Appendix P:	Diagnosis
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# 2 **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?

# 7 P.1 Evidence tables

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

# 9 **P.1.1 A**

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Abdel-Aziz K, Larner Psychogeriatr 2015;	r AJ: Six-Item Cognitive Impairment Test (6CIT): pragmatic diagnostic accuracy study for dementia and MCI. Int 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 no	n-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	rall 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 Co	ognitive Impairmen	t Test (6CI1	Г) (>9)						
6-item Cognitive Impa	irment Test (6CIT) (	>9)							
Results	True positives:	42	False negatives:	6	False positives:	43	True negatives:	154	
Additional comme 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								

1

 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 Neurosurg Psychiatry 2014; 85: 923–927.

 Study type
 Retrospective cohort

Country UK

Alexander SK, Rittm degeneration. J Neu	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 po	ssible) versus CBD mimic (corticobasal syndrome, but not CBD pathology)							
Index Test: CBD con	isensus 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	Not stated								
Sex	Not stated	Not stated								
Age	Mean age 53.4 yea	rs (SD 13.1	)							
Presentation	Suspected CADAS	IL								
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 CA	DASIL-like syndror	nes								
Index Test: Skin bio	psy									
Skin biopsy, immunos	staining pattern typic	al for CADA	SIL							
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,Mintho markers for Alzheim	on L,Davidsson P,V er disease in clinic	anmechelei al practice.	n E,Van-derstichel ArchNeurol 2001;	e H,Winblad B, 58: 373–9.	et al. Evaluation of C	SF-tau and	CSF-Abeta 42 as d	iagnostic		

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

1

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	45.6% male								
Age	73.4 years (SD 7.1	73.4 years (SD 7.1)								
Presentation	Suspected dement	ia								
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 var	ying certainty (prot	bable and p	ossible AD pooled	) verus non- AD	) (VaD, LBD, MCI and	l non-deme	ntia groups pooled	).		
Index Test: Amyloid	Beta 1-42									
The Amyloid/P- Tau r	atio was calculated ι	using the for	mula Amyloid Beta	42/(240 + [1.18×	T-tau])					
Results	True positives:	106	False negatives:	57	False positives:	32	True negatives:	43		
Additional comme nts	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 var	ying certainty (prob	bable and p	ossible AD pooled	) versus VaD						
Index Test: Amyloid	Beta 1-42									
The Amyloid/P- Tau r	atio was calculated u	using the for	mula Amyloid Beta	42/(240 + [1.18×	T-tau])					
Results	True positives:	106	False negatives:	57	False positives:	12	True negatives:	11		
Additional comme nts	Data on people dia	gnosed with	other neurological	conditions exclue	ded from analysis as n	not in access	sible format. N=3 peo	ople.		
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 var	ying certainty (prob	able and p	ossible AD pooled	) versus LBD				
Index Test: Amyloid The Amyloid/P- Tau r	Beta 1-42 atio was calculated ι	ising the for	mula Amyloid Beta	42/(240 + [1.18×	T-tau])			
Results	True positives:	106	False negatives:	57	False positives:	3	True negatives:	6
Additional comme nts	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 r	non- AD (VaD, LBD,	MCI and no	on-dementia group	os pooled).				
Index Test: Amyloid	Beta 1-42							
The Amyloid/P- Tau r	atio was calculated u	ising the for	mula Amyloid Beta	42/(240 + [1.18×	T-tau])			
Results	True positives:	99	False negatives:	6	False positives:	32	True negatives:	43
Additional comme nts	Data on people dia	gnosed with	other neurological	conditions exclu	ded from analysis as n	ot in access	ible format. N=3 peo	ople.
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	Low

Andreasen N,Mintho markers for Alzheim	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 ra	atio was calculated ι	using the for	mula Amyloid Beta	42/(240 + [1.18×	T-tau])				
Results	True positives:	99	False negatives:	6	False positives:	12	True negatives:	11	
Additional comme nts	Data on people dia	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 The Amyloid/P- Tau ra	Beta 1-42 atio was calculated u	using the for	mula Amvloid Beta	42/(240 + [1.18×	T-taul)				
Results	True positives:	99	False negatives:	6	False positives:	3	True negatives:	6	
Additional comme nts	Data on people dia	gnosed with	other neurological	conditions exclu	ded from analysis as r	not in access	ible format. N=3 pe	ople.	
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	Low	
Overall risk of bias	Not serious								

Andreasen N,Mintho markers for Alzheim	on L,Davidsson P,V er disease in clinic	anmechelei al practice.	n E,Van-derstichel ArchNeurol 2001;	e H,Winblad B,e 58: 373–9.	et al. Evaluation of C	SF-tau and	CSF-Abeta 42 as d	iagnostic		
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 comme nts	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 Va	)									
Index Test: Amyloid The Amyloid/P- Tau ra	<b>Beta 1-42</b> atio was calculated ι	ising the for	mula Amyloid Beta 4	42/(240 + [1.18×	T-tau])					
Results	True positives:	7	False negatives:	51	False positives:	12	True negatives:	11		
Additional comme nts	Data on people dia	gnosed with	other neurological	conditions exclue	ded from analysis as r	ot in access	ible format. N=3 peo	ople.		
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 comme nts	Data on people dia	gnosed with	other neurological	conditions exclue	ded from analysis as r	not in access	ible format. N=3 peo	ople.
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)

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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 p	oatients wer	e selected to be $\geq 60$	0 years old and	had on average only 4	.7 years of s	chooling)			
Index Test: 10-point 10-point cognitive scree off $\leq$ 6.	Cognitive Screene eener (10-CS), a mo	<b>r (10-CS) (</b> ≤ dified versio	6) on of the six-item scr	reener (Brazilian	Portuguese language	). Points add	led for education eff	ects. Cut-		
Results	True positives:	86	False negatives:	20	False positives:	20	True negatives:	104		
Additional comme nts										
Risk of bias	Patient selection:	High	Index test:	High	Reference standard:	Low	Flow and timing:	Low		
Overall risk of bias	Serious (Optimised	l thresholds	were calculated and	d people with mo	derate to severe demo	entia were e	xcluded from the stu	ıdy.)		
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low				
Overall	Serious (Included p	patients wer	e selected to be $\geq 60$	0 years old and	had on average only 4	.7 years of s	chooling)			

# 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  $\leq$  7.

Results	True positives:	100	False negatives:	6	False positives:	50	True negatives:	74	
Additional comme nts									
Risk of bias	Patient selection:	High	Index test:	High	Reference standard:	Low	Flow and timing:	Low	
Overall risk of bias	Serious (Optimised	I thresholds	were calculated and	people with mo	derate to severe demo	entia were e	xcluded from the stu	ıdy.)	
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	<b>Cognitive Screene</b>	r (10-CS) (≤	8)						
10-point cognitive scr off $\leq 8$ .	eener (10-CS), a mo	dified versio	on of the six-item scr	eener (Brazilian	Portuguese language	). Points add	ded for education eff	ects. Cut-	
Results	True positives:	103	False negatives:	3	False positives:	74	True negatives:	50	
Additional comme nts									
Risk of bias	Patient selection:	High	Index test:	High	Reference standard:	Low	Flow and timing:	Low	
Overall risk of bias	Serious (Optimised	I thresholds	were calculated and	people with mo	derate to severe demo	entia were e	xcluded from the stu	ıdy.)	
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low			
Overall indirectness	Serious (Included p	patients were	e selected to be $\geq 60$	) years old and	had on average only 4	.7 years of s	schooling)		

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Arslan E, Ekmekciog using 3-dimensiona Sciences, 2016; 45:	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, 0.3cm-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 w avoided; the index the reference stand	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, 0.3cm-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							

# 1 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<br/>possible vascular determination in the oldest-old.Study typeRetrospective cohortCountrySwitzerlandDepartment of Geriatrics and Psychiatry at the University of Geneva School of MedicineInclusion criteriaDiagnosis of dementia and subsequent autopsy examination; > 90 years old; evaluated within 6 months of death (including<br/>complete neuropsychological, neurology and mental status assessments).Exclusion criteriaPatients with major neuropsychiatric illness, alcoholism or Parkinson's disease.Sex19.1% 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 assessed 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-A NINDS-AIREN criteria	IREN 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 (Participan	its were sele	ected to be >90 year	s old)						
Index Test: ADDTC of ADDTC criteria (State	c <b>riteria</b> of California Alzheir	mer's Diseas	se Diagnostic and T	reatment Centre	s criteria)					
Results	True positives:	21	False negatives:	15	False positives:	19	True negatives:	55		
Additional comme nts										
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 (Participan	its were sele	ected to be >90 year	s 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 comme nts										
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 (Participan	ts were sele	ected to be >90 year	s old)						

Bahl JM, Heegaard I Christiansen M. The Aging 2009; 30:1834	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)	I								
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 (Exclu	usion of pose	sible CJD group fror	n index tests ma	y inflate test sensitivity	y; test cut of	f not pre-specified)		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								
Index Test: p-tau/tota CSF P-tau/total tau of	al tau above 0.04 is CJD <sub>l</sub>	positive							
Results	True positives:	18	False negatives:	3	False positives:	12	True negatives:	104	
Additional comme nts									
Risk of bias	Patient selection:	High	Index test:	High	Reference standard:	Low	Flow and timing:	High	
Overall risk of bias	Very serious (Exclu	usion of pose	sible CJD group fror	n index tests ma	y inflate test sensitivity	y; test cut of	f not pre-specified)		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								
Index Test: Neuron-s	specific enolase								
CSF neuron-specific e	enolase (NSE) using	35ng/ml cut	t 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 comme nts									
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 ind	ex tests may infl	ate test sensitivity)				
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious	Not serious							
Index Test: CSF 14-3 CSF 14-3-3 protein	3-3 immunoblotting								
Results	True positives:	18	False negatives:	1	False positives:	33	True negatives:	117	
Additional comme nts									
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 ind	ex tests may infl	ate test sensitivity)				
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								

1

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 Breuch the Original to Detec	ker S, Van den Berg t Dementia in a Fre	ge M, Fery F ench-Speak	P, Pepersack T, Bie ing Population. De	er JC. The Adde	enbrooke's Cognitive ogn Disord 2012; 34:	Examinatio	on Revised Is as Ef	fective as				
Inclusion criteria	People examined a had an MMSE scor	at the memo e of ≥20/30.	ry clinic between No	ovember 2007 ar	nd October 2011 that h	nad been foll	owed at least 6 mor	iths and				
Exclusion criteria	People with cogniti encephalitis seque	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 yea	ars (SD 13.0	)									
Presentation	Suspected dement	ia										
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 no	t dementia (includii	ng MCI)										
Index Test: Addenbr Addenbrooke's Cogni	<b>ooke's Cognitive E</b> tive Examination Rev	xamination	-Revised, ACE-R ( R), French version,	<b>&lt;83)</b> 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-off	s used.)									
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low						
Overall indirectness	Not serious											
Index Test: MMSE (< MMSE, 24/30	:24)											
Results	True positives:	50	False negatives:	78	False positives:	4	True negatives:	188				
Additional comme nts												

Bastide L, De Breuch the Original to Detect	ker S, Van den Berç t Dementia in a Fre	ge M, Fery F ench-Speak	P, Pepersack T, Bie ing Population. De	er JC. The Adde ment Geriatr C	enbrooke's Cognitive ogn Disord 2012; 34:	Examinatio	on Revised Is as Ef	fective as		
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 (< MMSE 27/30	<27)									
Results	True positives:	103	False negatives:	25	False positives:	49	True negatives:	143		
Additional comme nts										
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	s used.)							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									

1

Beinhoff U, Hilbert \ Cognitive Disorders	/, Bittner D, Gron G and Riepe MW. Screening for cognitive impairment: a triage for out patient care. Dementia and Geriatric 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 Cognitive Disorders	, Bittner D, Gron G 2005; 20: 278–285.	and Riepe	MW. Screening for	cognitive impa	airment: a triage for o	out patient o	care. Dementia and	Geriatric			
Age	mean age 64.7 yea	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 Dr	awing Test, CDT, S	hulman sco	oring method (>0)								
Clock Drawing Test, C	DT, Shulman scorir	ng method w	ith maximum score	of 6. Cut off sco	re 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 Dr Clock Drawing Test, C	<b>awing Test, CDT, S</b> CDT, Shulman scorir	<b>hulman sco</b> ig method w	oring method (>1) ith maximum score	of 6. Cut off sco	re 2/6 (>1).						
Results	True positives:	47	False negatives:	19	False positives:	20	True negatives:	146			
Additional comme nts											
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low			
Overall risk of bias	Serious (Use of mureference tests were	Itiple non-pr e interprete	e-specified threshol d independently of e	lds; interval betw each other.)	veen tests was unclea	r and it was i	unclear whether the	index and			
Indirectness	Patient	Low	Index test:	Low	Reference	Low					

