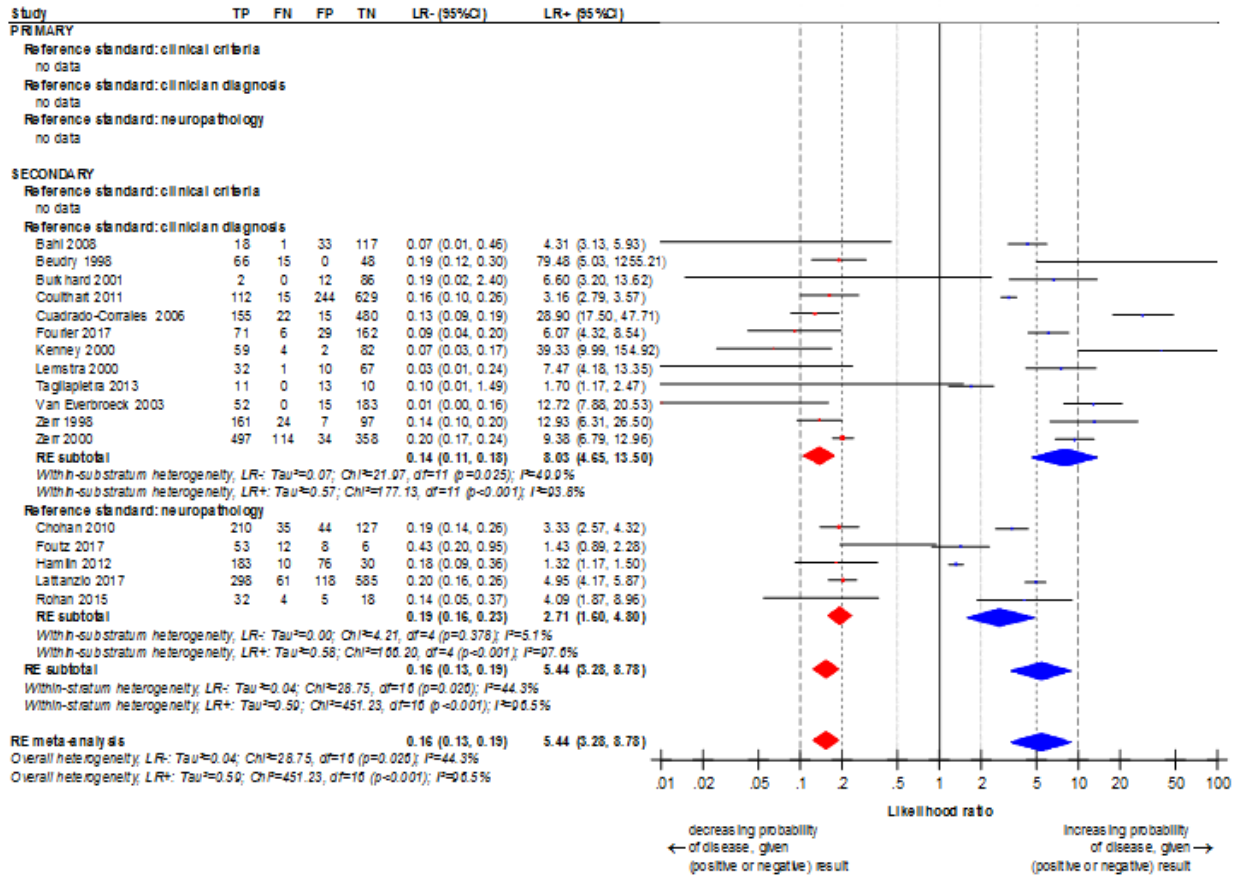


Figure 85CJD versus non-CJD: CSF 14-3-3 immunoblotting – forest plot: likelihood ratios

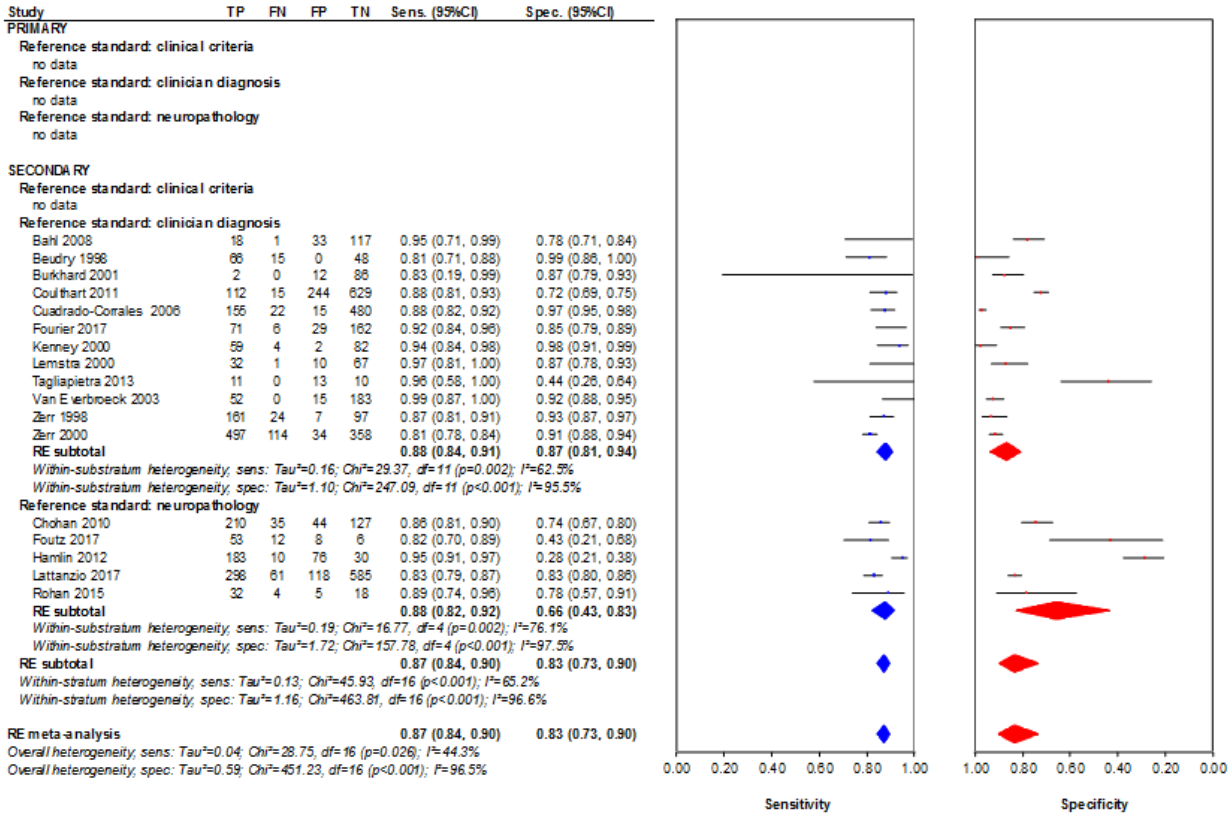


Figure 86CJD versus non-CJD: CSF 14-3-3 immunoblotting – forest plot: sensitivity and specificity