Beinhoff U, Hilbert V Cognitive Disorders	, Bittner D, Gron G 2005; 20: 278–285.	and Riepe	MW. Screening for	r cognitive impa	airment: a triage for o	out patient o	care. Dementia and	Geriatric
	selection:				standard:			
Overall indirectness	Not serious							
Index Test: Clock Dr	awing Test, CDT, S	Shulman sco	oring method (>2)					
Clock Drawing Test, C	CDT, Shulman scorir	ng method w	ith maximum score	of 6. Cut off sco	re 3/6 (>2).			
Results	True positives:	19	False negatives:	47	False positives:	4	True negatives:	162
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (Use of mu reference tests we	ultiple non-pr re interprete	re-specified thresho d independently of e	lds; interval betv each other.)	veen tests was unclear	and it was	unclear whether the	index and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Letter Sc	orting Test, LST (<3	5)						
LST (letter sorting test	t), < 3. The task is to	spell a 5-le	tter word forwards, I	backwards and i	n alphabetical order. C	)ne point pe	r correct answer.	
Results	True positives:	53	False negatives:	13	False positives:	52	True negatives:	114
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (Use of mureference tests were	ultiple non-pr re interprete	re-specified thresho d independently of e	lds; interval betv each other.)	veen tests was unclear	and it was	unclear whether the	index and
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 So	orting Test, LST (<2	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 comme nts										
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low		
Overall risk of bias	Serious (Use of mu reference tests we	ultiple non-pore interprete	re-specified thresho d independently of e	lds; interval betw each other.)	veen tests was unclea	r and it was	unclear whether the	index and		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									
Index Test: Letter So	orting Test, LST (<1	)								
LST (letter sorting tes	t), < 1. The task is to	spell a 5-le	tter word forwards,	backwards and i	n alphabetical order. C	One point pe	r correct answer.			
Results	True positives:	8	False negatives:	58	False positives:	2	True negatives:	164		
Additional comme nts										
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low		
Overall risk of bias	Serious (Use of mu reference tests we	ultiple non-pa re interprete	re-specified thresho d independently of e	lds; interval betw each other.)	veen tests was unclear	r and it was	unclear whether the	index and		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									
Index Test: Orientati	ion, OR (<8)									

Beinhoff U, Hilbert V Cognitive Disorders	, Bittner D, Gron G 2005; 20: 278–285.	and Riepe	MW. Screening for	<sup>·</sup> cognitive impa	airment: a triage for o	out patient o	care. Dementia and	Geriatric			
OR (Orientation), <8.	Eight questions abou	ut time, plac	e and situation withi	n about a minute	e. Score out of 8. Uses	s a subsection	on of the ADAS-Cog	test.			
Results	True positives:	43	False negatives:	23	False positives:	16	True negatives:	150			
Additional comme nts											
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low			
Overall risk of bias	Serious (Use of mu reference tests wer	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 (Orientation), <7.	i <b>on, OR (&lt;7)</b> Eight questions abou	ut time, plac	e and situation withi	n about a minute	e. Score out of 8. Uses	a subsectio	on of the ADAS-Cog	test.			
Results	True positives:	26	False negatives:	40	False positives:	2	True negatives:	164			
Additional comme nts											
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low			
Overall risk of bias	Serious (Use of murreference tests wer	iltiple non-pi e interprete	re-specified threshold independently of e	lds; interval betw each other.)	een tests was unclear	and it was	unclear whether the	index and			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										
Index Test: Memory MIS (Memory Impairm	Impairment Screen nent Screen), 8. Test	, <b>MIS (&lt;8)</b> is delayed fr	ee and cued recall o	of 4 items. Score	out of 12.						
Results	True positives:	65	False	1	False positives:	113	True negatives:	53			

Beinhoff U, Hilbert V Cognitive Disorders	, Bittner D, Gron G 2005; 20: 278–285.	and Riepe	MW. Screening for	r cognitive impa	airment: a triage for o	out patient o	care. Dementia and	Geriatric		
			negatives:							
Additional comme nts										
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low		
Overall risk of bias	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 MIS (Memory Impairm	Impairment Screen nent Screen), 7. Test	, <b>MIS (&lt;7)</b> is delayed fr	ee and cued recall	of 4 items. Score	e out of 12.					
Results	True positives:	61	False negatives:	5	False positives:	78	True negatives:	88		
Additional comme nts										
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low		
Overall risk of bias	Serious (Use of mureference tests were	Iltiple non-pr e interprete	re-specified thresho d independently of e	lds; interval betv each other.)	veen tests was unclear	r and it was	unclear whether the	index and		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									
Index Test: Memory	Impairment Screen	, MIS (<6)								
MIS (Memory Impairm	nent Screen), 6. Test	s delayed fr	ee and cued recall	of 4 items. Score	e 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 mureference tests were	ultiple non-pr re interprete	re-specified threshold independently of e	lds; interval betw each other.)	veen tests was unclear	r and it was	unclear whether the	index and			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										
Index Test: Memory MIS (Memory Impairm	Impairment Screen nent Screen), 5. Test	n, <b>MIS (&lt;5)</b> ts delayed fr	ee and cued recall o	of 4 items. Score	e out of 12.						
Results	True positives:	54	False negatives:	12	False positives:	31	True negatives:	135			
Additional comme nts											
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low			
Overall risk of bias	Serious (Use of mureference tests were	ultiple non-pr re interprete	re-specified threshold independently of e	lds; interval betw each other.)	veen tests was unclear	r and it was	unclear whether the	index and			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										
Index Test: Boston M	Naming Test, BNT (	<15)									
Boston Naming Test,	15. Tests ability to n	ame 15 line	drawings. Score ou	t of 15.							
Results	True positives:	47	False negatives:	19	False positives:	62	True negatives:	104			
Additional comme nts											
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 mureference tests were	ultiple non-pure interprete	re-specified threshol d independently of e	lds; interval betv each other.)	ween tests was unclear	r and it was	unclear whether the	index and		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									
Index Test: Boston N	Naming Test, BNT (	<14)								
Boston Naming Test,	14. Tests ability to n	ame 15 line	drawings. Score ou	t of 15.						
Results	True positives:	36	False negatives:	30	False positives:	27	True negatives:	139		
Additional comme nts										
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low		
Overall risk of bias	Serious (Use of mu reference tests wer	ultiple non-pr re interprete	re-specified threshol d independently of e	lds; interval betv each other.)	ween tests was unclear	r and it was	unclear whether the	index and		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									
Index Test: Boston I Boston Naming Test,	Naming Test, BNT ( 13. Tests ability to n	<b>&lt;13)</b> ame 15 line	drawings. Score ou	t of 15.						
Results	True positives:	26	False negatives:	40	False positives:	11	True negatives:	155		
Additional comme nts										
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low		
Overall risk of bias	Serious (Use of mu	ultiple non-pr	re-specified threshol	lds; interval betv	ween tests was unclear	r 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 comme nts										
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low		
Overall risk of bias	Serious (Use of mureference tests were	ultiple non-pr re interprete	e-specified thresho	lds; interval betw each other.)	veen tests was unclea	r and it was	unclear whether the	index and		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									
Index Test: Verbal ca Verbal category fluent was 60 secs.	ategory fluency (an cy, <23. Tests ability	i <b>mal namin</b> y to generate	<b>g), VF (&lt;23)</b> e as many category	names in given	time. In this case the o	category was	s animals and time d	uration		
Results	True positives:	64	False negatives:	2	False positives:	102	True negatives:	64		
Additional comme nts										
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low		
Overall risk of bias	Serious (Use of mu	ultiple non-pr	e-specified thresho	lds; interval betw	veen tests was unclea	r and it was	unclear whether the	index and		

Beinhoff U, Hilbert V Cognitive Disorders	, Bittner D, Gron G 2005; 20: 278–285.	and Riepe	MW. Screening for	r cognitive impa	airment: a triage for o	out patient o	care. Dementia and	Geriatric	
	reference tests we	re interprete	d independently of e	each other.)					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								
Index Test: Verbal ca Verbal category fluend was 60 secs.	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 comme nts									
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low	
Overall risk of bias	Serious (Use of mureference tests were	ultiple non-pr re interprete	e-specified thresho	lds; interval betv each other.)	veen tests was unclea	r and it was	unclear whether the	index and	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								
Index Test: Verbal ca Verbal category fluent was 60 secs.	ategory fluency (an cy, <21. Tests ability	<b>imal namin</b> y to generate	g), VF (<21) e as many category	names in given	time. In this case the o	category was	s animals and time d	uration	
Results	True positives:	62	False negatives:	4	False positives:	79	True negatives:	87	
Additional comme nts									
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low	
Overall risk of bias	Serious (Use of mu	ultiple non-pr	e-specified thresho	lds; interval betv	veen tests was unclea	r and it was	unclear whether the	index and	

Beinhoff U, Hilbert V Cognitive Disorders	, Bittner D, Gron G 2005; 20: 278–285.	and Riepe	MW. Screening for	cognitive imp	airment: a triage for o	out patient o	care. Dementia and	Geriatric
	reference tests we	e interprete	d independently of e	each other.)				
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Verbal c	ategory fluency (an	imal namin	g), VF (<20)					
Verbal category fluent was 60 secs.	cy, <20. Tests ability	y to generate	e as many category	names in given	time. In this case the c	category was	s animals and time d	luration
Results	True positives:	62	False negatives:	4	False positives:	70	True negatives:	96
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (Use of mureference tests we	Iltiple non-pi	re-specified threshold independently of e	lds; interval betv each other.)	veen tests was unclear	r and it was	unclear whether the	index and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: <b>Verbal ca</b> Verbal category fluent was 60 secs.	tegory fluency (ani cy, <19. Tests ability	<b>mal naming</b> / to generate	<b>g), VF (&lt;19)</b> e as many category	names in given	time. In this case the o	category was	s animals and time d	luration
Results	True positives:	56	False negatives:	10	False positives:	61	True negatives:	105
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (Use of mu	Iltiple non-pi	re-specified threshol	lds; interval betv	veen tests was unclear	r and it was	unclear whether the	index and

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Beinhoff U. Hilbert V	. Bittner D. Gron G	and Riepe	MW. Screening for	r cognitive imp	airment: a triage for (	out patient o	are. Dementia and	Geriatric
Cognitive Disorders	2005; 20: 278–285.	and thepe						Contactio
	reference tests wer	re interprete	d independently of e	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 th	he clock drawir	ig test: the relevance	e of "Time se	etting" in screening	9
dementia. J of Geria	tr Pscych and Neur	ology 2008	; 21: 250-260.					
Study type	Prospective cohort							
Country	Germany							
Setting	Memory clinic of th	e University	of Frankfurt am Ma	in				
Inclusion criteria	People vising the n	nemory clini	c with suspected de	mentia.				
Exclusion criteria	People who receive	ed a final dia	ignosis of FTD, DLE	3 or MCI.				
Sex	38.0% male							
Age	Mean age 71.5 yea	ars (SD 8.9)						
Presentation	Suspected dement	ia						
Reference standard	Dementia was diag	nosed using	the DSM-IV criteria	a and AD using I	NINCDS-ADRDA; Va[	O using NIND	S-AIREN.	
Dementia versus not	t dementia							
Index Test: Clock Dr	awing Test, CDT, S	hulman sc	oring method (>3)					
Clock Drawing Test, C	CDT (Shulman metho	od), cut-off 2	2/3 (>3), time setting	included (1 per	fect, 6 no reasonable i	representatio	on of a clock)	
Results	True positives:	301	False	33	False positives:	56	True negatives:	72

Results	i rue positives:	301	Faise	33	Faise positives:	50	True negatives:	72
			negatives.					
Risk of bias	Patient	High	Index test:	Low	Reference	Low	Flow and	Low
	selection:				standard:		timing:	
Overall risk of bias	Serious (People wi	no received	a final diagnosis of I	FTD, DLB or MC	I were excluded from	the study.)		
Indirectness	Patient	Low	Index test:	Low	Reference	Low		
	selection:				standard:			

Berger G, Frolich L, dementia. J of Geria	Weber B, Pantel J. tr Pscych and Neui	Diagnostic ology 2008	test accuracy of th ; 21: 250-260.	ne clock drawin	g test: the relevance	of "Time se	etting" in screening	9
Overall indirectness	Not serious							
Index Test: Clock Dr	awing Test, CDT, L	in scoring	method (<3)					
Clock Drawing Test, C	CDT (Lin method), cu	ut-off 3/2 (<3	<ol><li>time setting include</li></ol>	ded (scores 0-3,	higher better)			
Results	True positives:	294	False negatives:	40	False positives:	65	True negatives:	63
Additional comme nts								
Risk of bias	Patient selection:	High	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (People whether the serious se	no received	a final diagnosis of I	TD, DLB or MC	I were excluded from	the study.)		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Clock Dr Clock Drawing Test, C	<b>awing Test, CDT, N</b> CDT (Manos and Wu	<b>lanos and \</b> ı method),cu	<b>Wu scoring method</b> it-off 8/7 (<8), time s	<b>t (&lt;8)</b> etting included,	(0 to 10, higher better)	)		
Results	True positives:	271	False negatives:	63	False positives:	51	True negatives:	77
Additional comme nts								
Risk of bias	Patient selection:	High	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (People whether the serious se	no received	a final diagnosis of I	TD, DLB or MC	I were excluded from	the study.)		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Clock Dr	awing Test, CDT, N	lanos and V	Nu scoring method	d (<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, 0	CDT (Manos and Wu	i method), c	ut-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 comme nts									
Risk of bias	Patient selection:	High	Index test:	High	Reference standard:	Low	Flow and timing:	Low	
Overall risk of bias	Very serious (Peop was used.)	le who rece	ived a final diagnos	is of FTD, DLB c	r MCI were excluded	from the stud	dy and an optimised	threshold	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								
Index Test: Clock Dr Clock Drawing Test, C	<b>rawing Test, CDT, V</b> CDT (Wolf-Klein met	Volf-Klein s hod), cut-off	coring method (<7 7/6 (<7), time settir	) Ig not included (s	scores 0-10, higher be	etter)			
Results	True positives:	194	False negatives:	140	False positives:	24	True negatives:	104	
Additional comme nts									
Risk of bias	Patient selection:	High	Index test:	Low	Reference standard:	Low	Flow and timing:	Low	
Overall risk of bias	Serious (People whether the serious serious serious serious series and s	no received	a final diagnosis of I	FTD, DLB or MC	I were excluded from	the study.)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								
Index Test: Clock Dr Clock Drawing Test, (	rawing Test, CDT, V CDT (Watson method	Vatson sco d), cut-off 3/	ring method (>4) 4 (>4), time setting i	not included (sco	ore 0-7, lower better)				
Results	True positives:	240	False negatives:	94	False positives:	46	True negatives:	82	

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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 comme nts									
Risk of bias	Patient selection:	High	Index test:	Low	Reference standard:	Low	Flow and Low timing:		
Overall risk of bias	Serious (People wh	no received	a final diagnosis of	FTD, DLB or MC	I 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-H	IMPAO SPECT
99mTc-HMPAO SPE according to the Holm	CT imaged using a single-headed camera. Data obtained over a 360 degree rotation and 64x 64 matrix. Results were classified nan (1992) system. Pattern A was considered normal. Images classified by 2 nuclear medicine specialists.
Results	True positives:39False19False positives:29True negatives:13

Bergman H, Chertko Alzheimer's disease	ow H, Wolfson C, St . J Am Geriatr Soc	ern J, Rush 1997; 45: 15	C, Whitehead V, D –20	ixon R. HM-PA	O (CERETEC) SPEC	T brain sca	nning in the diagno	osis of
			negatives:					

Additional comme nts	The control group of on a subset of SPE using pattern A (no	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										

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Beaudry P, Cohen F Creutzfeldt-Jakob d	, Brandel JP, et al. 1 isease. Dement Geria	4-3-3 prote atr Cogn E	ein, neuron-specifi Disord 1999; 10: 40	ic enolase, and –46.	S-100 protein in cere	ebrospinal f	luid of patients wit	h
Study type	Prospective cohort							
Country	France							
Setting	Not stated, but sam	ples provid	ed by the French na	ational CJD surve	eillance network			
Inclusion criteria	People with suspect	ted CJD						
Exclusion criteria	Not stated							
Sex	47.3% male							
Age	Not stated							
Presentation	Rapidly progressive	dementia	leading to suspected	d CJD				
Reference standard	Criteria for CJD base	ed on Mas	ters et al. (1979)					
CJD (definite, proba	ble and possible) ve	ersus not C	JD					
Index Test: CSF 14-	3-3 immunoblotting							
CSF 14-3-3 protein d	etected by immunoblo	ected by immunoblotting						
Results	True positives:	66	False negatives:	15	False positives:	0	True negatives:	48

Beaudry P, Cohen P, Creutzfeldt-Jakob di	, Brandel JP, et al. sease. Dement Ger	14-3-3 prote iatr Cogn D	ein, neuron-specifi Disord 1999; 10: 40	c enolase, and –46.	S-100 protein in cere	brospinal f	luid of patients wit	h
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Unclear	Flow and timing:	Low
Overall risk of bias	Serious (Optimised inappropriate exclu or the reference sta	l test cut-offs sions avoide andard resul	s were used and it w ed; the index test re ts were interpreted	vas unclear whe sults were interp without knowled	ther: a consecutive or reted without knowled ge of the results of the	random sam ge of the res index test.)	ple of patients was outs of the reference	enrolled or e standard
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
CJD (excluding poss	ible CJD) versus n	ot CJD						
Index Test: CSF 14-3	-3 immunoblotting							
CSF 14-3-3 protein de	etected by immunobl	otting						
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 inappropriate exclu or the reference sta <10% population se	l test cut-off sions avoide andard resul o not downg	s were used and it were used and it were index test rests were interpreted raded for risk of bia	vas unclear whe sults were interp without knowled s.)	ther: a consecutive or reted without knowled ge of the results of the	random sam ge of the res index test. :	ple of patients was sults of the reference Subgroup analysis e	enrolled or e standard excluding
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
CJD versus not CJD								
Index Test: Neuron-s neuron-specific enolas	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 meas	sure in 1 san	nple					

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 comme nts	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 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.								
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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
<b>Overall risk of bias</b> 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 index test.)								
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Overall Not serious							
CJD (excluding poss	sible CJD) versus n	ot CJD						
Index Test: S100B, 2.5ng/ml								
S-100 glial protein, >2	.5ng/ml, measured u	using an imn	nuno-luminometric a	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 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	verall Not serious							

1

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 Larne	er AJ. Applause sig	n: screenin	g utility for demen	tia and cognitiv	ve impairment. Postg	raduate Me	dicine 2016; 128: 2	50–253.
Setting	Cognitive disorders	clinic						
Inclusion criteria	New referrals to the	e cognitive d	lisorders clinic seen	over a 12-mont	h period (January 2014	4–January 2	015).	
Exclusion criteria	None							
Sex	49.2% male							
Age	Median age 61 yea	rs (range 18	3-91)					
Presentation	Cognitive impairme	ent						
Reference standard	Clinician diagnosis	using DSM-	-IV for dementia and	l Petersen (1999	<ol> <li>for mild cognitive im</li> </ol>	pairment.		
Dementia versus not	t dementia							
Index Test: Applause Applause sign, <3	e 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							

1

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

Boutoleau-Bretonnie CSF biomarkers for 36.	ere C, Lebouviera T, Delaroche O, Lamy E, Evrard C, Charriau T, et al. Value of neuropsychological testing, imaging, and the differential diagnosis and prognosis of clinically ambiguous dementia. Journal of Alzheimer's Disease 2012; 28(2):323-
	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 $\geq$ 4) and in global cognitive functioning (drop in MMSE score $\geq$ 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	3	False positives:	10	True negatives:	39	
			negatives:						
Additional comme	Patients tested at b	Patients tested at baseline and formal reference diagnosis made at 24 months follow up.							
nts	Calculations for FT	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 fo made at 24 month	Serious (Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis nade 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 comme nts	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 comme nts	Patients tested at b	aseline and	formal reference di	agnosis made at	t 24 months follow up.			
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	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.)							e group
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
FTD versus non-FTD	dementia plus uno	classifiable						
Index Test: 99mTc-H	MPAO 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-Bretonnie CSF biomarkers for 36.	ere C, Lebouviera T the differential diag	, Delaroche jnosis and	e O, Lamy E, Evrard prognosis of clinic	d C, Charriau T, ally ambiguous	, et al. Value of neuro s dementia. Journal o	opsychologi of Alzheime	ical testing, imagin r's Disease 2012; 2	g, and 8(2):323-
			negatives:					
Additional comme nts	Patients tested at b	aseline and	formal reference di	agnosis made a	t 24 months follow up.			
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	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 d	lementia plus uncla	ssifiable						
Index Test: 99mTc-H	IMPAO SPECT							
99mTc-HMPAO SPEC Sixty-four 20 s views of fixation was analysed fixation, results were of lobes); hypoperfusion pattern used for analy	CT. Images taken wir over a 360° elliptical regionally for frontal classified in four cate of the FTD type (fro sis here.	th a multiple orbit taken u , parietal, te egories: Hyp ntal±tempor	headed camera. Thusing a three-heade mporal and occipita operfusion of the AI al hypoperfusion, no	nreshold is pre-s d gamma camer l regions on the D type (temporop D posterior defec	pecified; visual interpr a and reformatted into left and right. Accordin parietal hypoperfusion t); hypoperfusion of ar	etation of the a matrix of ng to the pat , whatever the nother type;	e SPECT images. D 128×128. 99 mTc-H tern of 99mTc-HMP/ ne perfusion of the fr normal SPECT. FTE	etails: MPAO AO ontal ) type
Results	True positives:	14	False negatives:	4	False positives:	13	True negatives:	25
Additional comme nts	Patients tested at b	aseline and	formal reference di	agnosis made a	t 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 fo made at 24 month but <10% study po	llow up of 6/ follow up wit pulation disc	69 patients; unclear h index tests carrie carded)	about consecut d out at baseline	ive versus random en and again at 24 mont	rolment of pa hs in some o	atients; reference dia cases; subgroup ana	agnosis Ilysis used
Indirectness	Patient	Low	Index test:	Low	Reference	Low		

Boutoleau-Bretonnie CSF biomarkers for 36.	ere C, Lebouviera T the differential diag	, Delaroche Inosis and I	O, Lamy E, Evrard prognosis of clinic	d C, Charriau T ally ambiguous	, et al. Value of neuro s dementia. Journal o	opsycholog of Alzheime	ical testing, imagin r's Disease 2012; 2	g, and 8(2):323-
	selection:				standard:			
Overall indirectness	Not serious							
AD versus VaD								
Index Test: 99mTc-H	MPAO 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 comme nts	Patients tested at b	aseline and	formal reference di	agnosis made a	t 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

1

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 comme nts	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-Bretonnie CSF biomarkers for	ere C, Lebouviera T, Delaroche O, Lamy E, Evrard C, Charriau T, et al. Value of neuropsychological testing, imaging, and 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 $\geq$ 4) and in global cognitive functioning (drop in MMSE score $\geq$ 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 vorsus non-AD d	lomontia 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 comme nts	Patients tested at b	aseline and	l formal reference di	agnosis made a	t 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 fo made at 24 month	llow up of 6/ follow up wi	/69 patients; unclear th index tests carrie	<sup>r</sup> about consecut d out at baseline	ive versus random en and again at 24 mont	rolment of p hs in some	atients; reference dia cases)	agnosis
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus non-AD d	lementia not includ	ing unclass	sifiable 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

**Risk of bias** 

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 comme nts	Patients tested at b	baseline and	formal reference di	agnosis 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 diagnosis made at analysis used with	to follow up 24 month fo >10% study	of 6/69 patients; un llow up with index te population discarde	clear about consects carried out a	secutive versus randor at baseline and again a	m enrolment at 24 months	of patients; references in some cases; sub	ce ogroup
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
FTD versus non-FTD	) dementia plus un	classifiable	group					
Index Test: MRI								
MRI scans were made sequence was availab averaged. The degree	e on different 1.0 and ble (55/60 patients), e of white	d 1.5 Tesla s using Schelt	ens score ranging f	veral clinics. MTL rom 0 (no atroph	A was rated visually v y) to 4 (severe atrophy	vhen a coror y). Scores of	nal T1-weighted grad f the left and right sid	lient echo de were
matter hyperintensitie ranging from grade 0	s severity was rated (no lesion) to grade	visually on a 3 (confluent	axial T2-weighted or lesions).	r fluid-attenuated	l inversion recovery (F	LAIR) image	es using the Fazeka	s scale,
Results	True positives:	2	False negatives:	9	False positives:	17	True negatives:	28
Additional comme nts	Patients tested at b	baseline and	formal reference di	agnosis made at	24 months follow up.			