P.3.6.3 EEG

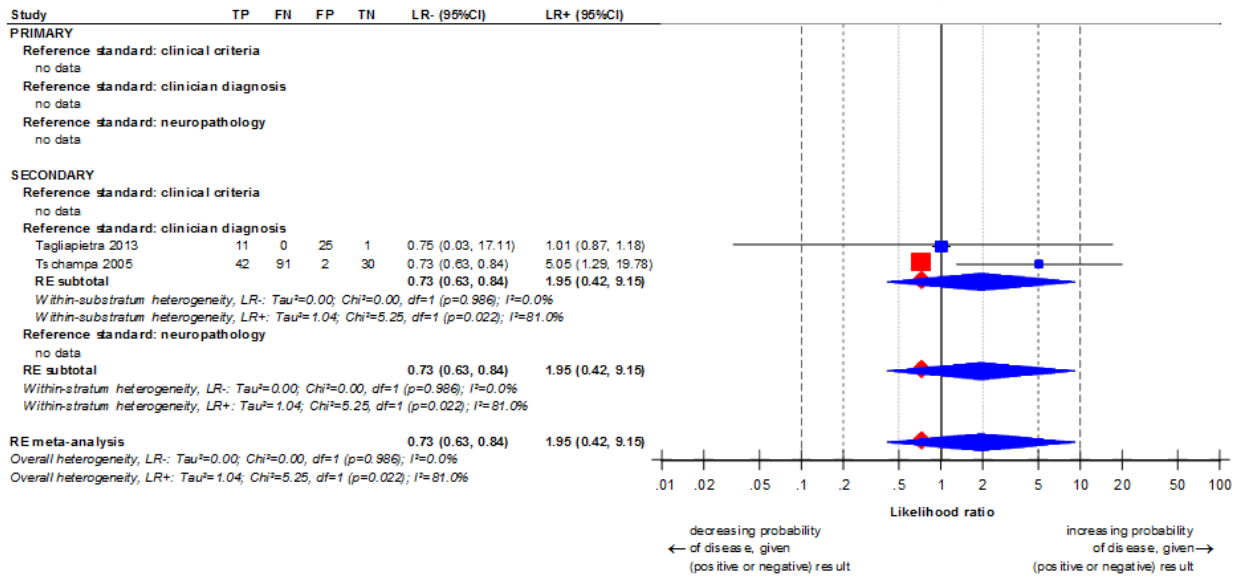


Figure 87CJD versus non-CJD: EEG – forest plot: likelihood ratios

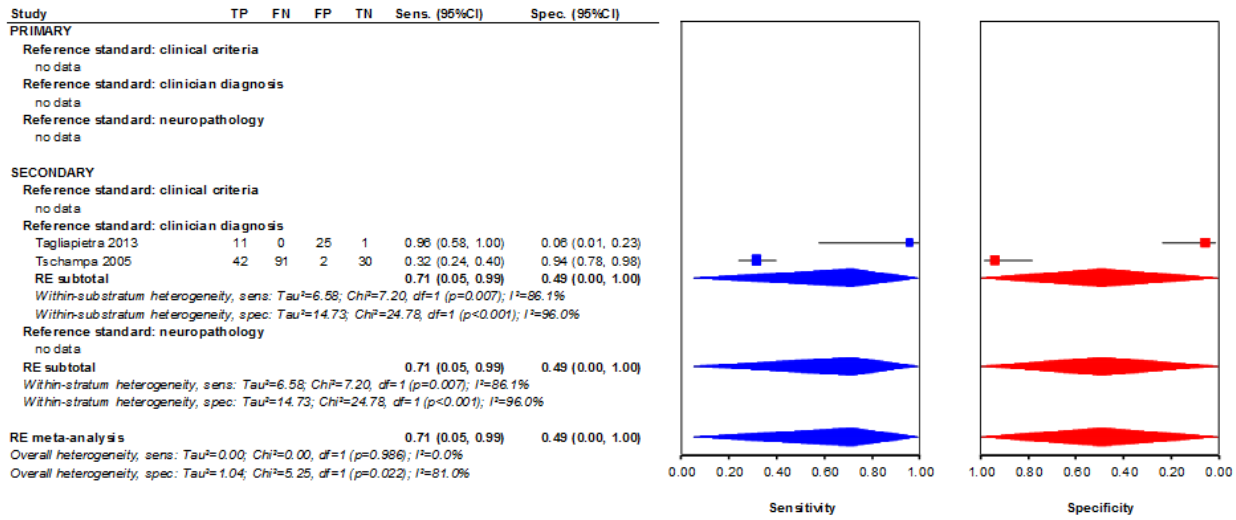


Figure 88CJD versus non-CJD: EEG – forest plot: sensitivity and specificity

P.3.6.4 MRI

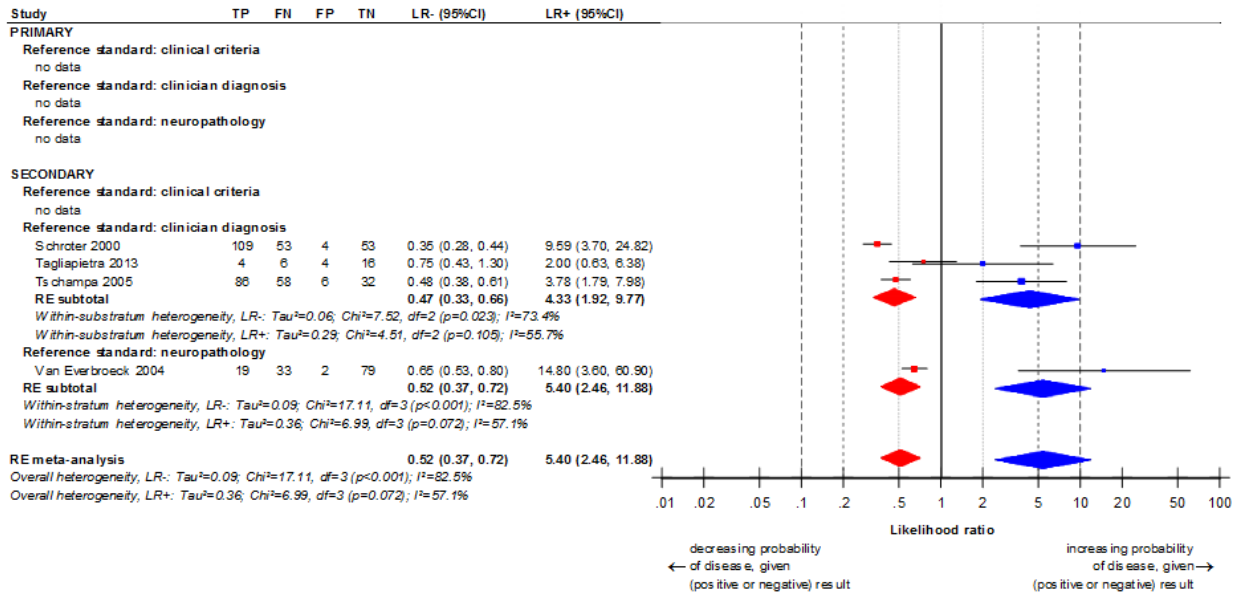


Figure 89CJD versus non-CJD: EEG – forest plot: sensitivity and specificity

P.3.6.5 MRI

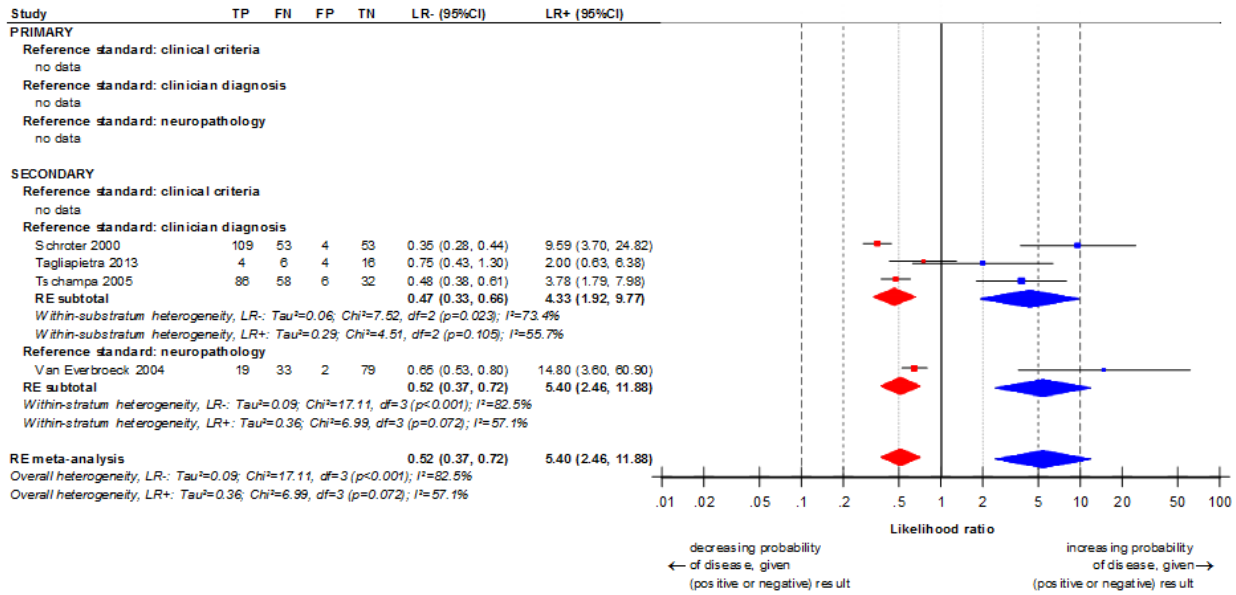


Figure 90CJD versus non-CJD: MRI – forest plot: likelihood ratios

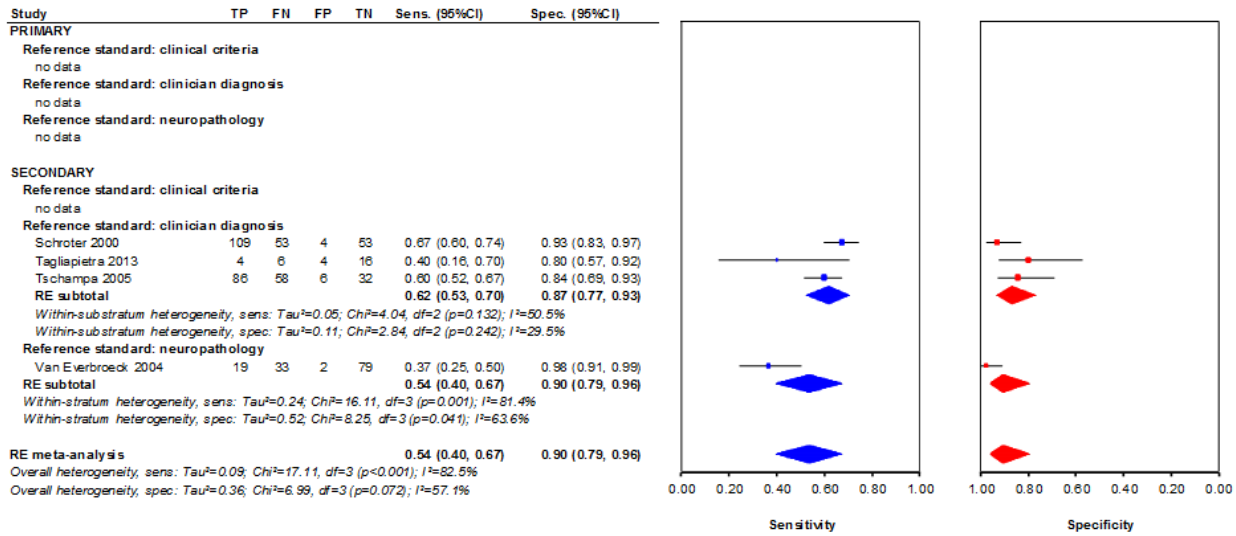


Figure 91 CJD versus non-CJD: MRI – forest plot: sensitivity and specificity

P.3.6.6 Neuron-specific enolase

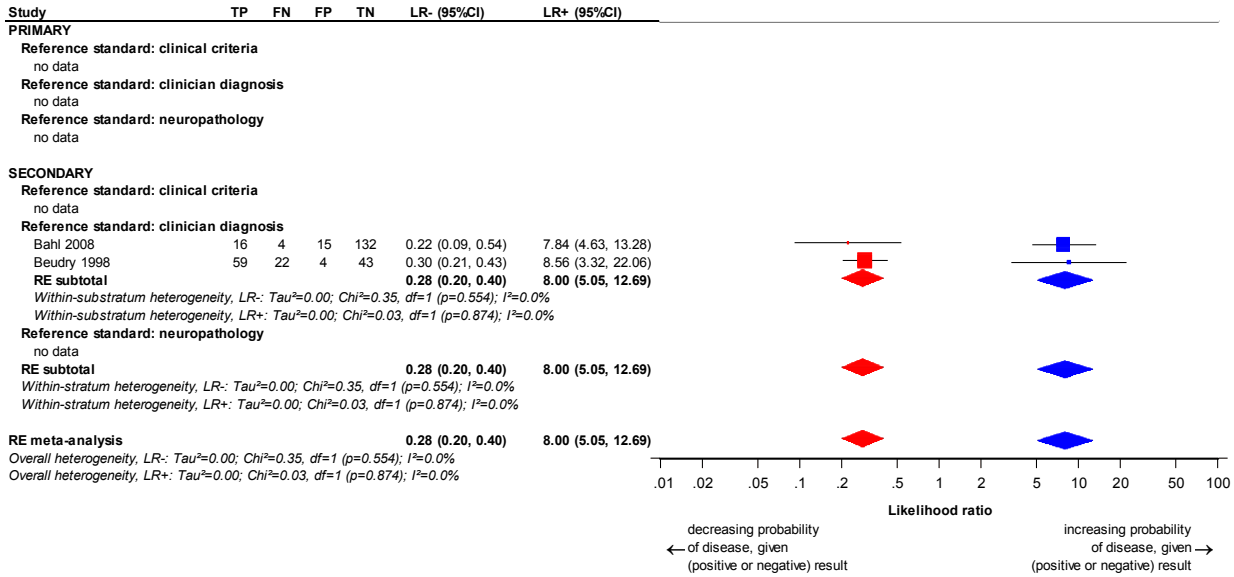


Figure 92CJD versus non-CJD: Neuron-specific enolase – forest plot: likelihood ratios

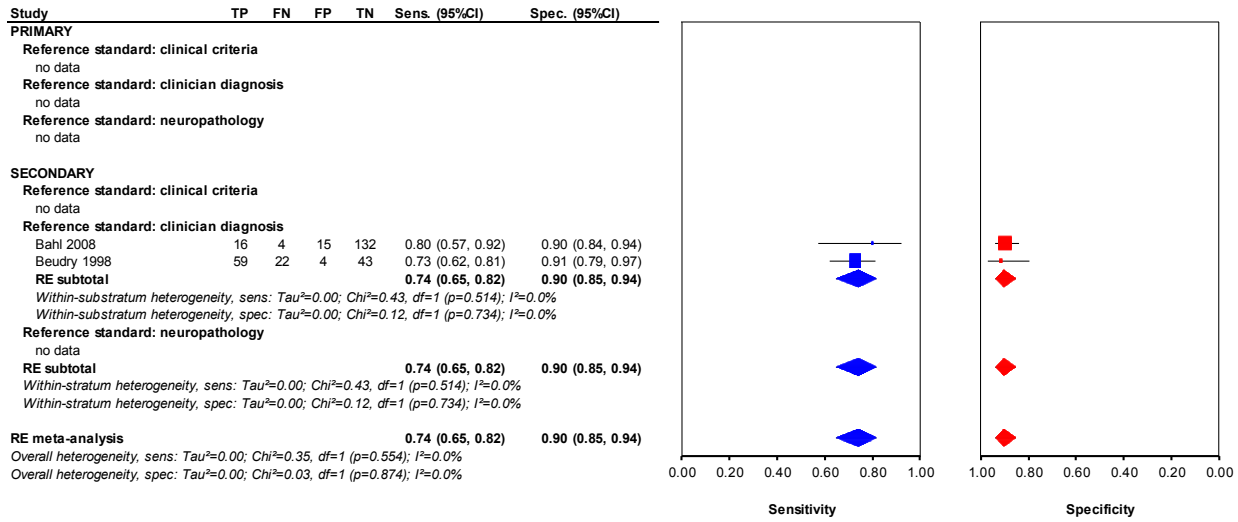


Figure 93CJD versus non-CJD: Neuron-specific enolase – forest plot: sensitivity and specificity

P.3.6.7 p-tau/total tau

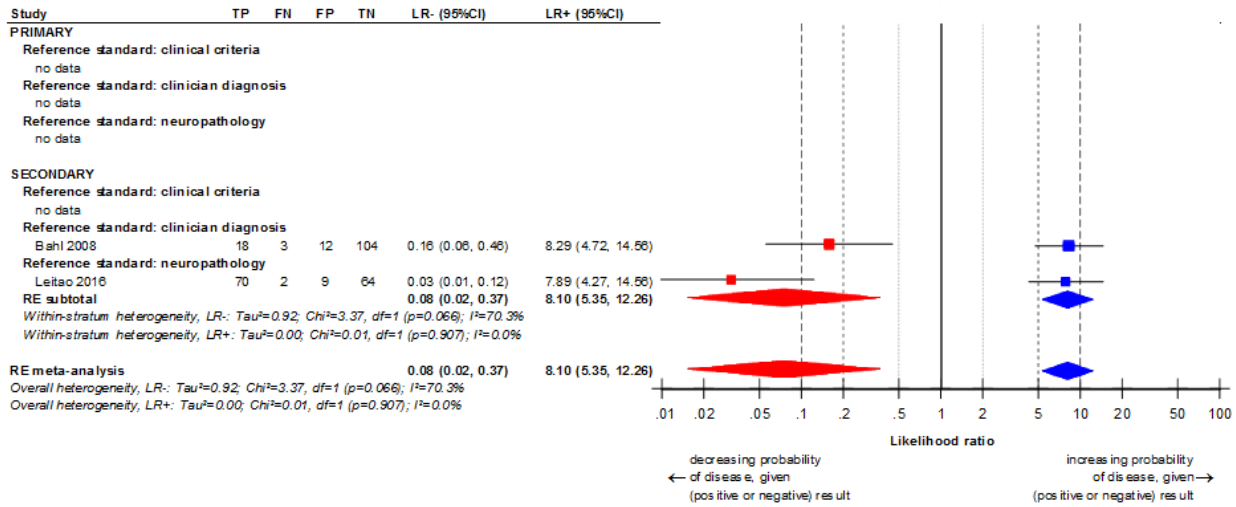


Figure 94CJD versus non-CJD: p-tau/total tau – forest plot: likelihood ratios

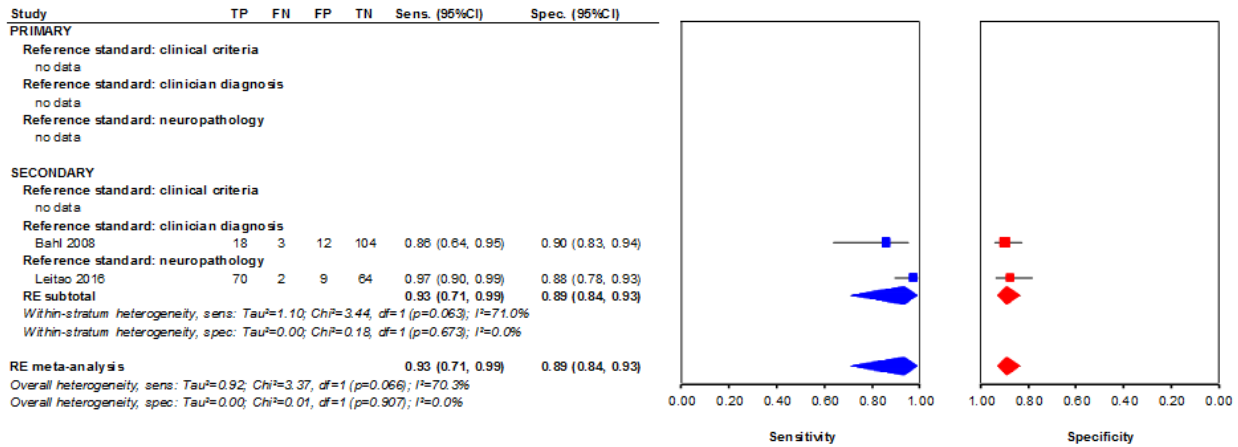


Figure 95CJD versus non-CJD: p-tau/total tau – forest plot: sensitivity and specificity