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Patient Unclear

Reference

Low

Flow and High

Index test: Low

Boutoleau-Bretonnie CSF biomarkers for t	ere C, Lebouviera T the differential diag	, Delaroche jnosis and j	O, Lamy E, Evrard prognosis of clinic	d C, Charriau T, ally ambiguous	et al. Value of neuro dementia. Journal o	opsychologi of Alzheime	ical testing, imaging r's Disease 2012; 2	g, and 8: 323-36.
	selection:				standard:		timing:	
Overall risk of bias	Serious (Loss to fo made at 24 month	llow up of 6/ follow up wit	69 patients; unclear th index tests carried	<sup>.</sup> about consecut d out at baseline	ive versus random en and again at 24 mont	rolment of pa hs in some o	atients; reference dia cases.)	agnosis
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
VaD versus non-VaD	dementia plus uno	classifiable	group					
Index Test: MRI								
MRI scans were made sequence was availab averaged. The degree	e on different 1.0 and le (55/60 patients), i e of white	d 1.5 Tesla s using Schelt	scanners across sev ens score ranging fi	veral clinics. MTL rom 0 (no atroph	A was rated visually w y) to 4 (severe atrophy	vhen a coror y). Scores of	nal T1-weighted grac f the left and right sic	lient echo de were
matter hyperintensities ranging from grade 0 (	s severity was rated (no lesion) to grade :	visually on a 3 (confluent	axial T2-weighted or lesions).	r fluid-attenuated	l inversion recovery (F	LAIR) image	es using the Fazekas	s scale,
Results	True positives:	7	False negatives:	1	False positives:	12	True negatives:	36
Additional comme nts	Patients tested at b	aseline and	formal reference di	agnosis made a	t 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 fo made at 24 month	llow up of 6/ follow up wit	69 patients; unclear th index tests carried	<sup>.</sup> about consecut d out at baseline	ive versus random en and again at 24 mont	rolment of pa hs in some o	atients; reference dia cases.)	agnosis
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus non AD d	ementia (FTD, VaD	, psychiatri	c disease)					
Index Test: Amyloid	Beta 1-42							
CSF Amyloid Beta 1-4	2 measured by com	mercially av	vailable sandwich EL	_ISAs (Innotest,	Innogenetics, Ghent, E	Belgium). Cu	t off <500 pg/ml.	
Results	True positives:	14	False	4	False positives:	9	True negatives:	17

Boutoleau-Bretonnie CSF biomarkers for	ere C, Lebouviera T the differential diag	, Delaroche Inosis and	O, Lamy E, Evrard prognosis of clinic	d C, Charriau T, ally ambiguous	et al. Value of neuro dementia. Journal o	psychologi of Alzheime	cal testing, imagin r's Disease 2012; 2	g, and 8: 323-36.
			negatives:					
Additional comme nts	Patients tested at b	aseline and	formal reference di	agnosis made a	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 diagnosis made at analysis used with	to follow up 24 month fo >10% study	of 6/69 patients; un llow up with index to population discardo	clear about consects carried out a	secutive versus randor at baseline and again a	m enrolment at 24 months	of patients; reference in some cases; sub	ce ogroup
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Total tau CSF Total tau measur	red by commercially	available sa	ndwich ELISAs (Inn	otest, Innogene	ics,Ghent, Belgium). l	Jsual test cu	t off >350 pg/ml pre	specified,
Results	True positives:	18	False negatives:	0	False positives:	7	True negatives:	19
Additional comme nts	Patients tested at b	aseline and	formal reference di	agnosis made a	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 diagnosis made at analysis used with	to follow up 24 month fo >10% study	of 6/69 patients; un llow up with index te population discarde	clear about consects carried out a	secutive versus randor at baseline and again a	m enrolment at 24 months	of patients; reference in some cases; sub	ce ogroup
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Total tau CSF Total tau measur	red by commercially	available sa	ndwich ELISAs (Inn	otest, Innogene	tics, Ghent, Belgium).	Optimised te	est cut off of > 480pc	j/ml here
Results	True positives:	16	False	2	False positives:	3	True negatives:	23

Boutoleau-Bretonnie CSF biomarkers for	ere C, Lebouviera T the differential diag	, Delaroche jnosis and j	O, Lamy E, Evrard prognosis of clinic	d C, Charriau T, ally ambiguous	et al. Value of neuro dementia. Journal o	psycholog of Alzheime	ical testing, imagin r's Disease 2012; 2	g, and 8: 323-36.
			negatives:					
Additional comme nts	Patients tested at b	aseline and	formal reference dia	agnosis made a	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 diagnosis made at analysis used with	to follow up 24 month fo >10% study	of 6/69 patients; un llow up with index te population discarde	clear about consects carried out a	secutive versus randor It baseline and again a	m enrolment at 24 months	t of patients; references s in some cases; sub	ce ogroup
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: p-tau 18	1							
CSF P- tau measured	by commercially ava	ailable sand	wich ELISAs (Innote	est, Innogenetics	, Ghent, Belgium). Us	ual test cut	off >50 pg/ml.	
Results	True positives:	18	False negatives:	0	False positives:	9	True negatives:	17
Additional comme nts	Patients tested at b	aseline and	formal reference dia	agnosis made a	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 diagnosis made at analysis used with	to follow up 24 month fo >10% study	of 6/69 patients; un llow up with index te population discarde	clear about consects carried out a	secutive versus randor at baseline and again a	m enrolment at 24 month	t of patients; references s in some cases; sub	ce ogroup
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: p-tau 18	1 by commercially av	ailable sand	wich FLISAs (Innote	est Innogenetics	Ghent Belgium) Op	timised test	cut off >68 pg/ml	
Results	True positives:	17	False	1	False positives:	4	True negatives:	22

Boutoleau-Bretonnie	ere C, Lebouviera T the differential diag	, Delaroche mosis and	O, Lamy E, Evrard	d C, Charriau T, ally ambiguous	et al. Value of neuro dementia, Journal of	opsychologi of Alzheime	ical testing, imagin r's Disease 2012: 2	g, and 8: 323-36.	
			negatives:	any annoigue a					
Additional comme nts	Patients tested at b	aseline and	formal reference di	agnosis made a	t 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 The INNOTEST Amyl ELISAs (Innotest, Inno	<b>Beta 1-42</b> oid Tau Index (IATI) ogenetics, Ghent, Be	was calcula elgium). Cut	ted using Amyloid E off <0.8.	8eta 42/(240 + [1	.18×T-tau]) ratio. Mea	sured by co	mmercially available	sandwich	
Results	True positives:	17	False negatives:	1	False positives:	8	True negatives:	18	
Additional comme nts	Patients tested at b	aseline and	formal reference di	agnosis made a	t 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 diagnosis made at analysis used with	to follow up 24 month fo >10% study	of 6/69 patients; un llow up with index te population discarde	clear about consects carried out a	secutive versus randor at baseline and again a	m enrolment at 24 months	of patients; references in some cases; sub	ce ogroup	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								
Index Test: CSF 14-3	3-3, total Tau and p-	-tau							
≥2 abnormal CSF bio	markers, conventiona	al cut offs, A	myloid beta 1-42 50	00pg/ml, total tau	i 350pg/ml, P-tau 50pg	g/ml			

Boutoleau-Bretonnie CSF biomarkers for	ere C, Lebouviera T the differential diag	, Delaroche gnosis and p	O, Lamy E, Evrard prognosis of clinic	d C, Charriau T, ally ambiguous	et al. Value of neuro dementia. Journal o	psychologi of Alzheime	ical testing, imagin r's Disease 2012; 2	g, and 8: 323-36.
Results	True positives:	18	False negatives:	0	False positives:	8	True negatives:	18
Additional comme nts	Patients tested at b	baseline and	formal reference di	agnosis made a	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 diagnosis made at analysis used with	to follow up 24 month fo >10% study	of 6/69 patients; un llow up with index te population discarde	clear about consects carried out a	secutive versus randor at baseline and again a	m enrolment at 24 months	of patients; references of sin some cases; sub	ce ogroup
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: CSF 14-3 ≥2 abnormal CSF bio	<b>3-3, total Tau and p</b> markers, optimised c	<b>-tau</b> cut offs Amyl	loid beta 1-42 500pg	g/ml, total tau 48	0pg/ml, P-tau 68pg/ml	l		
Results	True positives:	17	False negatives:	1	False positives:	3	True negatives:	23
Additional comme nts	Patients tested at b	aseline and	formal reference di	agnosis made a	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 diagnosis made at analysis used with	to follow up 24 month fo >10% study	of 6/69 patients; un llow up with index te population discarde	clear about consects carried out a	secutive versus randor at baseline and again a	m enrolment at 24 months	of patients; references in some cases; sub	ce ogroup
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

1

Brandel JP, Delasne incidence estimates	rie-Laupretre N, La . Neurology 2000; 5	planche JL 54: 1095–10	, Hauw JJ, Alperov 99.	vitch A. Diagnos	sis of Creutzfeldt-Jak	ob disease	effect of clinical c	riteria on		
Study type	Retrospective coho	ort								
Country	France	rance								
Setting	Not stated, but sam	nples provid	ed by the French na	tional CJD surve	eillance network					
Inclusion criteria	Suspicion of spora	dic CJD								
Exclusion criteria	Genetic or iatrogen	nic CJD								
Sex	Not stated									
Age	Not stated									
Presentation	Not reported									
Reference standard	Histopathological e	examination	of autopsy samples							
CJD versus not CJD										
Index Test: Master's	criteria for CJD									
Master's criteria for C	JD (Masters, 1979).									
Results	True positives:	193	False negatives:	3	False positives:	36	True negatives:	4		
Additional comme nts	Data for the non-au	utopsy cases	s was excluded as t	he clinician diagi	nosis used the index te	est				
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 of French criteria for CJI	French criteria for CJD ria for CJD (Cathala, 1979)									
Results	True positives:	173	False negatives:	23	False positives:	20	True negatives:	20		

Brandel JP, Delasne incidence estimates.	rie-Laupretre N, La Neurology 2000; 5	planche JL, 4: 1095–10	, Hauw JJ, Alperov 99.	itch A. Diagnos	sis of Creutzfeldt-Jak	ob disease:	effect of clinical c	riteria on
Additional comme nts	Data for the non-au	itopsy cases	s was excluded as th	ne clinician diagr	nosis used the index te	est		
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: Europea	n criteria for CJD							
European criteria for (	CJD							
Results	True positives:	179	False negatives:	17	False positives:	29	True negatives:	11
Additional comme nts	Data for the non-au	utopsy cases	s was excluded as th	ne clinician diagr	nosis used the index te	est		
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	s not CJD (possible	e CJD exclu	ded)					
Index Test: Master's	criteria for CJD							
Master's criteria for C.	JD (Masters, 1979).							
Results	True positives:	145	False negatives:	6	False positives:	18	True negatives:	4
Additional comme nts	Data for the non-au	itopsy cases	s was excluded as th	ne clinician diagr	nosis used the index te	est		

Brandel JP, Delasne incidence estimates.	rie-Laupretre N, La Neurology 2000; 5	planche JL, 4: 1095–10	, Hauw JJ, Alperov 99.	itch A. Diagnos	sis of Creutzfeldt-Jak	ob disease	effect of clinical o	riteria on
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Serious (Unclear ris	sk of bias fo	r patient selection a	s we could only	use data for autopsied	l patients; su	bgroup analysis tha	t excluded
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: French c	riteria for CJD							
French criteria for CJE	D (Cathala, 1979)							
Results	True positives:	99	False negatives:	52	False positives:	1	True negatives:	21
Additional comme nts	Data for the non-au	itopsy cases	s was excluded as th	ne clinician diagr	nosis used the index te	est		
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Serious (Unclear ris	sk of bias fo	r patient selection a	s we could only	use data for autopsied	l patients; su	bgroup analysis tha	t excluded
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: European European criteria for C	n criteria for CJD							
Results	True positives:	99	False negatives:	52	False positives:	1	True negatives:	21
Additional comme nts	Data for the non-au	itopsy cases	s was excluded as th	ne clinician diagr	nosis used the index te	est		
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	High

Brandel JP, Delasne incidence estimates	rie-Laupretre N, La . Neurology 2000; 5	planche JL 4: 1095–10	, Hauw JJ, Alperov 99.	vitch A. Diagnos	sis of Creutzfeldt-Jak	ob disease	: effect of clinical o	riteria on		
Overall risk of bias	Serious (Unclear ris	erious (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, H Geriatr Cogn Disord	leegaard NH, Walde 2008; 25: 553-558.	emar G, Joh	annsen P. Usabili	ty of cerebrosp	inal fluidbiomarkers	in a tertiary	memoryclinic. De	ment		
Study type	Retrospective coho	ort								
Country	Denmark									
Setting	Copenhagen Memo	ory Clinic , C	Copenhagen Univers	sity Hospital						
Inclusion criteria	Participants underg	oing initial o	liagnosis for demen	tia, or referred fr	om other dementia sp	ecialists for	a second opinion			
Exclusion criteria	Not stated									
Sex	57.1% male									
Age	Mean age 63.1 yea	irs (no SD d	ata provided, but ag	es of participant	s ranged from 27-86 y	ears old)				
Presentation	suspected dementi	а								
Reference standard	AD was diagnosed FTD consensus cri depression used th	according to teria (Neary e ICD-10 ar	o NINCDS-ADRDA et al); DBL used the id other diagnostic o	criteria; VaD was e DLB consensu criteria are not sp	s diagnosed using NIN s criteria (McKeith et a becified.	IDS-AIREN; al); MCI used	diagnosis of FTD us the Peterson criter	se the ia;		
AD versus non-AD (i	including depression	on, MCI, oth	er forms of demer	ntia and unspec	ified diagnoses)					
Index Test: Amyloid	Beta 1-42									
Beta Amyloid 1-42 in	CSF, < 400pg/ml, d	etermined u	sing an ELISA assa	ay (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, Delasne incidence estimates.	rie-Laupretre N, La Neurology 2000; 5	planche JL, 4: 1095–109	, Hauw JJ, Alperov 99.	ritch A. Diagnos	sis of Creutzfeldt-Jak	ob disease	: effect of clinical c	riteria on
Overall indirectness	Not serious							
Index Test: Total Tau Total -tau in CSF, <51	<b>ı</b> years >300pg/ml, 5	1-70 years >	>450pg/ml, >70 yea	rs >530pg/ml, d	etermined using an EL	ISA assay (I	Innotest hTau Ag)	
Results	True positives:	25	False negatives:	23	False positives:	11	True negatives:	88
Additional comme 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							
Index Test: p-tau 181 p-tau 181 in CSF, >80	l pg/ml, determined u	sing an ELIS	SA assay (Innotest I	Phospho-tau 18	I)			
Results	True positives:	16	False negatives:	32	False positives:	8	True negatives:	92
Additional comme 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							
Index Test: 2 out of 3	3 abnormal (Amylo	id Beta 1–4	2, Total Tau, p-tau)					
2 out of 3 abnormal (E	Seta Amyloid 1–42, T	otal- tau, p-	tau). For total -tau c	ut offs were <51	years >300pg/ml, 51-	70 years >4	50pg/ml, >70 years	