P.3.6.8 RT-QuIC

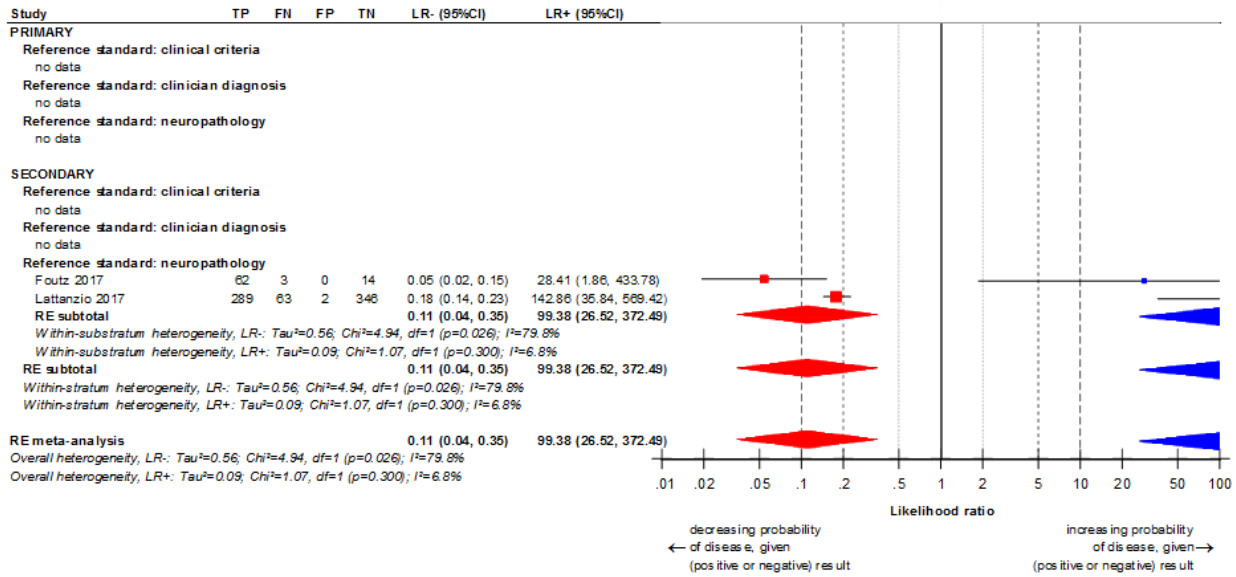


Figure 96CJD versus non-CJD: RT-QuIC – forest plot: likelihood ratios

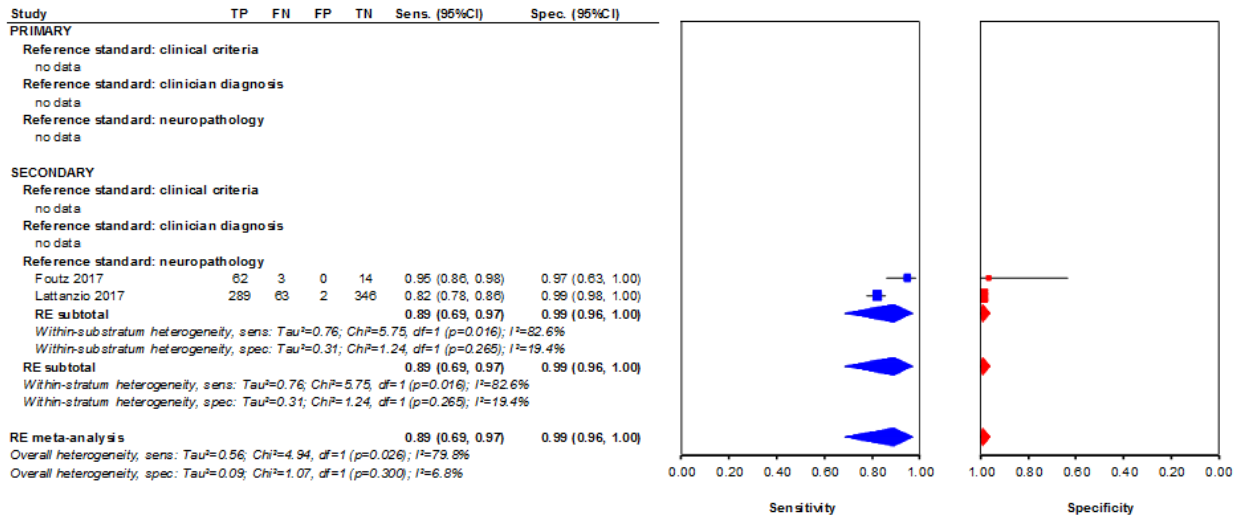


Figure 97CJD versus non-CJD: RT-QuIC – forest plot: sensitivity and specificity

P.3.6.9 S100B, 2.5ng/ml

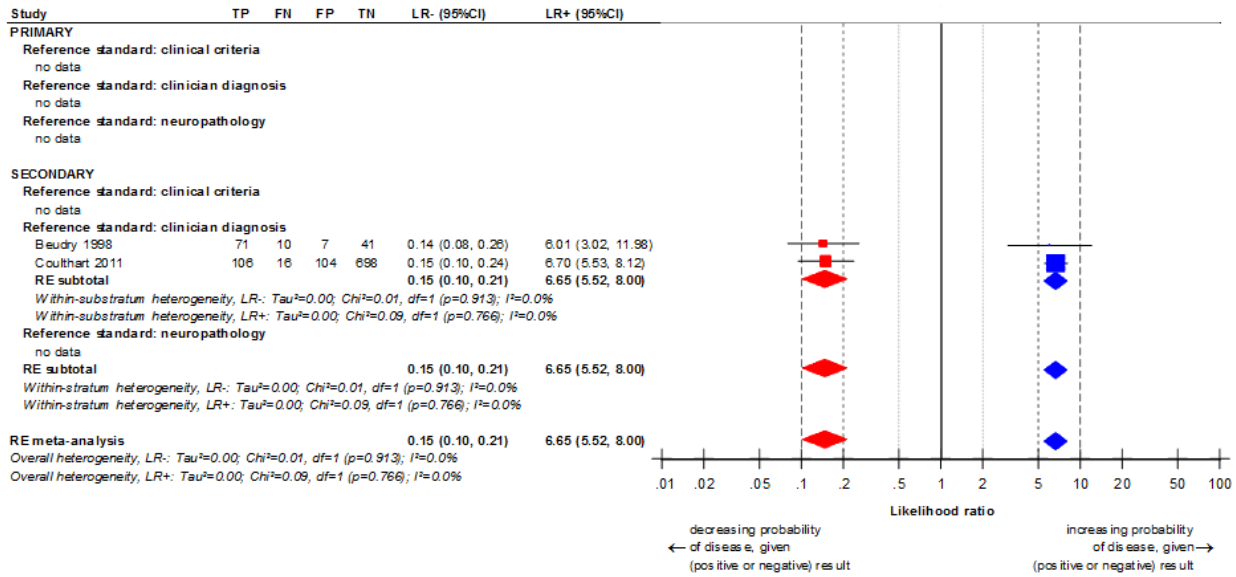


Figure 98CJD versus non-CJD: S100B, 2.5ng/ml – forest plot: likelihood ratios

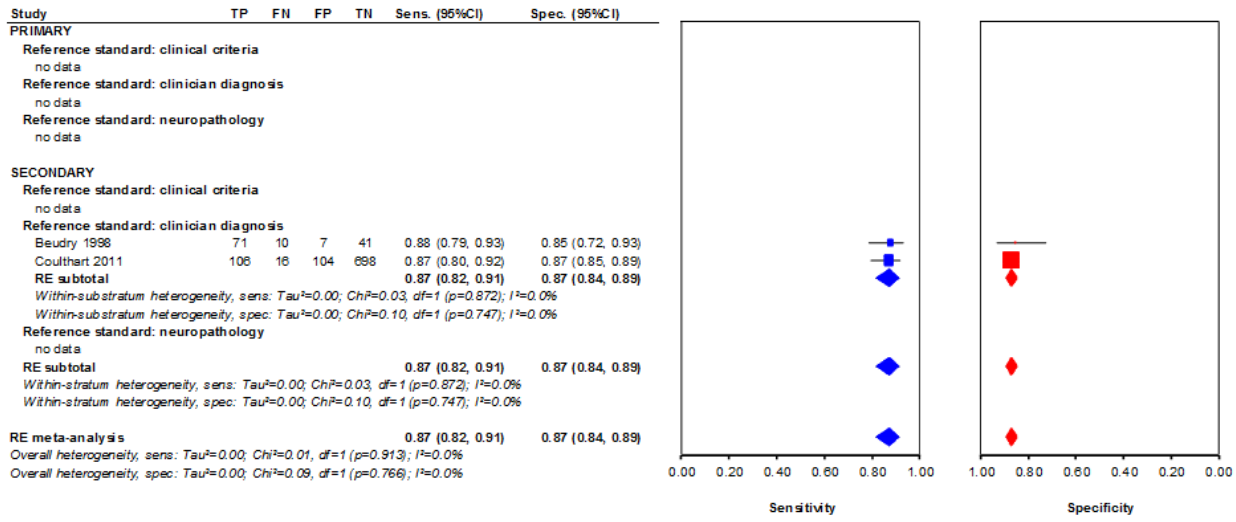


Figure 99CJD versus non-CJD: S100B, 2.5ng/ml – forest plot: sensitivity and specificity

P.3.6.10 Total Tau

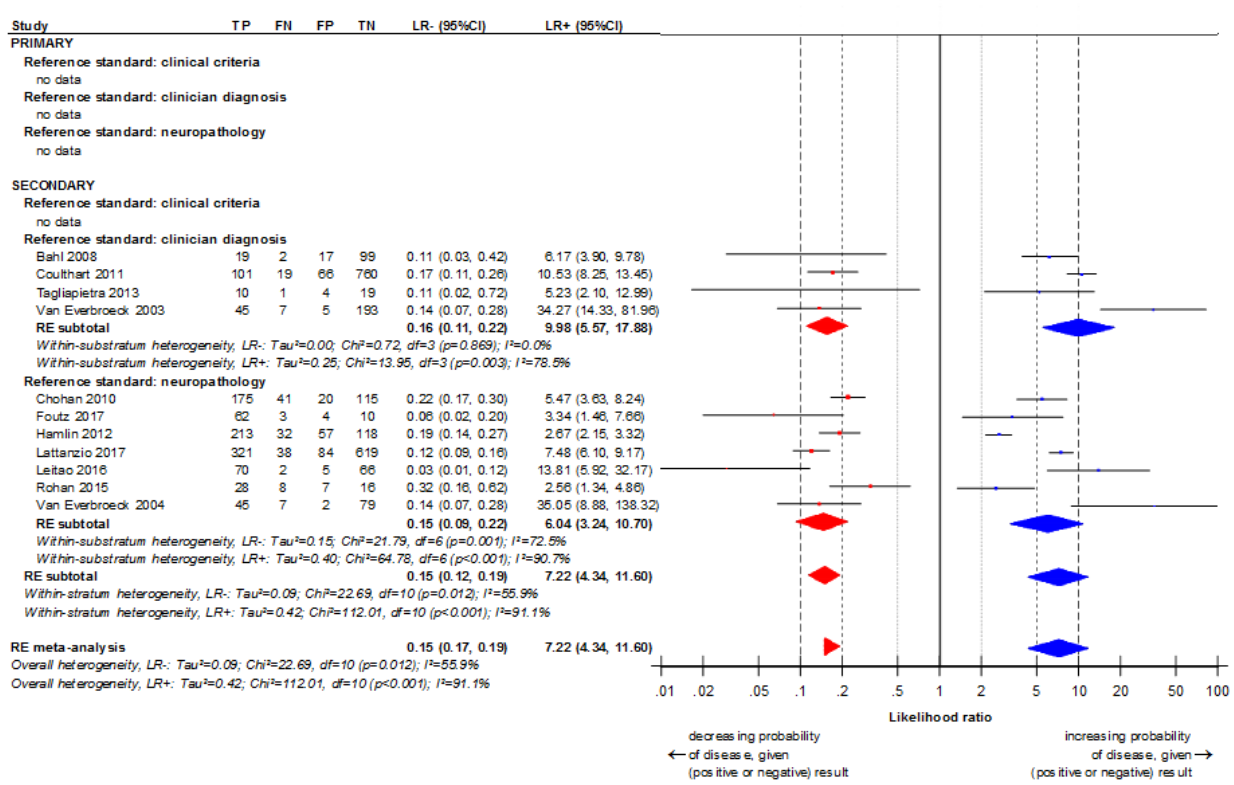


Figure 100 CJD versus non-CJD: Total Tau – forest plot: likelihood ratios

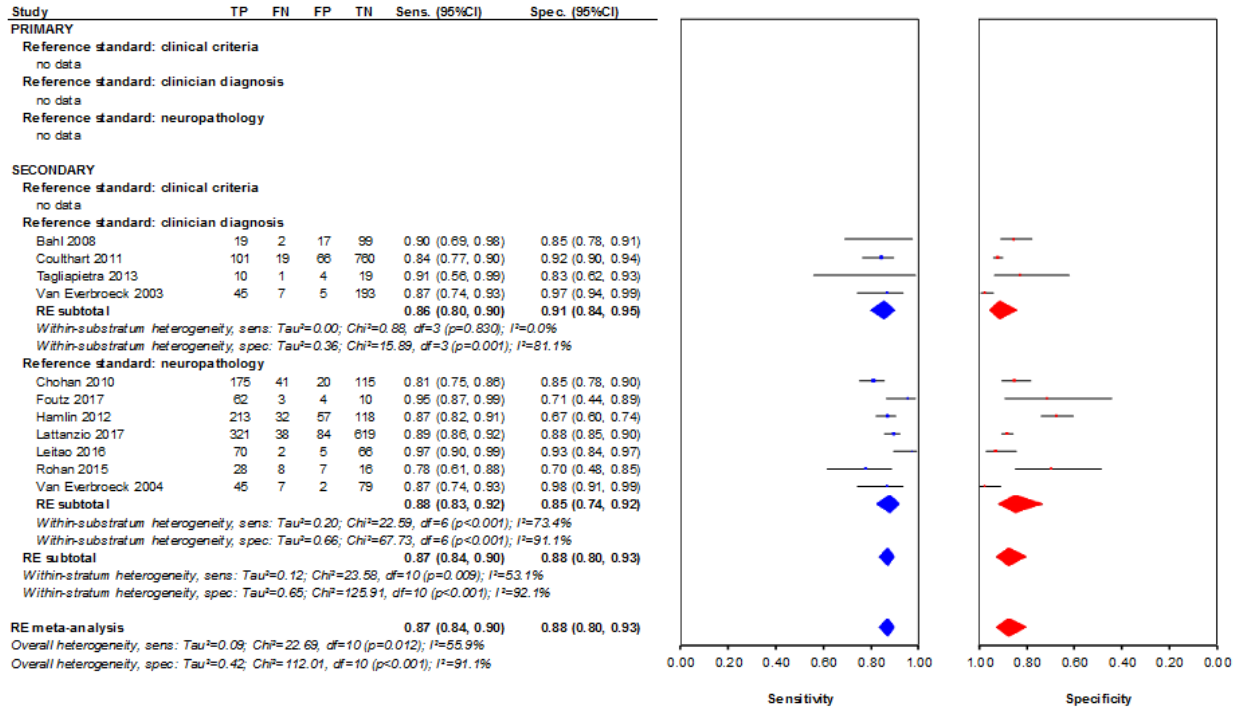


Figure 101 CJD versus non-CJD: Total Tau – forest plot: sensitivity and specificity

P.3.6.11 WHO CJD criteria

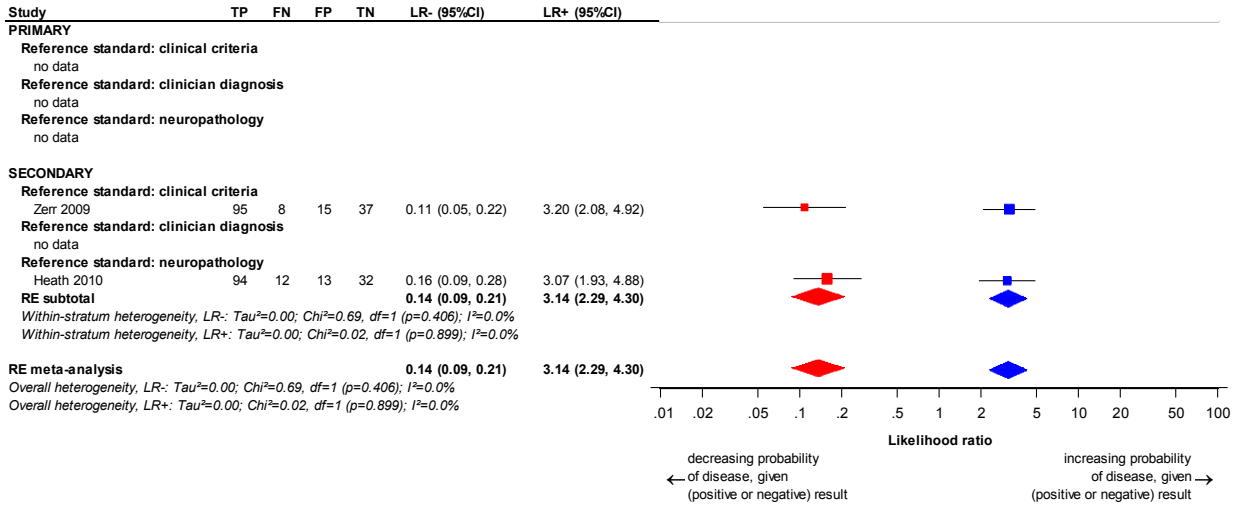


Figure 102 CJD versus non-CJD: WHO CJD criteria – forest plot: likelihood ratios

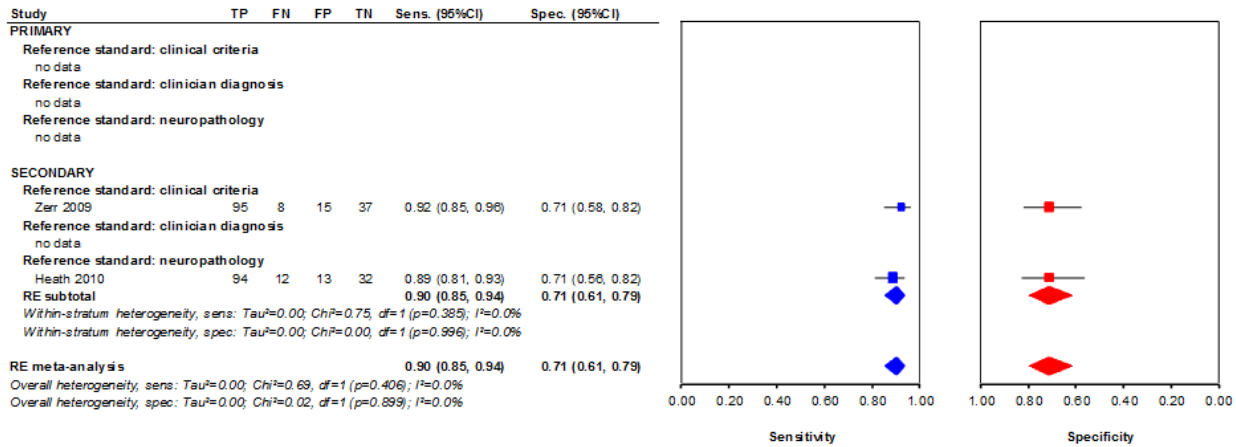


Figure 103 CJD versus non-CJD: WHO CJD criteria – forest plot: sensitivity and specificity

P.3.7 DLB versus non-DLB

P.3.7.1 123I-FP-CIT SPECT

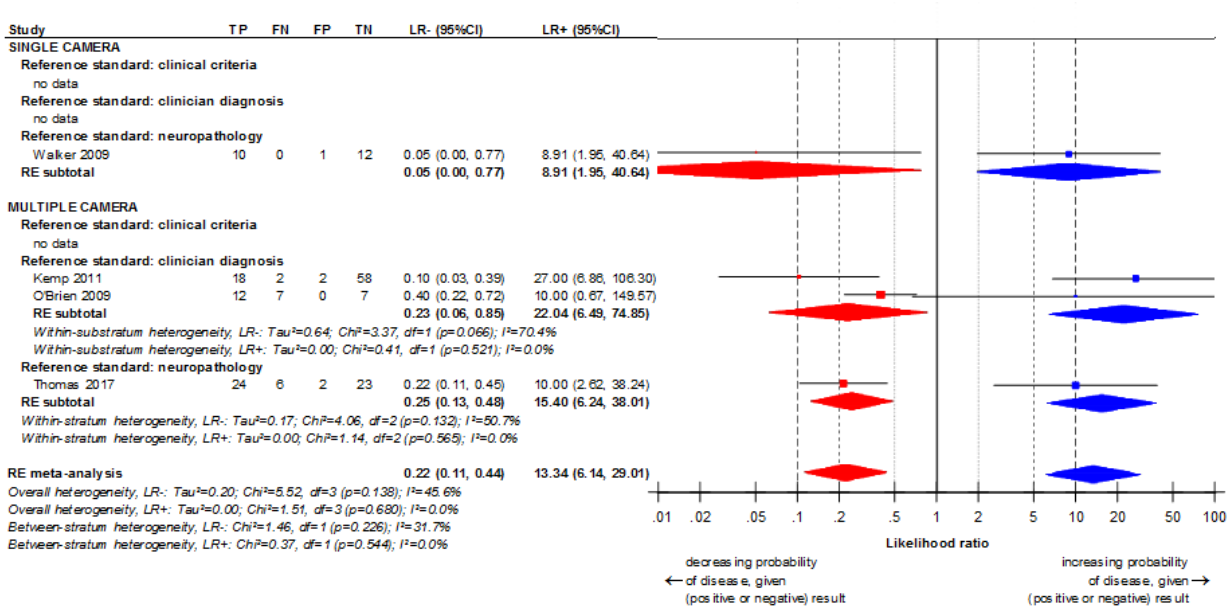


Figure 104 DLB versus non-DLB: 123I-FP-CIT SPECT – forest plot: likelihood ratios

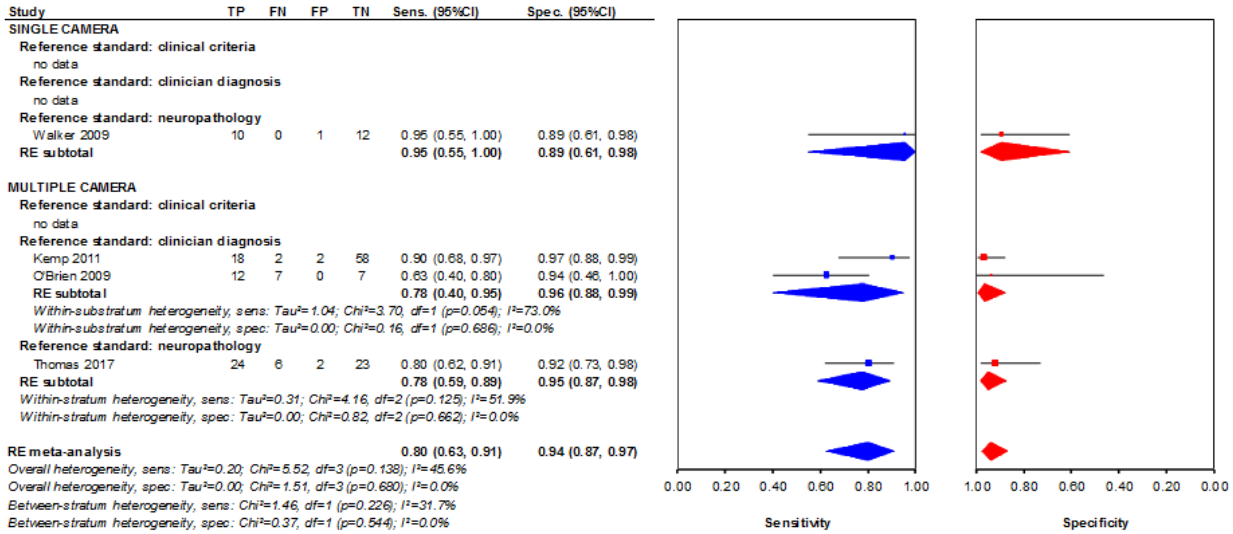


Figure 105 DLB versus non-DLB: 123I-FP-CIT SPECT – forest plot: sensitivity and specificity