Brandel JP, Delasner incidence estimates.	rie-Laupretre N, La Neurology 2000; 5	planche JL, 54: 1095–10	, Hauw JJ, Alperov 99.	itch A. Diagnos	sis of Creutzfeldt-Jak	ob disease	: effect of clinical o	riteria on
>530pg/ml; Beta Amyl	oid 1–42 , < 400pg/r	ml; p-tau 18 <sup>-</sup>	1, >80pg/ml					
Results	True positives:	20	False negatives:	28	False positives:	10	True negatives:	89
Additional comme 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							
Index Test: Amyloid	Beta 1-42, Total Ta	u and p-tau	ı abnormal					
3 out of 3 abnormal (B >530pg/ml; Beta Amyl	eta Amyloid 1–42, T oid 1–42 , < 400pg/r	<sup>⊤</sup> otal- tau, p- ml; p-tau 18 <sup>·</sup>	tau). For total -tau c 1, >80pg/ml	ut offs were <51	years >300pg/ml, 51-	70 years >4	50pg/ml, >70 years	
Results	True positives:	13	False negatives:	35	False positives:	1	True negatives:	98
Additional comme 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							

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; Sanch 2001; 56: 1528-33	nez JC; Landis T; H	ochstrasse	r DF. CSF detectio	n of the 14-3-3	protein in unselected	l patients w	ith dementia.Neuro	logy.
Country	Switzerland							
Setting	Not stated							
Inclusion criteria	Patients with ongoi	ng cognitive	e impairment referre	d for further inve	stigation			
Exclusion criteria	Not stated							
Sex	59.0% male							
Age	Mean age 66 years	s (range 17-	85)					
Presentation	Patients with ongoi	ng cognitive	e impairment					
Reference standard	Criteria not specifie	riteria not specified						
CJD versus not CJD								
Index Test: CSF 14-3 CSF 14-3-3 protein, ir	3-3 immunoblotting mmunoblotting							
Results	True positives:	2	False negatives:	0	False positives:	12	True negatives:	86
Risk of bias	Patient selection:	Patient selection:LowIndex test:YesReference standard:UnclearFlow and timing:Low						
Overall risk of bias	Not serious							
Indirectness	Patient selection:	PatientHighIndex test:LowReferenceLowselection: </th						
Overall indirectness	Serious (Patients d	lo not have :	suspected CJD at b	aseline)				

# 1 **P.1.3 C**

 Callahan CM, Unverzet FW, Hui SL, et al. Six-item screener to identify cognitive impairment among potential subjects for clinical research.

 Med Care. 2002;40():771-81. PMID: 12218768.

 Study type
 Prospective cohort

 Country
 USA

 Setting
 Indiana Alzheimer's Disease Centre

Callahan CM, Unverz Med Care. 2002;40(9	zagt FW, Hui SL, et ):771-81. PMID: 122	al. Six-item 18768.	n screener to ident	ify cognitive im	pairment among pote	ential subje	cts for clinical rese	arch.
Inclusion criteria	People referred to t	eople referred to the Indiana Alzheimer's Disease Centre for evaluation for dementia.						
Exclusion criteria	Inability to complete	e assessme	ents due to severe co	ognitive impairm	ent.			
Sex	42.9% male							
Age	Mean age 69.6 yea	rs (SD not p	provided)					
Presentation	Suspected dement	ia						
Reference standard	Dementia diagnose informant reported cognition; or (3) the impairment in the p deviations (SD) bel	formant reported a clinically significant decline in cognition; (2) the physician detected a clinically significant impairment in ognition; or (3) the participant's scores on cognitive testing fell below the 7th percentile; and if there was no clinically important opairment in the performance of activities of daily living.17 The 7th percentile is approximately equivalent to 1.5 standard eviations (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 so 6 item screener, $\ge 0$	eener (≥0)							
Results	True positives:	345	False negatives:	0	False positives:	306	True negatives:	0
Additional comme nts	The data for cohort have suspected de no dementia and co	one was ex mentia at ba ognitive imp	cluded as the peop aseline. For the ana airment no dementia	le consisted of a lysis presented t a or if it is just th	community- based sa he paper does not sta e non-dementia group	imple screer te whether th alone.	ned for dementia and ne comparator group	l did not includes
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (It was unc reference tests wer	lear whethe	r a consecutive or r ent of each other an	andom sample o d the test thresh	of patients was enrolled old was not pre-specif	d in the stud fied.)	y; whether the index	and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: 6 item so 6 item screener, $\geq 1$	creener (≥1)							

Callahan CM, Unverz Med Care. 2002;40(9	zagt FW, Hui SL, et ):771-81. PMID: 122	al. Six-item 18768.	screener to identi	ify cognitive im	pairment among pote	ential subje	cts for clinical rese	earch.
Results	True positives:	334	False negatives:	11	False positives:	143	True negatives:	163
Additional comme nts	The data for cohort have suspected de no dementia and co	one was ex mentia at ba ognitive imp	cluded as the peop aseline. For the anal airment no dementia	le consisted of a lysis presented t a or if it is just the	community- based sa he paper does not stat e non-dementia group	mple screer te whether th alone.	ned for dementia and ne comparator group	d did not o includes
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (It was und reference tests wer	lear whethe	r a consecutive or ra ent of each other an	andom sample o d the test thresh	f patients was enrolled old was not pre-specif	d in the stud ïed.)	y; whether the index	and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: 6 item so 6 item screener, $\ge 2$	creener (≥2)							
Results	True positives:	309	False negatives:	36	False positives:	63	True negatives:	243
Additional comme nts	The data for cohort have suspected de no dementia and co	one was ex mentia at ba ognitive imp	cluded as the peop aseline. For the anal airment no dementia	le consisted of a lysis presented t a or if it is just the	community- based sa he paper does not stat e non-dementia group	mple screer te whether th alone.	ned for dementia and ne comparator group	d did not o includes
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (It was und reference tests wer	lear whethe	r a consecutive or ra ent of each other an	andom sample o d the test thresh	f patients was enrolled old was not pre-specif	d in the stud ied.)	y; whether the index	and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: 6 item so 6 item screener, $\geq 3$	creener (≥3)							

Callahan CM, Unverz Med Care. 2002;40(9	zagt FW, Hui SL, et ):771-81. PMID: 122	al. Six-item 18768.	screener to identi	ify cognitive im	pairment among pote	ential subje	cts for clinical rese	earch.
Results	True positives:	278	False negatives:	67	False positives:	28	True negatives:	278
Additional comme nts	The data for cohort have suspected de no dementia and co	one was ex mentia at ba ognitive imp	cluded as the peopl aseline. For the anal airment no dementia	le consisted of a lysis presented t a or if it is just the	community- based sa he paper does not stat e non-dementia group	mple screer te whether th alone.	ned for dementia and ne comparator group	d did not o includes
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (It was unc reference tests wer	lear whethe	r a consecutive or ra ent of each other an	andom sample o d the test thresh	f patients was enrolled old was not pre-specif	d in the stud ïed.)	y; whether the index	and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: 6 item so 6 item screener, $\ge 4$	creener (≥4)							
Results	True positives:	233	False negatives:	112	False positives:	12	True negatives:	294
Additional comme nts	The data for cohort have suspected de no dementia and co	one was ex mentia at ba ognitive imp	cluded as the peoplaseline. For the anal airment no dementia	le consisted of a lysis presented t a or if it is just the	community- based sa he paper does not stat e non-dementia group	mple screer te whether th alone.	ned for dementia and ne comparator group	d did not o includes
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (It was und reference tests wer	lear whethe	r a consecutive or ra ent of each other an	andom sample o d the test thresh	f patients was enrolled old was not pre-specif	d in the stud ied.)	y; whether the index	and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: 6 item so 6 item screener, $\geq 5$	creener (≥5)							

Callahan CM, Unverz Med Care. 2002;40(9	zagt FW, Hui SL, et ):771-81. PMID: 122	al. Six-item 18768.	screener to identi	fy cognitive im	pairment among pote	ential subje	cts for clinical rese	earch.
Results	True positives:	169	False negatives:	176	False positives:	4	True negatives:	302
Additional comme nts	The data for cohort have suspected de no dementia and co	one was ex mentia at ba ognitive imp	cluded as the peop aseline. For the anal airment no dementia	le consisted of a lysis presented t a or if it is just the	community- based sa he paper does not stat e non-dementia group	mple screer te whether tl alone.	ned for dementia and ne comparator group	did not includes
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (It was und reference tests wer	lear whethe	r a consecutive or ra ent of each other an	andom sample c d the test thresh	f patients was enrolled old was not pre-specif	d in the stud īed.)	y; whether the index	and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: 6 item so 6 item screener, 6	creener (≥6)							
Results	True positives:	105	False negatives:	240	False positives:	2	True negatives:	304
Additional comme nts	The data for cohort have suspected de no dementia and co	one was ex mentia at ba ognitive imp	cluded as the peop aseline. For the anal airment no dementia	le consisted of a lysis presented t a or if it is just the	community- based sa he paper does not stat e non-dementia group	mple screer te whether tl alone.	ned for dementia and ne comparator group	l did not includes
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (It was und reference tests wer	lear whethe	r a consecutive or ra ent of each other an	andom sample c d the test thresh	f patients was enrolled old was not pre-specif	d in the stud īed.)	y; whether the index	and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE, ≤ 27	28)							

Callahan CM, Unverz Med Care. 2002;40(9	zagt FW, Hui SL, et ):771-81. PMID: 122	al. Six-item 218768.	n screener to identi	ify cognitive im	pairment among pot	ential subje	cts for clinical rese	earch.
Results	True positives:	338	False negatives:	7	False positives:	107	True negatives:	199
Additional comme nts	The data for cohort have suspected de no dementia and co	one was ex mentia at ba ognitive imp	cluded as the peop aseline. For the anal airment no dementia	le consisted of a lysis presented t a or if it is just the	community- based sa he paper does not sta e non-dementia group	mple screer te whether tl alone.	ned for dementia and ne comparator group	did not includes
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (It was unc reference tests wer	lear whethe	er a consecutive or ra ent of each other an	andom sample c d the test thresh	f patients was enrolled old was not pre-specit	d in the stud fied.)	y; whether the index	and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE, ≤ 26	:27)							
Results	True positives:	326	False negatives:	19	False positives:	67	True negatives:	239
Additional comme nts	The data for cohort have suspected de no dementia and co	one was ex mentia at ba ognitive imp	cluded as the peop aseline. For the anal airment no dementia	le consisted of a lysis presented t a or if it is just the	community- based sa he paper does not sta e non-dementia group	mple screer te whether tl alone.	ned for dementia and ne comparator group	d did not includes
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (It was unc reference tests wer	lear whethe	er a consecutive or ra ent of each other an	andom sample o d the test thresh	f patients was enrolled old was not pre-specit	d in the stud fied.)	y; whether the index	and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE, ≤ 25	:26)							

Callahan CM, Unverz Med Care. 2002;40(9	zagt FW, Hui SL, et ):771-81. PMID: 122	al. Six-item 18768.	screener to identi	fy cognitive im	pairment among pote	ential subje	cts for clinical rese	earch.
Results	True positives:	308	False negatives:	37	False positives:	49	True negatives:	257
Additional comme nts	The data for cohort have suspected de no dementia and co	one was ex mentia at ba ognitive imp	cluded as the peop aseline. For the anal airment no dementia	le consisted of a lysis presented t a or if it is just the	community- based sa he paper does not sta e non-dementia group	imple screer te whether tl alone.	ned for dementia and ne comparator group	did not includes
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (It was unc reference tests wer	lear whethe	r a consecutive or ra ent of each other an	andom sample c d the test thresh	of patients was enrolled old was not pre-specif	d in the stud fied.)	y; whether the index	and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE, ≤ 24	:25)							
Results	True positives:	292	False negatives:	53	False positives:	30	True negatives:	276
Additional comme nts	The data for cohort have suspected de no dementia and co	one was ex mentia at ba ognitive imp	cluded as the peop aseline. For the anal airment no dementia	le consisted of a lysis presented t a or if it is just the	community- based sa he paper does not sta e non-dementia group	imple screer te whether tl alone.	ned for dementia and ne comparator group	l did not includes
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (It was und reference tests wer	lear whethe	r a consecutive or ra ent of each other an	andom sample c d the test thresh	of patients was enrolled old was not pre-specif	d in the stud fied.)	y; whether the index	and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE, ≤ 23	:24)							