P.3.7.2 123I-MIBG cardiac scintigraphy

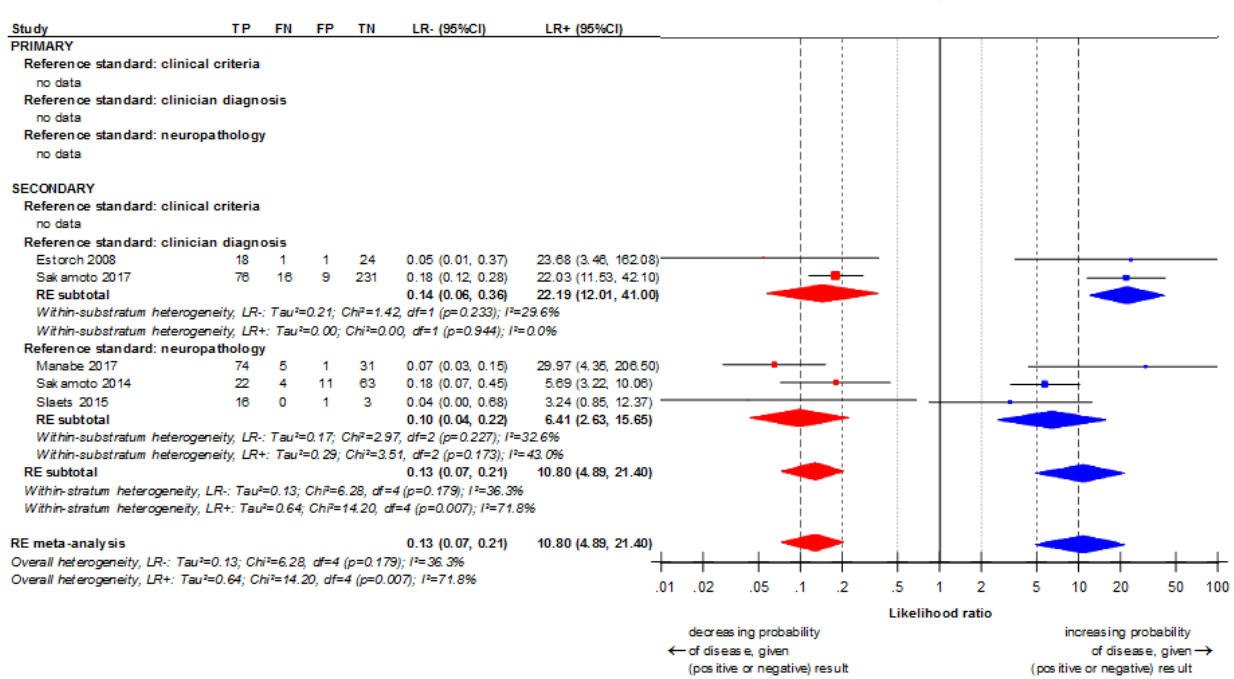


Figure 106 DLB versus non-DLB: 123I-MIBG cardiac scintigraphy – forest plot: likelihood ratios

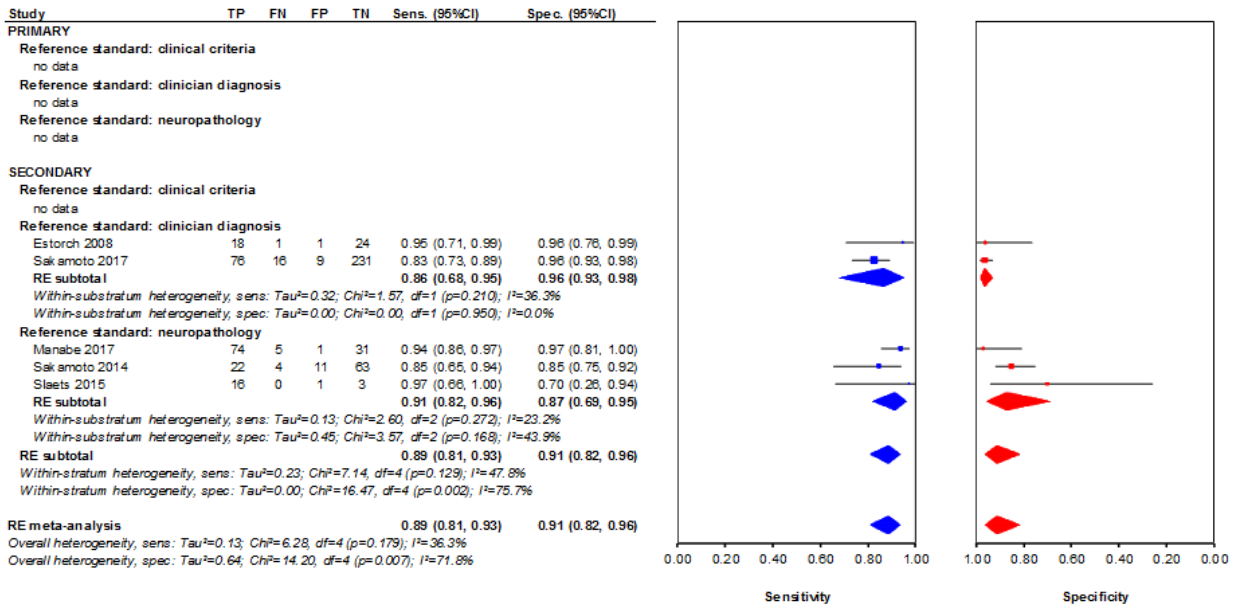


Figure 107 DLB versus non-DLB: 123I-MIBG cardiac scintigraphy – forest plot: sensitivity and specificity

P.3.7.3 FDG-PET

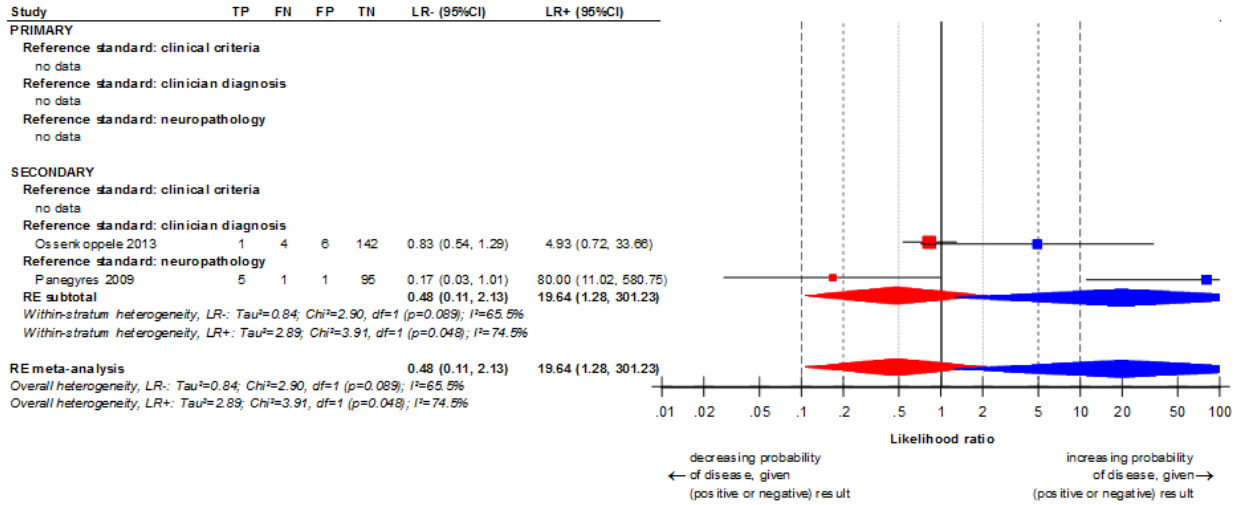


Figure 108 DLB versus non-DLB: FDG-PET – forest plot: likelihood ratios

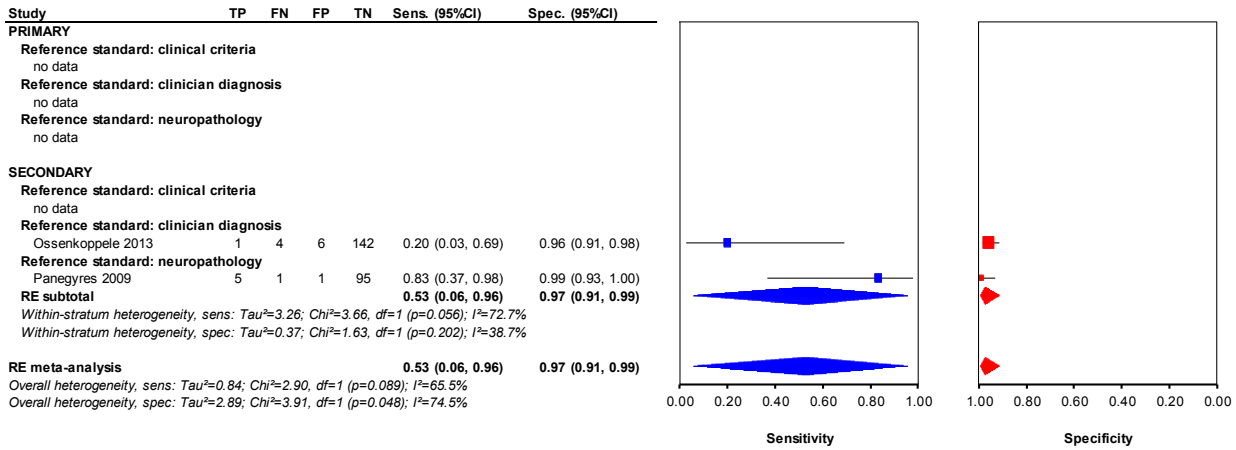


Figure 109 DLB versus non-DLB: FDG-PET – forest plot: sensitivity and specificity

P.3.8 DLB versus other dementias

P.3.8.1 123I-FP-CIT SPECT

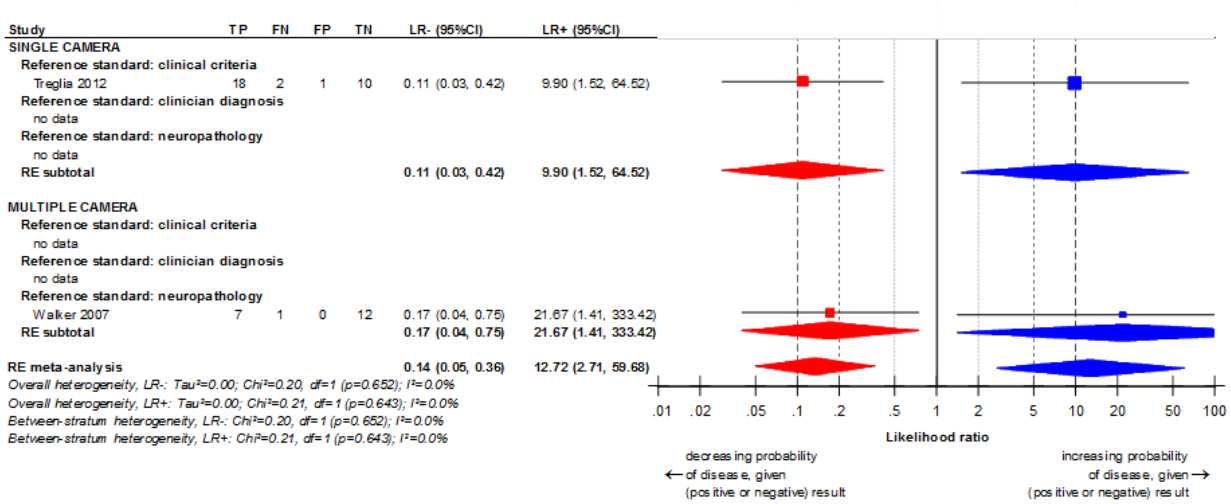


Figure 110 DLB versus other dementias: 123I-FP-CIT SPECT – forest plot: likelihood ratios

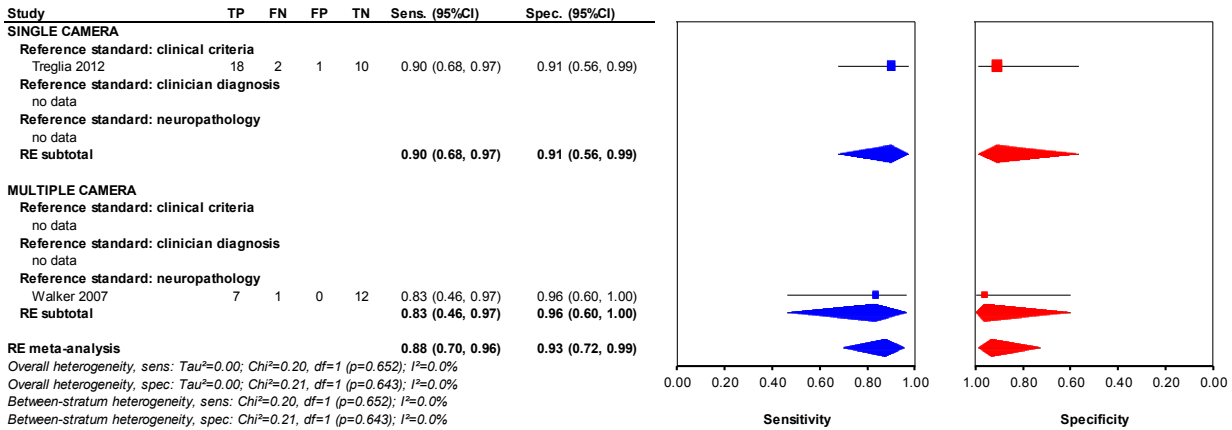


Figure 111 DLB versus other dementias: 123I-FP-CIT SPECT – forest plot: sensitivity and specificity

P.3.9 FTD versus AD

P.3.9.1 99mTc-HMPAO SPECT

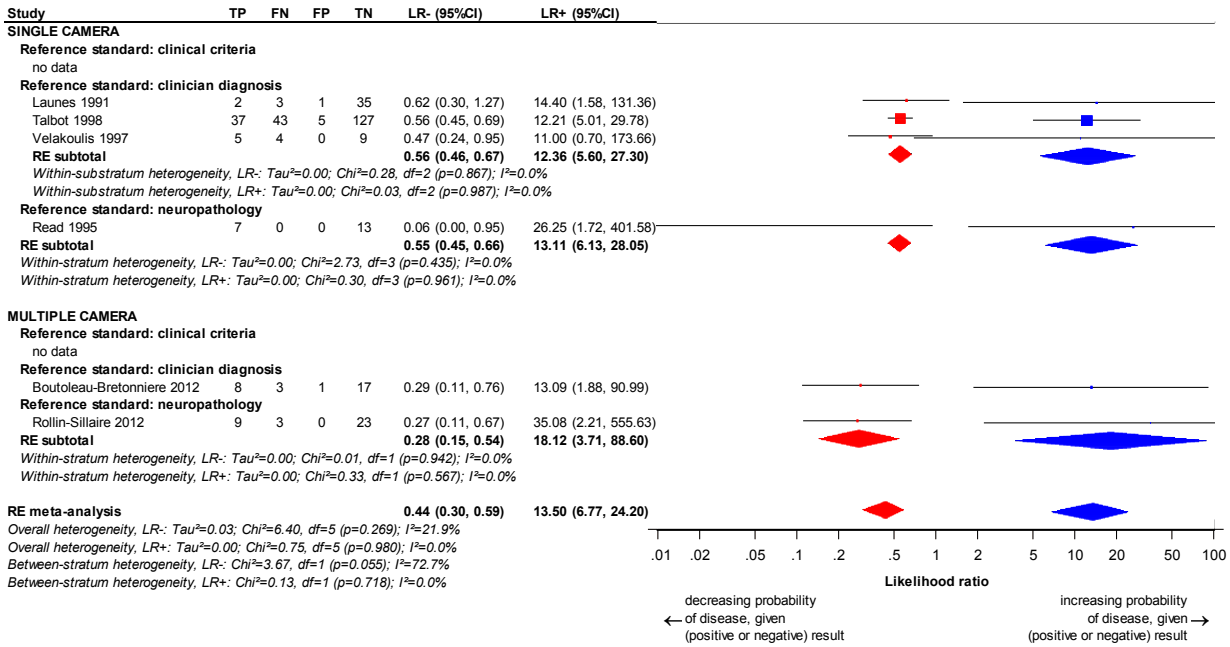


Figure 112 FTD versus AD: 99mTc-HMPAO SPECT – forest plot: likelihood ratios

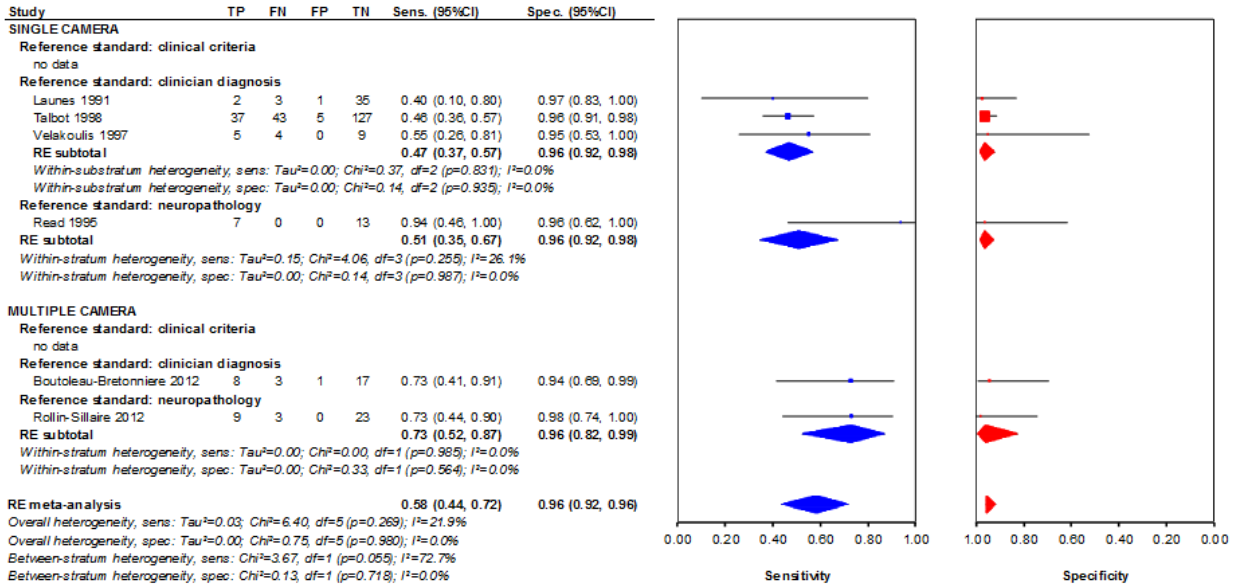


Figure 113 FTD versus AD: 99mTc-HMPAO SPECT – forest plot: sensitivity and specificity

P.3.10 FTD versus non-FTD

P.3.10.1 99mTc-HMPAO SPECT

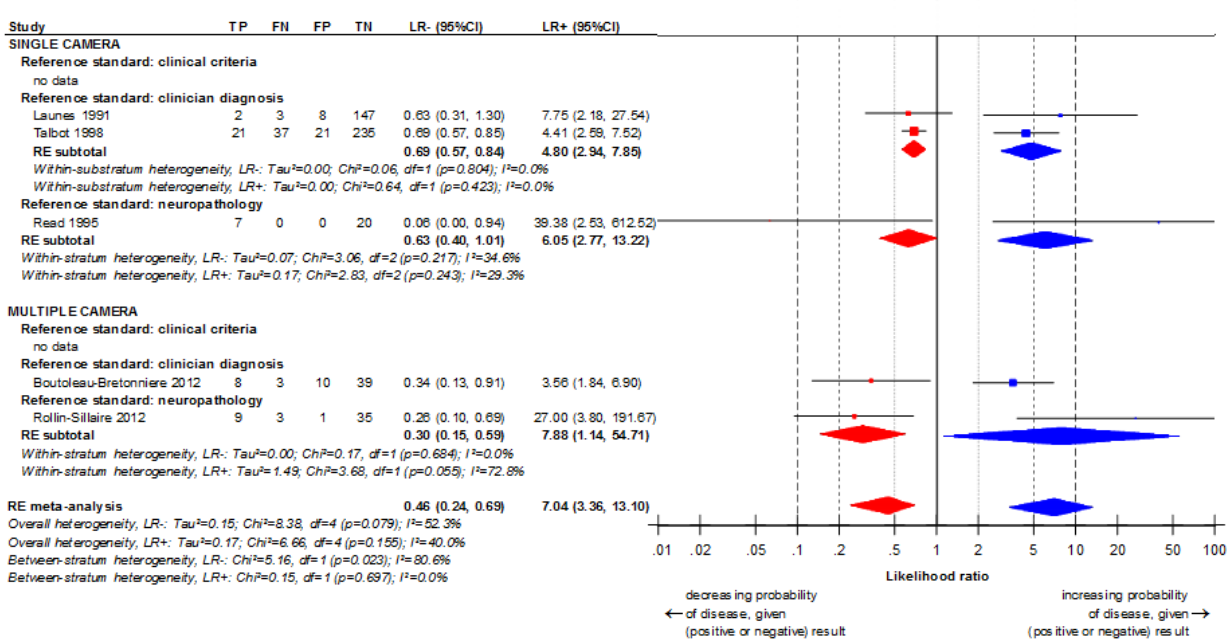


Figure 114 FTD versus non-FTD: 99mTc-HMPAO SPECT – forest plot: likelihood ratios

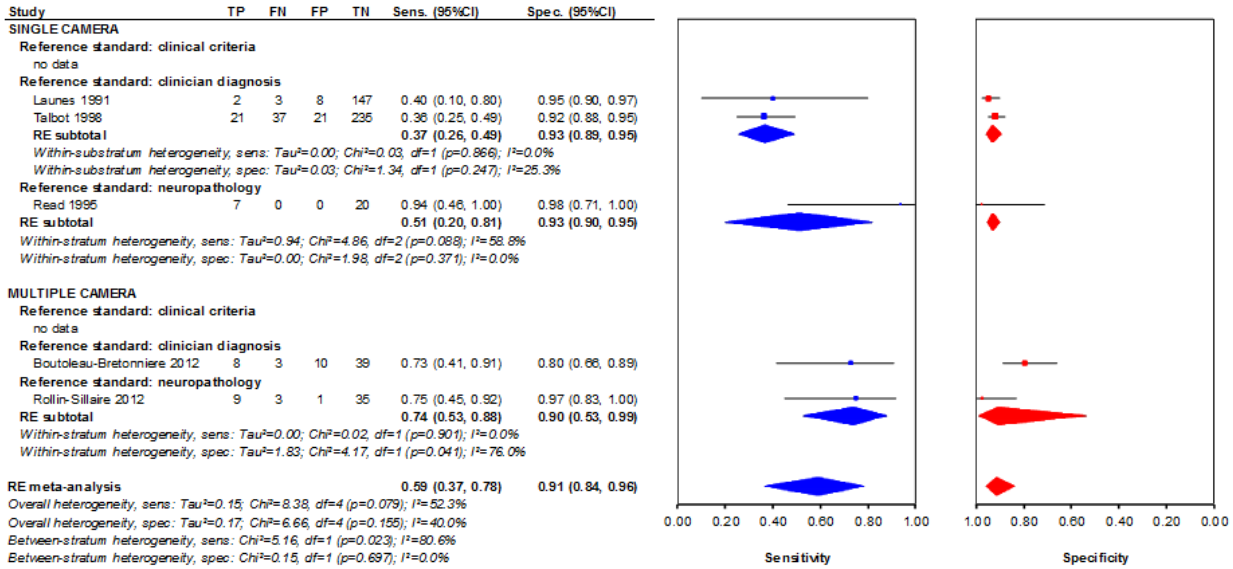


Figure 115 FTD versus non-FTD: 99mTc-HMPAO SPECT – forest plot: sensitivity and specificity

P.3.10.2 FDG-PET

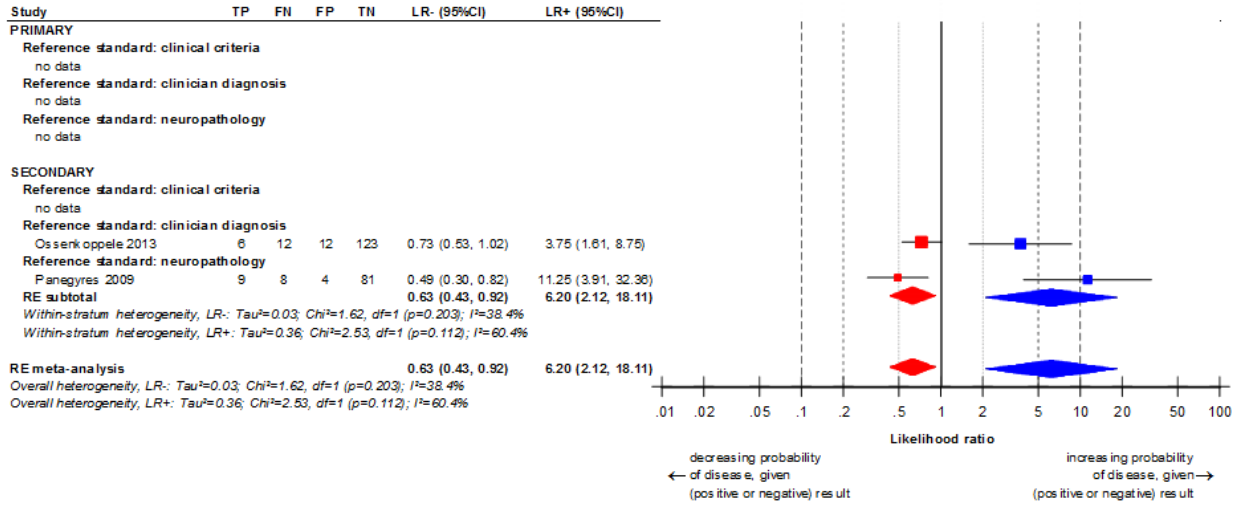


Figure 116 FTD versus non-FTD: FDG-PET – forest plot: likelihood ratios

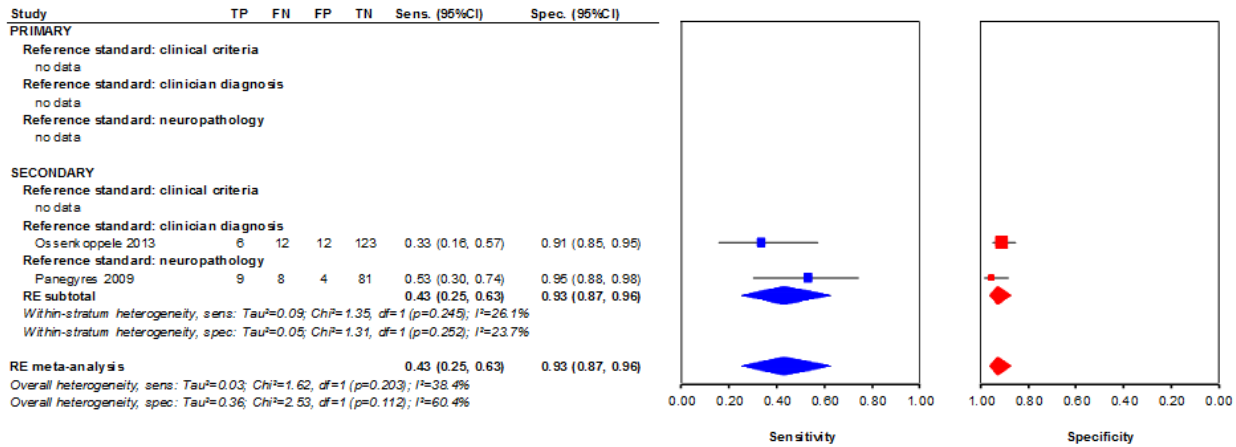


Figure 117 FTD versus non-FTD: FDG-PET – forest plot: sensitivity and specificity