Callahan CM, Unverz Med Care. 2002;40(9	zagt FW, Hui SL, et ):771-81. PMID: 122	al. Six-item 218768.	screener to identi	fy cognitive im	pairment among pote	ential subje	cts for clinical rese	earch.
Results	True positives:	281	False negatives:	64	False positives:	20	True negatives:	286
Additional comme nts	The data for cohort have suspected de no dementia and co	t one was ex mentia at ba ognitive imp	cluded as the peop aseline. For the anal airment no dementia	le consisted of a lysis presented t a or if it is just the	community- based sa he paper does not stat e non-dementia group	mple screer te whether th alone.	ned for dementia and ne comparator group	l did not includes
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (It was und reference tests wer	clear whethe	r a consecutive or ra ent of each other an	andom sample c d the test thresh	f patients was enrolled old was not pre-specif	d in the stud fied.)	y; whether the index	and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE, ≤ 22	23)							
Results	True positives:	265	False negatives:	80	False positives:	14	True negatives:	292
Additional comme nts	The data for cohort have suspected de no dementia and co	t one was ex mentia at ba ognitive imp	cluded as the peop aseline. For the anal airment no dementia	le consisted of a lysis presented t a or if it is just the	community- based sa he paper does not stat e non-dementia group	imple screer te whether th alone.	ned for dementia and ne comparator group	l did not includes
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (It was und reference tests wer	clear whethe	r a consecutive or ra ent of each other an	andom sample c d the test thresh	f patients was enrolled old was not pre-specif	d in the stud fied.)	y; whether the index	and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE, ≤ 21	22)							

Callahan CM, Unverz Med Care. 2002;40(9	allahan CM, Unverzagt FW, Hui SL, et al. Six-item screener to identify cognitive impairment among potential subjects for clinical research. ed Care. 2002;40(9):771-81. PMID: 12218768.							
Results	True positives:	252	False negatives:	93	False positives:	9	True negatives:	297
Additional comme nts	The data for cohort have suspected de no dementia and co	one was ex mentia at ba ognitive impa	cluded as the peopl aseline. For the anal airment no dementia	e consisted of a ysis presented to a or if it is just the	community- based sa he paper does not sta e non-dementia group	imple screer te whether t alone.	ned for dementia and he comparator group	d did not o includes
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (It was und reference tests wer	lear whethe	r a consecutive or ra ent of each other an	andom sample o d the test thresh	f patients was enrolled old was not pre-specif	d in the stud fied.)	y; whether the index	and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

1

Carnero-Pardo C, Es phototest in dement	pejo-Martinez B, Lopez-Alcalde S, Espinosa-Garcia M, Saez-Zea C, Vilchez-Carrillo R, et al. Effectiveness and costs of ia 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, Es	spejo-Martinez B, Lo ia and cognitive im	opez-Alcalo	le S, Espinosa-Gar creening BMC Neu	cia M, Saez-Zea urology 2011: 1	a C, Vilchez-Carrillo I 1 <sup>.</sup> 92	R, et al. Effe	ectiveness and cos	ts of	
Index Test: phototes	st (<27)		brooming. Dino not						
phototest ≤ 26. Spanis	sh 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 Impairm	nent Screen), cut off	3/4. Spanisl	า						
Results	True positives:	28	False negatives:	2	False positives:	17	True negatives:	70	
Additional comme 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 Not serious									
Index Test: Memory	Impairment Screen	, MIS (<5)							
MIS (Memory Impairm	nent Screen), cut off	4/5. Spanisl	า						
Results	True positives:	29	False negatives:	1	False positives:	25	True negatives:	62	
Additional comme									

1

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:77False0False positives:175True negatives:108										

Carnero-Pardo 2013 {published and unpublished data} Carnero-Pardo C, Espejo-Martinez B, Lopez-Alcalde S, Espinosa-Garcia M, Saez-Zea C,											
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 comme	Includes unpublish	ed data from	n Madrid (174 subje	cts) from 1 healt	h centre between April	2000 and C	ctober 2002; publis	hed			
nts	Granada data from February 2008 to January 2009.										
Dick of hice			I OIIS DOWINED 14 as	normal not pres	Beforence			lles.			
RISK OF DIAS	selection:	LOW	index test.	High	standard:	LOW	timing:	LOW			
Overall risk of bias	Serious (Multiple te	est threshold	ls 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 23/2	24, Spanish	version								
Results	True positives:	77	False negatives:	0	False positives:	153	True negatives:	130			
Additional comme	Includes unpublish	ed data from	n Madrid (174 subje	cts) from 1 healt	h centre between April	2000 and C	october 2002; publisl	hed			
nts	Additional data from	February 2 allable for cu	t offs down to 14 as	9. normal not pres	ented here as these c	ut offs are n	ot used in other stud	lies			
Risk of bias	Patient		Index test:	High	Reference		Flow and	Low			
	selection:	2011		g.i	standard:	2011	timing:	2011			
Overall risk of bias	Serious (Multiple te	est threshold	ls were used)								
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall	Not serious										
Indirectness	(00)										
MMSE (Folstein 1975	<23) version), cut off 22/2	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,											
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 comme	Includes unpublish	ed data from	n Madrid (174 subje	cts) from 1 healt	h centre between April	2000 and C	ctober 2002; publis	hed			
nts	Granada data from February 2008 to January 2009.										
Dick of hice			It ons down to 14 as	normal not pres	Beforence			lles.			
RISK OF DIAS	selection:	LOW	index test:	High	standard:	LOW	timing:	LOW			
Overall risk of bias	Serious (Multiple te	est threshold	ls 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 21/2	22, Spanish	version								
Results	True positives:	74	False negatives:	3	False positives:	93	True negatives:	190			
Additional comme	Includes unpublish	ed data from	n Madrid (174 subje	cts) from 1 healt	h centre between April	2000 and C	october 2002; publis	hed			
nts	Additional data from	ilable for cu	to January 2008 It offs down to 14 as	9. normal not pres	ented here as these c	ut offs are no	ot used in other stud	lies.			
Risk of bias	Patient	Low	Index test:	High	Reference	Low	Flow and	Low			
	selection:			5	standard:		timing:				
Overall risk of bias	Serious (Multiple te	est threshold	ls 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 20/2	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,											
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 comme	Includes unpublish	ed data from	n Madrid (174 subje	cts) from 1 healt	h centre between April	2000 and C	ctober 2002; publis	hed			
nts	Granada data from February 2008 to January 2009.										
Dick of hice			I OIIS OOWII LO 14 as	normal not pres	Beforence			lles.			
RISK OF DIAS	selection:	LOW	index test.	High	standard:	LOW	timing:	LOW			
Overall risk of bias	Serious (Multiple te	est threshold	ls 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 19/2	20, Spanish	version.								
Results	True positives:	72	False negatives:	5	False positives:	51	True negatives:	232			
Additional comme	Includes unpublish	ed data from	n Madrid (174 subje	cts) from 1 healt	h centre between April	2000 and C	october 2002; publis	hed			
IIIS	Additional data ava	ilable for cu	t offs down to 14 as	normal not pres	ented here as these c	ut offs are no	ot used in other stud	lies.			
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low			
Overall risk of bias	Serious (Multiple te	est threshold	ls were used)								
Indirectness	Patient	Low	Index test:	Low	Reference standard:	Low					
Overall	Not serious				Standard.						
indirectness											
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,													
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 comme	Includes unpublish	ed data from	n Madrid (174 subje	cts) from 1 healt	h centre between April	2000 and C	ctober 2002; publis	hed					
nts	Granada data from February 2008 to January 2009.												
Dick of hice			l ons down to 14 as	normal not pres	Peference			lles.					
RISK OT DIAS	selection:	LOW	index test:	High	standard:	LOW	timing:	LOW					
Overall risk of bias	Serious (Multiple te	est threshold	ls 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 comme	Includes unpublish	ed data from	n Madrid (174 subje	cts) from 1 healt	h centre between April	2000 and C	october 2002; publis	hed					
nts	Additional data ava	ilable for cu	t offs down to 14 as	normal not pres	ented here as these c	ut offs are n	ot used in other stud	lies.					
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low					
Overall risk of bias	Serious (Multiple te	est threshold	ls were used)		otandaran		tining.						
Indirectness	Patient		Index test	Low	Reference	Low							
	selection:	2011		2011	standard:	2011							
Overall indirectness	Not serious												
Index Test: MMSE (<	<17)	17 Spaniah			Index Test: MMSE (<17)								
	VESSING		Version										
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]													
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			negatives:										
Additional comme nts	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 ava	liable for cu	t ons down to 14 as	normal not pres	ented here as these c	ut ons are n	ot used in other stud	lies.					
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low					
Overall risk of bias	Serious (Multiple te	est threshold	s were used)										
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low							
Overall indirectness	Not serious												

1

Carnero-Pardo C, Cu cognitive impairmer	ruz-Orduña I, Espejo-Martínez B, Martos-Aparicio C, López-Alcalde S, Olazarán J. Utility of the Mini-Cog for detection of It 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-Co	g (≤2)

1

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 comme nts	The data presented primary study. The to the Granada stud known by the indivi was only available The data for the CE dementia together	d here was of published p dy sites as p duals comp in the Grana DT and MMS in their anal	obtained from an un rimary study include part of the Mini-Cog leting the reference ada sample and the SE were not extracte ysis and we could n	bublished Cochra es data from 2 st test (the CDT) w standard. Also, t data was made ed here as the pr ot separate them	ane review using publi udy sites, but the Cocl /as included as part of the diagnosis of demen available to the CR gro rimary study authors gro with the information p	shed and un nrane review the reference ntia separat pup by the a rouped mild provided.	npublished data from v authors used data ce standard in Madri e from cognitive impo uthors. cognitive impairmer	n the confined d and was airment nt and	
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low	
Overall risk of bias	Serious ( The test t	hreshold wa	as not pre-specified,	but was optimis	ed 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 diagnosi	s 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							

1

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	Clinician diagnosis based on DSM-IV
standard	
Dementia vs no dem	ientia

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)

1

## 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 comme nts	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 (Uncle index and referenc analysis.)	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.

1240-0.	
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, Penningt other proteins in the 1243-8.	on C, Mackenzie JM diagnosis of spora	M, Andrews adic Creutzt	M, Everington D, V feldt-Jakob diseas	Will RG, Knight e in the UK: a 1	RS, Green AJ. The ro 0-year review. J Neu	ole of cereb rol Neurosu	rospinal fluid 14-3 Irg Psychiatry. 2010	-3 and 0; 81:			
Presentation	Rapidly progressive	apidly progressive dementia leading to suspected CJD									
Reference standard	Confirmed CJD bas basis for probable (	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	8-3 immunoblotting										
Presence of a detecta	ble 14-3-3 band in C	SF sample									
Results	True positives:	210	False negatives:	35	False positives:	44	True negatives:	127			
Additional comme nts	Age range was 28- confirmation.	89 years old	I. Analysis excludes	people diagnos	ed with probable CJD,	but lacking	neuropathological				
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	High			
Overall risk of bias	Serious (Subgroup unclear whether the	analysis wit e reference	h >10% population and index tests were	excluded and in e interpreted ind	the included groups p ependently of each oth	eople are mi ner.)	issing without explar	nation; it is			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										
Index Test: Total Tau CSF Total Tau (Innote	<b>u</b> est h-TAU -Ag assay	), >1260pg/ı	nl								
Results	True positives:	175	False negatives:	41	False positives:	20	True negatives:	115			
Additional comme nts	Age range was 28- confirmation.	89 years old	I. Analysis excludes	people diagnos	ed with probable CJD,	but lacking	neuropathological				
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	High			
Overall risk of bias	Serious (Subgroup unclear whether the	analysis wit e reference	h >10% population and index tests were	excluded and in e interpreted ind	the included groups p ependently of each oth	eople are mi ner.)	issing without explar	nation; it is			
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 u	using an ELISA, >1.0	Ong/ml									
Results	True positives:	158	False negatives:	85	False positives:	17	True negatives:	152			
Additional comme nts	Age range was 28- confirmation.	89 years old	I. Analysis excludes	people diagnos	ed with probable CJD,	but lacking	neuropathological				
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 Presence of a detecta	<b>3-3 (presence) and</b> a ble 14-3-3 band in C	<b>S100b (&gt;1.0</b> CSF sample	ng/ml) and CSF S100b as	sayed using an E	ELISA, >1.0ng/ml						
Results	True positives:	151	False negatives:	91	False positives:	9	True negatives:	160			
Additional comme nts	Age range was 28- confirmation.	89 years old	I. Analysis excludes	people diagnos	ed with probable CJD,	but lacking	neuropathological				
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	High			
Overall risk of bias	Serious (Subgroup unclear whether the	analysis wit e reference	h >10% population and index tests were	excluded and in e interpreted ind	the included groups p ependently of each oth	eople are mi ner.)	issing without explar	nation; it is			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					

Chohan G, Penningt other proteins in the 1243-8.	on C, Mackenzie JM diagnosis of spora	M, Andrews adic Creutz	M, Everington D, feldt-Jakob diseas	Will RG, Knight e in the UK: a 1	RS, Green AJ. The ro 0-year review. J Neu	ole of cereb rol Neurosu	prospinal fluid 14-3 Irg Psychiatry. 201	-3 and 0; 81:		
Overall indirectness	Not serious									
Index Test: Total Tau and S100b										
CSF Total Tau (Innote	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 comme nts	Age range was 28- confirmation.	89 years old	<ol> <li>Analysis excludes</li> </ol>	people diagnos	ed with probable CJD,	, but lacking	neuropathological			
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	High		
Overall risk of bias	Serious (Subgroup unclear whether the	analysis wit e reference	th >10% population and index tests wer	excluded and in e interpreted ind	the included groups p ependently of each oth	eople are m ner.)	issing without explar	nation; it is		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									
Index Test: CSF 14-3	3-3 and total Tau									
CSF Total Tau (Innote	est h-TAU -Ag assay	), >1260pg/	ml and presence of	a detectable 14-	3-3 band in CSF samp	ole.				
Results	True positives:	162	False negatives:	54	False positives:	16	True negatives:	119		
Additional comme nts	Age range was 28- confirmation.	89 years old	d. Analysis excludes	people diagnos	ed with probable CJD,	, but lacking	neuropathological			
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	High		
Overall risk of bias	Serious (Subgroup unclear whether the	analysis wit e reference	th >10% population and index tests wer	excluded and in e interpreted ind	the included groups p ependently of each otl	eople are m her.)	issing without explar	nation; it is		
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.