P.3.10.3 MRI

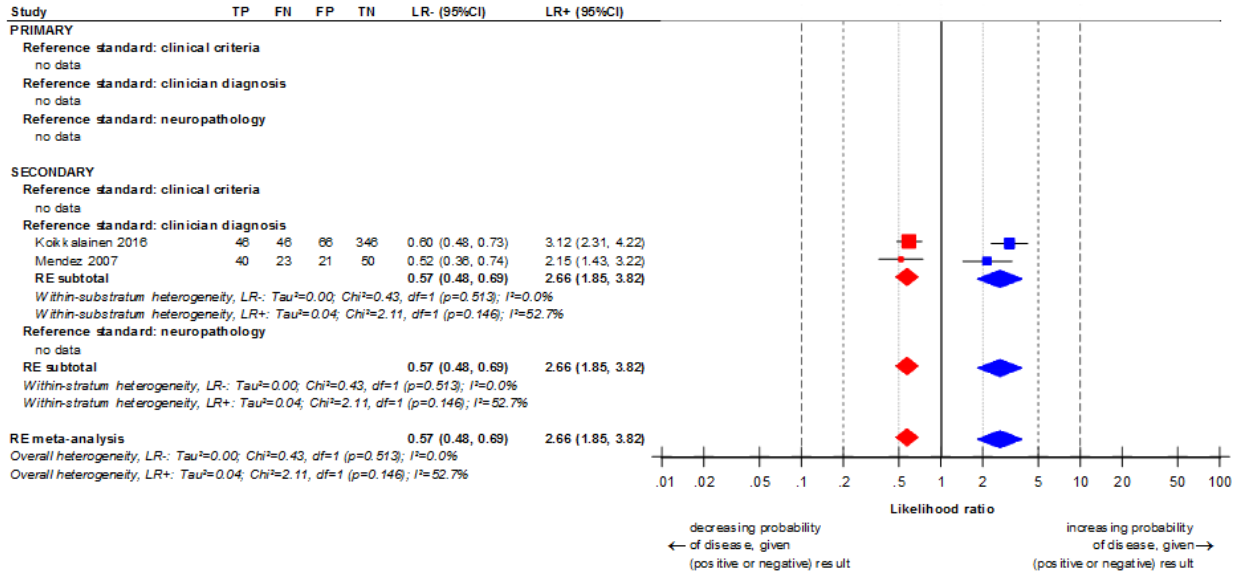


Figure 118 FTD versus non-FTD: MRI – forest plot: likelihood ratios

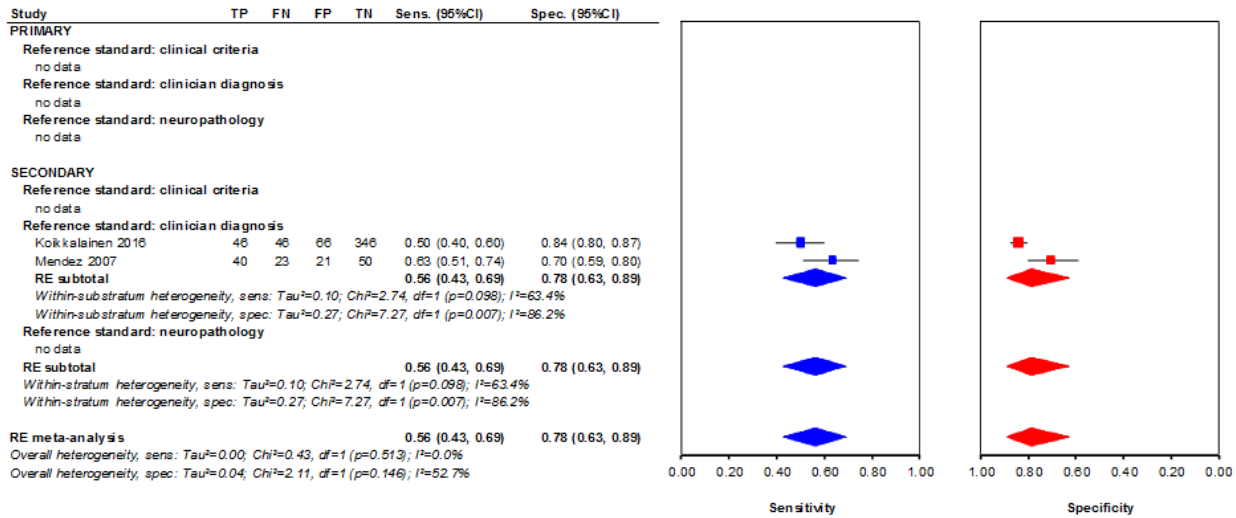


Figure 119 FTD versus non-FTD: MRI – forest plot: sensitivity and specificity

P.3.11 FTD versus other dementias

P.3.11.1 FDG-PET

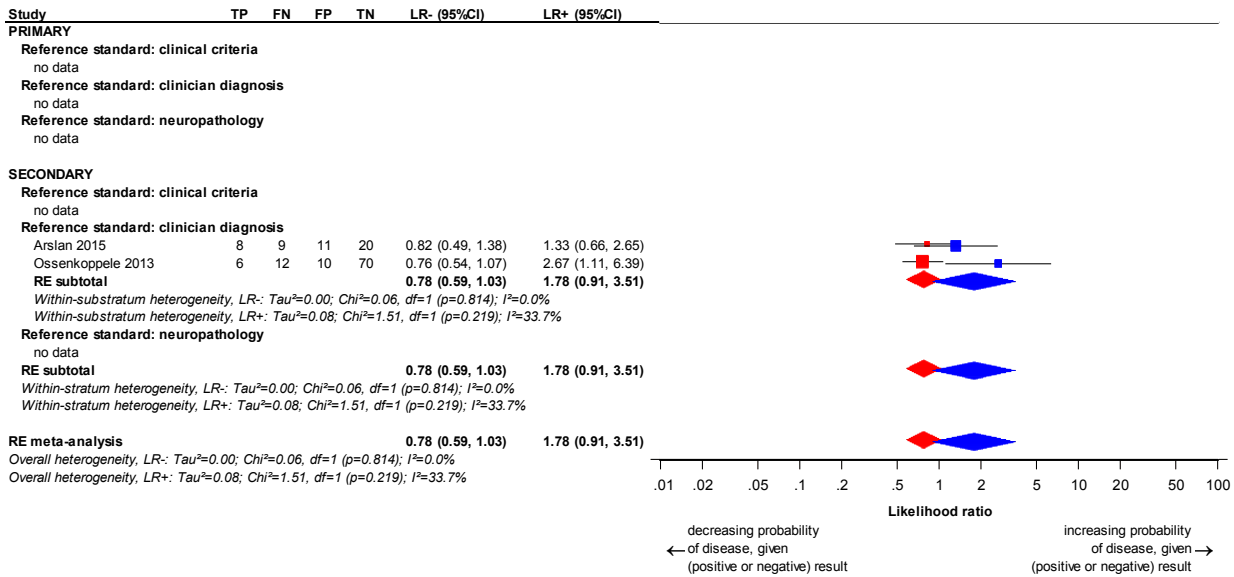


Figure 120 FTD versus other dementias: FDG-PET – forest plot: likelihood ratios

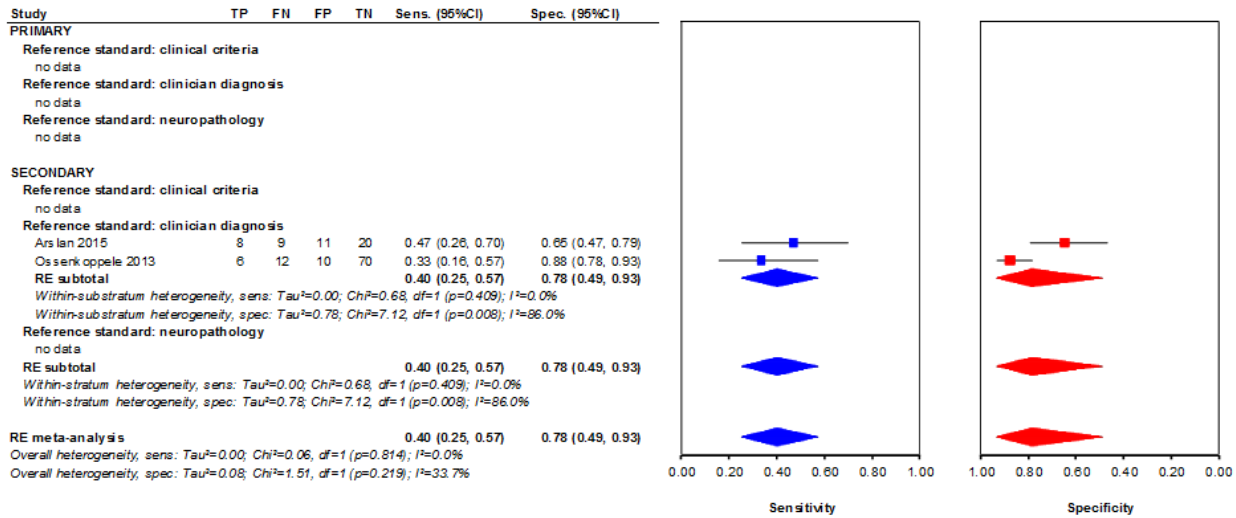


Figure 121 FTD versus other dementias: FDG-PET – forest plot: likelihood ratios

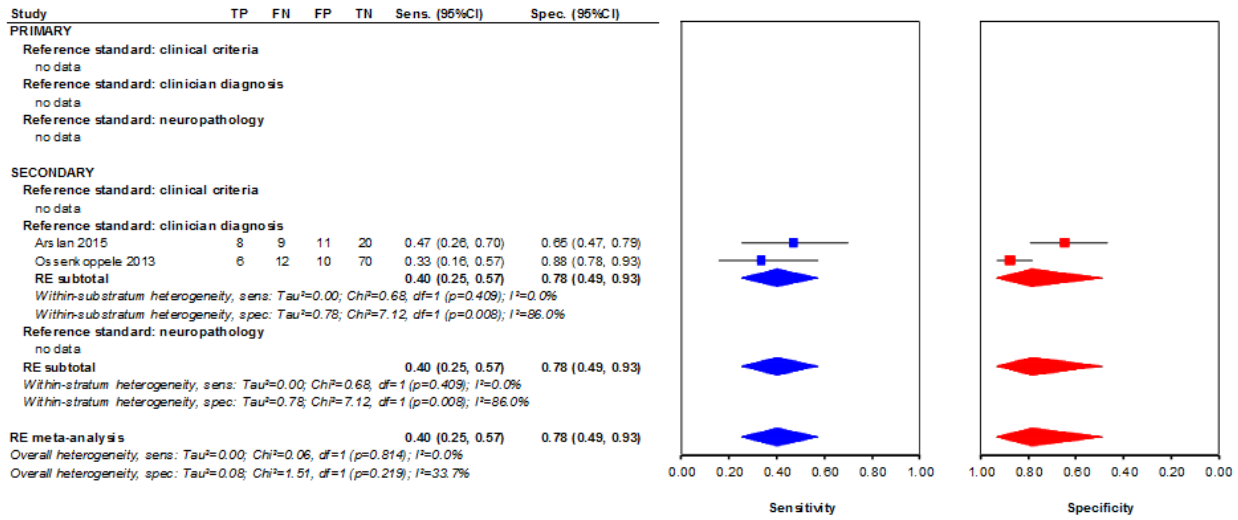


Figure 122 FTD versus other dementias: FDG-PET – forest plot: sensitivity and specificity