n.ong/nn.											
Results	True positives:	123	False negatives:	93	False positives:	6	True negatives:	129			
Additional comme nts	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, Lars BMC Geriatrics 2017	son E-M, Holm IE, I 7; 17: 129- 135.	Nielsen OB	F, Andersen S. Olf	actory testing i	n consecutive patien	ts referred	with suspected der	nentia.			
Study type	Prospective cohort										
Country	Denmark										
Setting	Aalborg University	Hospital gei	iatric outpatient clin	ic							
Inclusion criteria	Patients referred to	the geriatri	c outpatient clinic at	Aalborg Univers	sity Hospital for evalua	tion of cogn	itive decline.				
Exclusion criteria	A history of nose-th of the brain with un	nroat patholo consciousno	bgy with increasing seas, and cerebral su	sinusitis or chror ırgery.	nic sinusitis, a flue con	dition, previo	ous brain trauma, co	ncussion			
Sex	52% male										
Age	Mean age 79.1 yea	irs (no SD p	rovided)								
Presentation	Suspected dement	ia									
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, $\geq$ 3 errors

Olfactory test,  $\geq$  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 (Althou	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,  $\geq$  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 (Althou	ot 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: Olfactor	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,  $\geq$  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 (Althou	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									

1

Coulthart M, Jansen markers for sporadi	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							

Sex51.4% maleAgeMedian age ranged from 63-66 years across CJD and not CJD groups.

**Presentation** Rapidly progressive dementia leading to suspected CJD

**Reference** 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 stu	dy. BMC Neurology 2	2011, 11:13	3.				
Results	True positives:	112	False negatives:	15	False positives:	244	True negatives:	629			
Additional comme nts	ditional comme 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 do	wngraded f	or exclusions during	data analysis a	s <10% population exc	cluded.)					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										
Index Test: Total Tau tau in CSF, INNOTES	<b>ı</b> T hTau-Ag ELISA, c	ut off 976pg	/ml								
Results	True positives:	109	False negatives:	11	False positives:	99	True negatives:	727			
Additional comme nts	Data analysis exclu duplicate samples; diagnostic classifica result was used as case remained ope	ision criteria (iii) unconfir ation was ge a criterion to n at study c	consisted of situation med suspected CJE enetic prion diseases o classify such case losure.	ons where: i) the D at sample subr ; (vi) final diagno s, they could no	e sample was technical mission; (iv) the 14-3-3 ostic classification was t be included in the val	lly inadequa assay resu probable s0 idation stud	te for 14-3-3 testing; It was indeterminate CJD (as a positive 14 y for this marker); or	; (ii) ; (v) final 3-3 <sup>-</sup> (vii) the			
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low			
Overall risk of bias	Serious (Optimised CJD cases as not s	threshold u specified; no	sed to analyse Tau t downgraded for ex	results; unclear clusions during	whether the reference data analysis as <10%	standards v population	would correctly class excluded.)	ify non-			
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										
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 comme nts	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 S100B, Sangtec 100 B	<b>.5ng/ml</b> ELISA kit, cut off 2.5	ng/ml								
Results	True positives:	106	False negatives:	16	False positives:	104	True negatives:	698		
Additional comme nts 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 CJD cases as not s	threshold u specified; no	sed to analyse S100 t downgraded for ex	B results; uncle	ar whether the referer data analysis as <10%	nce standard 6 population	ls would correctly cla excluded.)	assify non-		

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	ot 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 comme nts	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 exclusions during d	ar whether tl lata analysis	ne reference standa as <10% populatio	rds would correct n excluded and s	tly classify non-CJD c standard threshold us	cases as not ed to analys	specified; not down e S100B results.)	graded for		
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 Olive Alzheimer's disease	eira-Souzs R, Moll J, Tovar-Moll F, Mattos P. Is it possible to identify individuals with mild cognitive impairment and 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,<br/>the FAQ and the IQCODE. Family Practice 2012; 29: 401-6.Study typeprospective cohortCountrySpainSettingSeven medical clinics of the Pena Prieta Primary Care Centre (Health District 1, Autonomous Community of Madrid).Inclusion criteriaAge >49 years; any complaint or suspicion raised by the patient, an informant or primary care physician related to cognition; a<br/>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	Not stated								
Sex	29.1% male	29.1% male								
Age	Mean age 72.2 yea	ars (SD 8.9)								
Presentation	Complaint or suspi	cion of cogn	itive impairment							
Reference standard	Formal neuropsych for dementia.	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 (Threshold	s were not p	pre-specified but we	re calculated to	give optimum sensitivi	ty and speci	ficity.)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									
Index Test: Informar Informant Questionna	nt Questionnaire on ire on Cognitive Dec	l <b>Cognitive</b> line, IQCOE	<b>Decline, IQCODE (</b> DE (26 item, 95/96).	<b>26 item, &gt;3.6)</b> Spanish						
Results	True positives:	12	False negatives:	3	False positives:	34	True negatives:	111		
Additional comme nts										
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low		
Overall risk of bias	Serious (Threshold	s were not p	pre-specified but we	re calculated to	give optimum sensitivi	ty and specif	ficity.)			
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 Activ	vities Questionnaire),	scored 0 to	33 (total dependen	ce). Spanish. Cι	ıt off 8/9.					
Results	True positives:	13	False negatives:	2	False positives:	26	True negatives:	119		
Additional comme nts										
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low		
Overall risk of bias	Serious (Threshold	ls were not j	ore-specified but we	re calculated to	give optimum sensitivi	ty and speci	ficity.)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									

1

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 issue.)	out due to p	problems with samp	les; <10 % exclu	ded from analysis for	possible CJ	D so not downgraded	d for this	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								

# 1 **P.1.4 D**

Davis HF, Skolasky grooved pegboard.	RL, Selnes OA, Burgess DM, McArthur JC. Assessing HIV-associated dementia: modified HIV dementia scale versus the 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 assessment					
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 unclear whether co	test cut-offs	s used; unclear whe r random patients w	ther the index te ere enrolled.)	st was interpreted with	nout knowled	dge of the reference	test;	
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low			
Overall indirectness	Serious (Study part	ticipants we	re aged from 33-47	years, median 3	9 years.)				
Index Test: Grooved	pegboard test								
Grooved pegboard tes	st, cut-off 1.5SD belo	ow the expect	cted age-and educa	tion- adjusted m	ean.				
Results	True positives:	102	False negatives:	42	False positives:	168	True negatives:	143	
Additional comme nts									
Risk of bias	Patient selection:	Unclear	Index test:	Unclear	Reference standard:	Low	Flow and timing:	Low	
Overall risk of bias	Serious (Unclear w random patients we	hether the iner the iner the iner enrolled.	ndex test was interp )	reted without kn	owledge of the referer	nce test; unc	lear whether consec	utive or	
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low			
Overall indirectness	Serious (Study part	ticipants we	re aged from 33-47	years, median 3	9 years.)				
Index Test: Modified	HIV dementia scale	e (m-HDS) a	and grooved pegbo	oard combined.					
Modified HIV dementian adjusted mean for the	a scale (m-HDS) and pegboard test.	d grooved pe	egboard combined.	A score of <7.5	on the m-HDS or 1.5S	D below the	expected age-and e	ducation-	
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 comme nts										
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 par	Serious (Study participants were aged from 33-47 years, median 39 years.)								

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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 comme nts	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 unclea avoided.)	ar whether a	consecutive or ran	dom sample of p	atients was enrolled a	ind whether	inappropriate exclus	ions were			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										
FDG-PET. Carried ou coronal images were by 2 experienced nuc consisting of 16 ROIs	t using a whole body reconstructed with a lear medicine physic . The qualitative imag	v scanner us n iterative re ians and for ge patterns	ing a mean dose of construction algorit quantitative analysi are described in det	190M Bq with a hm (slice thickne is the MI was me ail the methods.	cquisition starting 45 r ss 3.49mm, pixel size asure based on a star	nin post inje 1.03mm). S ndardized re	ction. Transaxial, sa Scans assess qualita gion of interest (RO	ggital and tively by I) analysis			
Results	True positives:	111	False negatives:	33.12	False positives:	186.6	True negatives:	124.4			
Additional comme nts	Additional subgroup	p analyses v	vere not carried out	as the numbers	of study participants v	vas very sm	all (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 unclea avoided.)	ar whether a	consecutive or ran	dom sample of p	atients was enrolled a	ind whether	inappropriate exclus	ions were			
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 comme nts	Additional subgrou	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-H	MPAO SPECT (all	dementia p	atterns)								
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	2	False positives:	4	True negatives:	2			

Results	True positives:	16	False negatives:	2	False positives:	4	True negatives:	2		
Additional comme nts	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	Not serious
ndirectness	

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## 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 demer	ntia (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 whether inappropri	analysis wi ate exclusio	th > 35% population ns were avoided.)	excluded; uncle	ear whether consecutiv	e or random	n patients were enrol	led or
Indirectness	Patient	Low	Index test:	Low	Reference	Low		

Duits FH, Teunissen Easily said, but what	CE, Bouwman FH, does it mean?Alzh	Visser P-J, neimer's &	Mattsson N, Zette Dementia 2014; 10	rberg H, Blenno : 713–723.	ow K et al. The cereb	rospinal flu	id "Alzheimer profi	ile":
	selection:				standard:			
Overall indirectness	Not serious							
AD versus other dem	nentias (excluding	MCI)						
Index Test: Amyloid Amyloid Beta 1-42, IN	<b>Beta 1-42</b> NOTEST ELISA, cu <sup>.</sup>	t-off < 550 p	g/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 whether inappropriate	analysis wit ate exclusio	h > 35% population ns were avoided.)	excluded; uncle	ar whether consecutiv	e or random	patients were enrol	led or
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus not AD (S	MC and other dem	entias, excl	uding MCI)					
Index Test: Amyloid Amyloid Beta 1-42, IN	<b>Beta 1-42</b> NOTEST ELISA, cu	t-off < 550 p	g/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 demen	itia (SMC, excludes	s MCI)						

Duits FH, Teunissen Easily said, but what	CE, Bouwman FH, t does it mean?Alzl	Visser P-J, heimer's &	, Mattsson N, Zette Dementia 2014; 10	rberg H, Blenno : 713–723.	ow K et al. The cereb	rospinal flu	iid "Alzheimer prof	le":		
Index Test: Total tau	l									
t-tau, INNOTEST ELIS	SA, 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	Overall Not serious									
AD versus other den	nentias (excluding	MCI)								
Index Test: Total tau	l i i i i i i i i i i i i i i i i i i i									
t-tau, INNOTEST ELIS	SA, 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 whether inappropri	analysis wit ate exclusio	th > 35% population ns were avoided.)	excluded; uncle	ar whether consecutiv	e or random	n patients were enrol	led or		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									
AD versus not AD (S	MC and other dem	entias, excl	luding 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	Not serious									
AD versus no demer	ntia (SMC, excludes	s MCI)									
Index Test: p-tau 187	1										
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 whether inappropri	analysis wil ate exclusio	th > 35% population ns were avoided.)	excluded; uncle	ar whether consecutiv	e or random	patients were enrol	led or			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										
AD versus other den	nentias (excluding	MCI)									
Index Test: p-tau 181	1										
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 wit	th > 35% population	excluded; uncle	ar whether consecutiv	e or random	patients were enrol	led or			

Duits FH, Teunissen Easily said, but what	CE, Bouwman FH, t does it mean?Alzl	Visser P-J, neimer's &	Mattsson N, Zette Dementia 2014; 10	rberg H, Blenno : 713–723.	ow K et al. The cereb	rospinal flu	id "Alzheimer prof	ile":				
	whether inappropri-	whether inappropriate exclusions were avoided.)										
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low						
Overall indirectness	Not serious											
AD versus not AD (S	versus not AD (SMC and other dementias, excluding MCI)											
Index Test: p-tau 18	1											
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 demen	ntia (SMC, excludes	s MCI)										
Index Test: Amyloid	Beta 1-42 and t-tau	i and/or p-ta	au abnormal									
Amyloid Beta 1-42 an 375 pg/ml; p-tau 181,	d t-tau and/or p-tau INNOTEST ELISA,	181 abnorma cut-off > 52	al. Amyloid Beta 1-4 pg/ml.	2, INNOTEST E	LISA, cut-off < 550 pg	g/ml; t-tau, IN	INOTEST ELISA, cu	ut-off >				
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 whether inappropri-	analysis wit ate exclusio	h > 35% population ns were avoided.)	excluded; uncle	ar whether consecutiv	e or random	patients were enrol	led or				
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low						