P.3.12 FTD versus VaD

P.3.12.1 99mTc-HMPAO SPECT

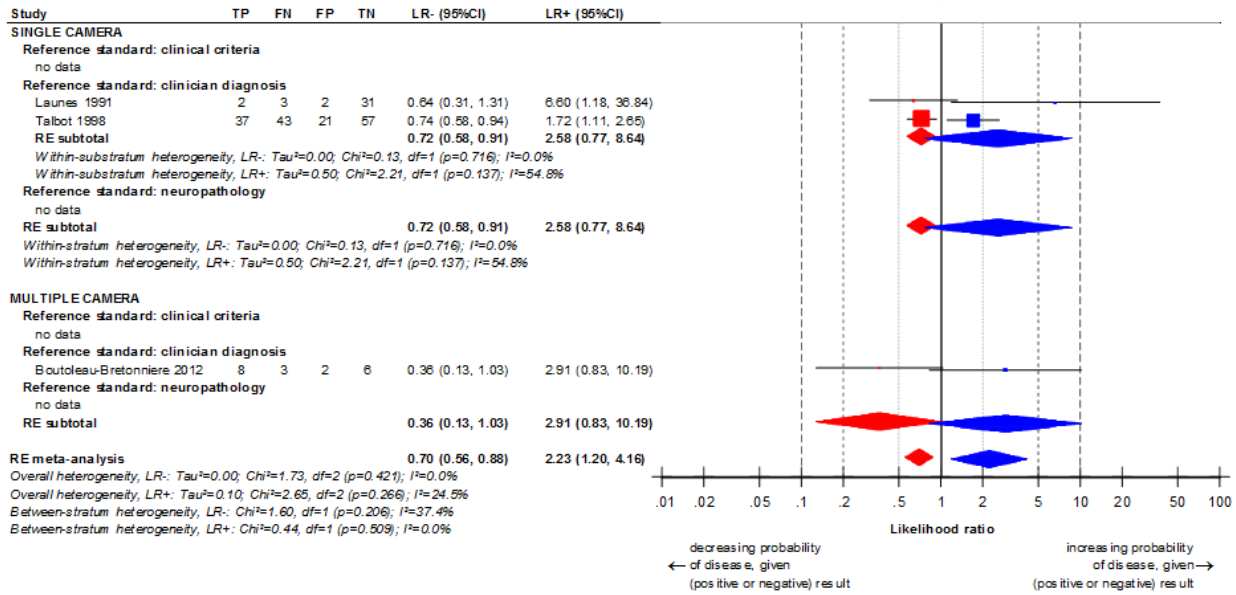


Figure 123 FTD versus VaD: 99mTc-HMPAO SPECT – forest plot: likelihood ratios

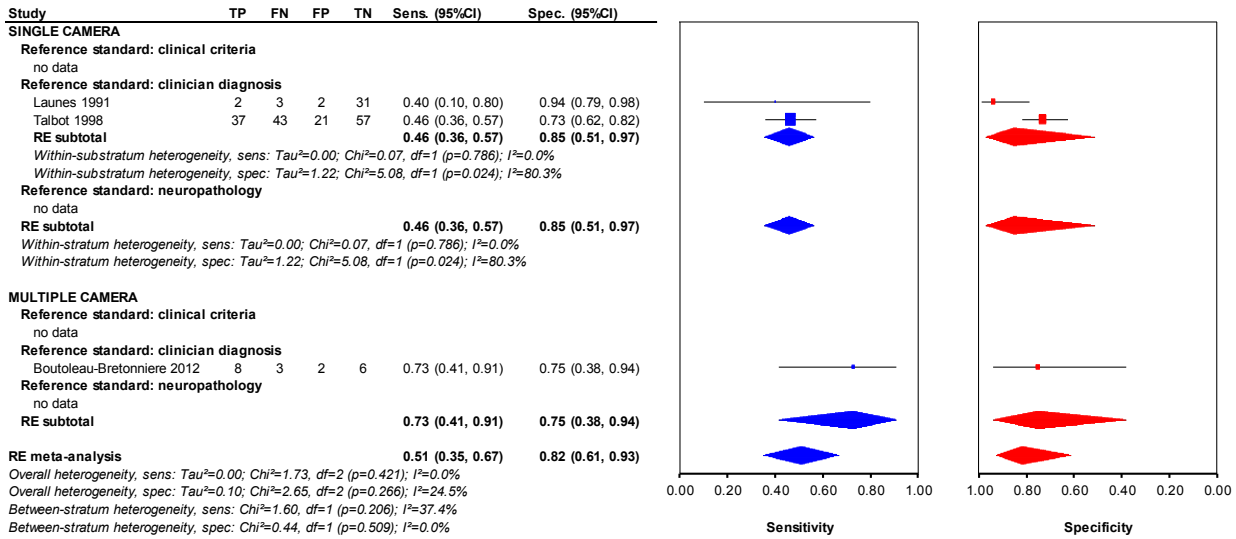


Figure 124 FTD versus VaD: 99mTc-HMPAO SPECT – forest plot: sensitivity and specificity

P.3.13 VaD versus AD

P.3.13.1 99mTc-HMPAO SPECT

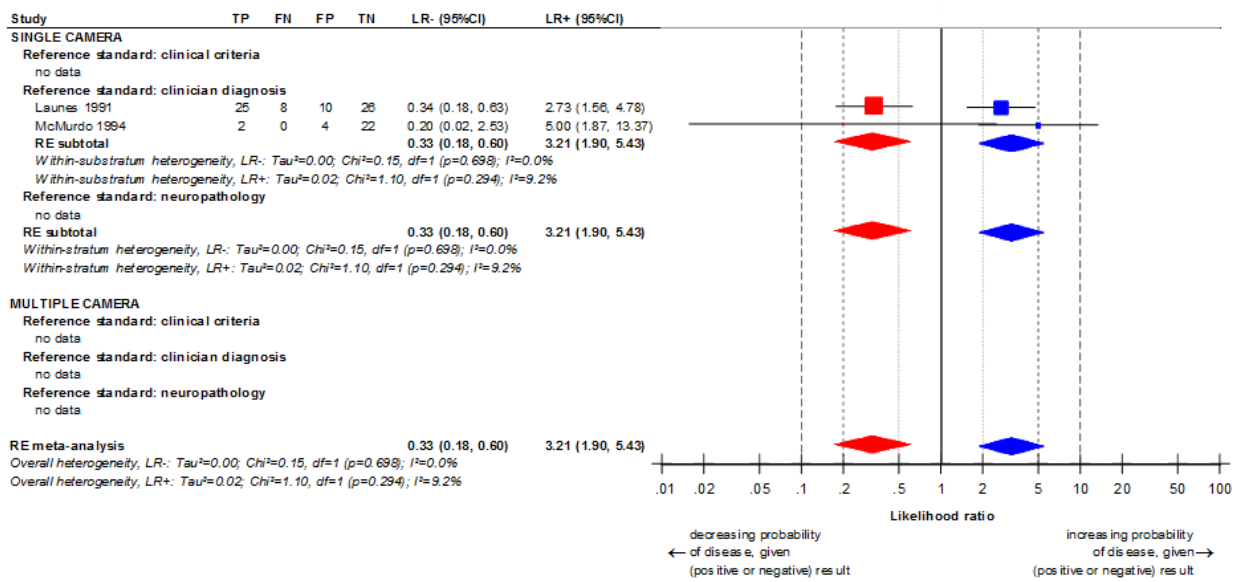


Figure 125 VaD versus AD: 99mTc-HMPAO SPECT – forest plot: likelihood ratios

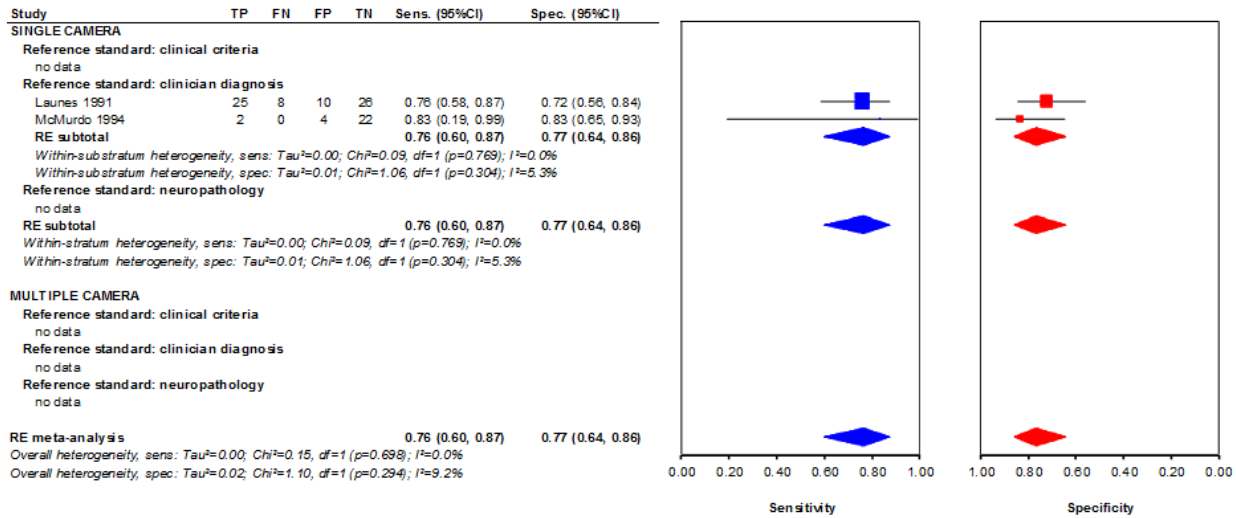


Figure 126 VaD versus AD: 99mTc-HMPAO SPECT – forest plot: sensitivity and specificity

P.3.14 VaD versus non-VaD

P.3.14.1 99mTc-HMPAO SPECT

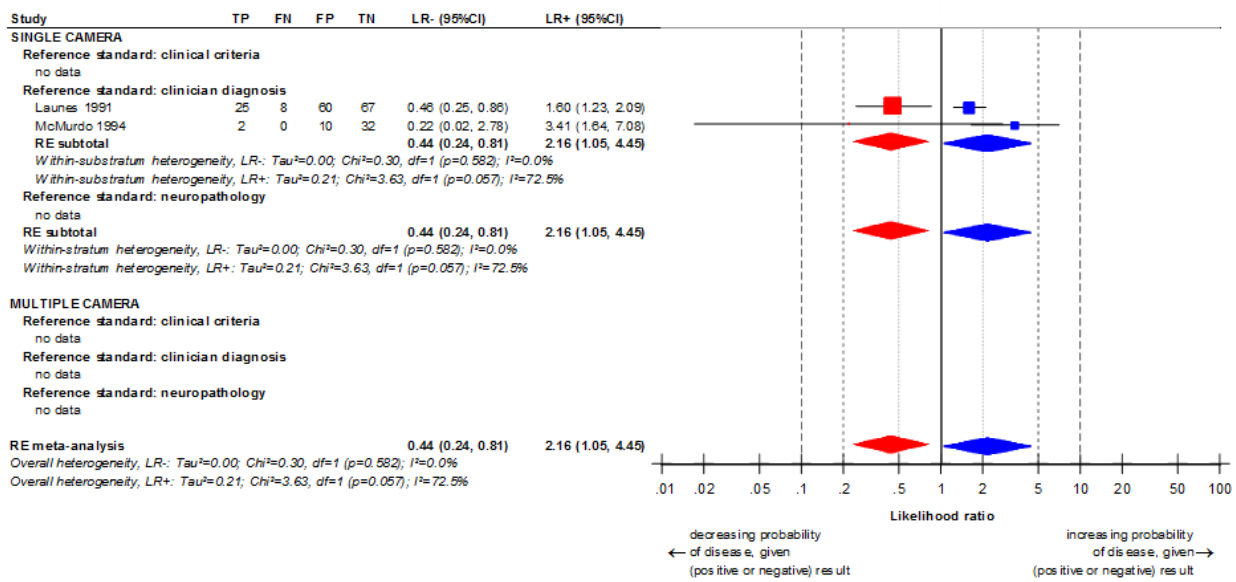


Figure 127 VaD versus non-VaD: 99mTc-HMPAO SPECT – forest plot: likelihood ratios

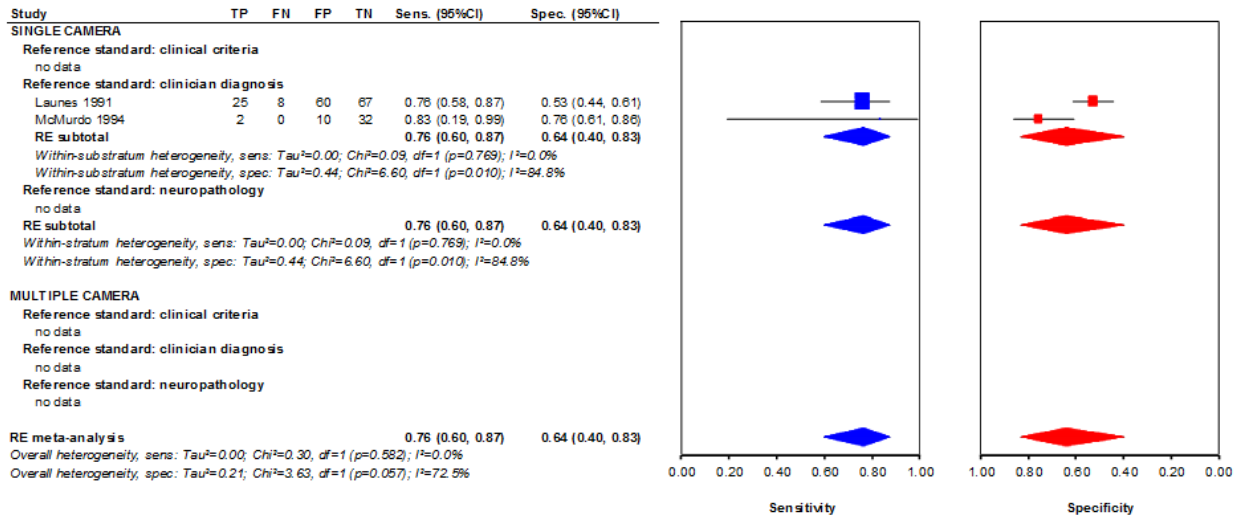


Figure 128 VaD versus non-VaD: 99mTc-HMPAO SPECT – forest plot: sensitivity and specificity