Duits FH, Teunissen	CE, Bouwman FH,	Visser P-J,	Mattsson N, Zette	rberg H, Blenn	ow K et al. The cereb	rospinal flu	id "Alzheimer profi	ile":			
Overall indirectness	Not serious			. 110-120.							
AD versus other dementias (excluding MCI)											
Index Test: Amyloid	Beta 1-42 and t-tau	and/or p-ta	au 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 whether inappropriate	analysis wit ate exclusio	h > 35% population ns were avoided.)	excluded; uncle	ear whether consecutiv	e or random	patients were enrol	led or			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										
AD versus not AD (S	MC and other dem	entias, excl	uding MCI)								
Index Test: Amyloid Amyloid Beta 1-42 an 375 pg/ml; p-tau 181,	Beta 1-42 and t-tau d t-tau and/or p-tau INNOTEST ELISA,	1 and/or p-ta 181 abnorma cut-off > 52	<b>au abnormal</b> al. Amyloid Beta 1-4 pg/ml.	2, INNOTEST E	ELISA, cut-off < 550 pg	ı/ml; t-tau, IN	INOTEST ELISA, cu	it-off >			
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 demen	ntia (SMC, excludes	s 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 den	nentias (excluding	MCI)								
Index Tests > 2 of 2 k			Data 4 40 t tau m	4						

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 whether inappropri-	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 (S	SMC and other dem	entias, exc	luding 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 Easily said, but wha	CE, Bouwman FH, t does it mean?Alzl	Visser P-J, heimer's &	, Mattsson N, Zette Dementia 2014; 10	rberg H, Blenno : 713–723.	ow K et al. The cereb	rospinal flu	uid "Alzheimer profi	ile":			
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	rectness Not serious										
AD versus no demen	ntia (SMC, excludes	s MCI)									
Index Test: Total Ta	u/Amyloid Beta 1-4	2									
t-tau/ Amyloid Beta 1-	42, cut-off 0.71. Am	yloid Beta 1-	42, INNOTEST ELI	SA; t-tau, INNOT	EST ELISA.						
Results	True positives:	536	False negatives:	95	False positives:	25	True negatives:	226			
Additional comme nts	Cut-off determined	for sensitivi	ty 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 whether inappropri-	analysis wit ate exclusio	h > 35% population: ns were avoided.)	excluded; uncle	ar whether consecutiv	e or randor	n patients were enrol	led or			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										
AD versus other der	nentias (excluding	MCI)									
Index Test: Total Ta	u/Amyloid Beta 1-4	2									
t-tau/ Amyloid Beta 1-	42, cut-off 0.71. Am	yloid Beta 1-	42, INNOTEST ELI	SA; t-tau, INNOT	EST 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 comme nts	Cut-off determined	for sensitivi	ty 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 (S	MC and other dem	entias, excl	uding MCI)							
Index Test: Total Tau Total tau/ Amyloid Bet	u/Amyloid Beta 1-42 ta 1-42, cut-off 0.71.	<b>2</b> Amyloid Be	ta 1-42, INNOTEST	ELISA; t-tau, IN	NOTEST ELISA.					
Results	True positives:	536	False negatives:	95	False positives:	92	True negatives:	426		
Additional comme nts	Cut-off determined	for sensitivi	ty 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 demer	ntia (SMC, excludes	s MCI)								
Index Test: Total Tau	u/Amyloid Beta 1-4	2								
t-tau/ Amyloid Beta 1-	42, cut-off 0.52. Amy	yloid Beta 1-	42, INNOTEST ELI	SA; t-tau, INNO	TEST 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 comme nts	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 den	nentias (excluding	MCI)							
Index Test: Total Tat t-tau/ Amyloid Beta 1-	u/ <b>Amyloid Beta 1-42</b> 42, cut-off 0.52. Amy	<b>2</b> /loid Beta 1-	42, INNOTEST ELI	SA; t-tau, INNO <sup>⁻</sup>	EST ELISA.				
Results	True positives:	587	False negatives:	44	False positives:	91	True negatives:	176	
Additional comme nts	Cut-off determined	for sensitivit	ty 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 whether inappropria	analysis wit ate exclusio	h > 35% population ns were avoided.)	excluded; uncle	ar whether consecutiv	e or random	patients were enrol	led or	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								
AD versus not AD (S	MC and other demo	entias, excl	uding 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 comme nts	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 demen	ntia (SMC, excludes	s MCI)								
Index Test: p-tau/Am	yloid Beta 1-42									
p-tau 181/ Amyloid Be	eta 1-42, cut-off 0.11	. Amyloid Be	eta 1-42, INNOTES	Г ELISA; p-tau 1	81, INNOTEST ELISA	۱.				
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 whether inappropriate	analysis wit ate exclusio	th > 35% population ns were avoided.)	excluded; uncle	ar whether consecutiv	e or random	i patients were enrol	led or		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall Not serious										
AD versus other den	nentias (excluding	MCI)								
Index Test: p-tau/Am	yloid Beta 1-42									
p-tau 181/ Amyloid Be	eta 1-42, cut-off 0.11	. Amyloid Be	eta 1-42, INNOTEST	Г ELISA; p-tau 1	81, INNOTEST ELISA	۱.				
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/Am	yloid Beta 1-42									
p-tau 181/ Amyloid Be	eta 1-42, cut-off 0.11	. Amyloid Be	eta 1-42, INNOTEST	Г ELISA; p-tau 1	81, INNOTEST ELISA	۱.				
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 demer	ntia (SMC, excludes	s MCI)								
Index Test: p-tau/Am	yloid Beta 1-42									
p-tau 181/ Amyloid Be	eta 1-42, cut-off 0.08	. Amyloid Be	eta 1-42, INNOTEST	۲ ELISA; p-tau 1	81, INNOTEST ELISA	۱.				
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	ias 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 (S	MC and other dem	entias, excl	uding MCI)							
Index Test: p-tau/An	nyloid Beta 1-42									
p-tau 181/ Amyloid Be	eta 1-42, cut-off 0.08	. Amyloid Be	eta 1-42, INNOTES <sup>-</sup>	Г ELISA; p-tau 1	81, INNOTEST ELISA	۱.				
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, 19	99. 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	as 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	Overall Not serious									
AD versus other den	nentias (excluding	MCI)								
Index Test: Formula	Hulstaert (biomark	ers)								
Formula Hulstaert, 19	99. 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 whether inappropri-	analysis wi ate exclusio	th > 35% population ns were avoided.)	excluded; uncle	ar whether consecutiv	e or randon	n patients were enrol	led or		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									
AD versus not AD (S	MC and other dem	entias, exc	luding 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 demen	ntia (SMC, excludes	s 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 whether inappropriate	analysis wit ate exclusio	h > 35% population ns were avoided.)	excluded; uncle	ar whether consecutiv	e or random	patients were enrol	led or		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall 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 Easily said, but what	CE, Bouwman FH, t does it mean?Alzl	Visser P-J, neimer's &	, Mattsson N, Zette Dementia 2014; 10	rberg H, Blenno : 713–723.	ow K et al. The cereb	rospinal flu	id "Alzheimer prof	ile":		
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Overall risk of bias	Serious (Subgroup whether inappropri-	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 (S	MC and other dem	entias, excl	uding MCI)							
Index Test: Formula	Mulder (biomarker	s)								
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 demen	ntia (SMC, excludes	s MCI)								
Index Test: Formula	Mattson (biomarke	ers)								
Formula Mattson, 3.69	94 + 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 Easily said, but what	CE, Bouwman FH, does it mean?Alzl	Visser P-J, neimer's & I	Mattsson N, Zette Dementia 2014; 10	rberg H, Blenno : 713–723.	ow K et al. The cereb	rospinal flu	id "Alzheimer prof	ile":
Overall indirectness	Not serious							
AD versus other den	nentias (excluding	MCI)						
Index Test: Formula	Mattson (biomarke	ers)						
Formula Mattson, 3.69	94 + 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 whether inappropri-	analysis wit ate exclusio	h > 35% population ns were avoided.)	excluded; uncle	ar whether consecutiv	e or random	patients were enrol	led or
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus not AD (S	MC and other dem	entias, excl	uding MCI)					
Index Test: Formula	Mattson (biomarke	ers)						
Formula Mattson, 3.69	94 + 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 demer	ntia (SMC, excludes	s MCI)						
Index Test: Formula	Schoonenboom (b	iomarkers)						

Duits FH, Teunissen Easily said, but wha	CE, Bouwman FH, t does it mean?Alz	Visser P-J, heimer's &	Mattsson N, Zette Dementia 2014; 10	rberg H, Blenno : 713–723.	ow K et al. The cereb	rospinal flu	id "Alzheimer profi	le":	
Formula Schoonenbo	om, 152+8.25x p-tau	ı = 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 den	nentias (excluding	MCI)							
Index Test: Formula Formula Schoonenbo	Schoonenboom (b om, 152+8.25x p-tau	<b>iomarkers)</b> ı = 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 whether inappropri	analysis wit ate exclusio	h > 35% population ns were avoided.)	excluded; uncle	ar whether consecutiv	e or random	n patients were enrol	led or	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								
AD versus not AD (S	MC and other dem	entias, excl	uding MCI)						
Index Test: Formula Formula Schoonenbo	Schoonenboom (b om, 152+8.25x p-tau	<b>iomarkers)</b> ı = 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 coho	ort							
Country	Canada								
Setting	Centre Hospitalier	de l' Univers	ite de Montreal (CH	IUM)					
Inclusion criteria	Early syphilis plus of cell count of < 350	one of blood cells/microli	l serum RPR titre ≥ tre.	1:32, neurologic	al and/or ophthalmic s	igns or symp	otoms of neurosyphil	lis or CD4	
Exclusion criteria	Syphilis of unknow	n duration, h	nistory of neurosyph	ilis, treatment wi	th penicillin prior to lur	nbar punctu	re.		
Sex	99.2% male								
Age	Median age 42 yea	rs (range 22	2-66)						
Presentation	Suspected neurosy	philis							
Reference standard	CSF-VDRL test rea	active							
Neurosyphilis versu	s not neurosyphilis	;							
Index Test: PCR for PCR for T. pallidum g	<b>T. pallidum genes:</b> enes: polA, Tpp47, a	<b>polA, Tpp4</b> and bmp.	7, and bmp.						
Results	True positives:	True positives:       6       False onegatives:       9       False positives:       36       True negatives:       57							
Risk of bias	Patient selection:	Patient selection:LowIndex test:UnclearReference standard:LowFlow and timing:Low							
Overall risk of bias	Not serious								

Dummaresq J, Lang HIV-Infected Patients	evin S, Gagnon S, S s with Early Syphili	Serhir B, De s. Journal o	eligne B, Tremblay of Clinical Microbio	C, Tsang RSW blogy 2013; 51:	et al. Clinical Predic 4060–4066.	tion and Dia	agnosis of Neurosy	philis in		
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low				
Overall indirectness	Serious (>99% me	erious (>99% men who have sex with men)								
Index Test: FTA-ABS	6									
FTA-ABS, fluorescent	treponemal antibod	y absorption	assay.							
Results	True positives:	15	False negatives:	0	False positives:	76	True negatives:	9		
Additional comme nts										
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% me	n who have	sex with men)							
Index Test: TPPA TPPA, Treponema pa	llidum particle agglu	tination assa	ay.							
Results	True positives:	10	False negatives:	5	False positives:	45	True negatives:	40		
Additional comme nts										
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% me	n 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 ass	INNO-LIA Syphilis assay.									
Results	True positives:	12	False negatives:	0	False positives:	63	True negatives:	8		
Additional comme nts										
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% me	n who have	sex with men)							

1

Dumurgier J, Schrae clinical setting of me	en S, Gabelle A, Vercruysse O, Bombois S, Laplanche J-L, Peoc'h K et al. Cerebrospinal fluid amyloid-β 42/40 ratio in emory 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/Am	nyloid 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 Am	CSF p-tau181 and Amyloid Beta 1-42 combined										
Results	True positives:	114	False negatives:	12	False positives:	9	True negatives:	150			
Additional comme nts	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	<b>c of bias</b> 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 CSF p-tau181 and Am	<b>Amyloid Beta 42/</b> Iyloid Beta 1-42/1-40	<b>40</b> ) ratio comb	ined								
Results	True positives:	118	False negatives:	17	False positives:	15	True negatives:	153			
Additional comme nts	The study descripti CSF was taken 1 m	on of test tin nonth after d	ning is unclear: the l liagnosis.	reference standa	rd diagnosis included	consideratio	on of the CSF results	s, but the			
	Data was only pres	ented as the	e combined results of	of the 3 centres f	or the use of combina	tions 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 patients with unknounclear and a subg	reference st own clinical o roup analys	andard diagnosis in diagnoses or MCI we is was carried out th	cluded considera ere excluded fro nat excluded >10	ation of the CSF result m the study; the timing % population (with inc	ts; the test c g of the refer determinate	ut offs were not pre- rence and index tests results).)	specified; s is			
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 comme nts	The study descripti CSF was taken 1 n	on of test tir nonth after o	ning is unclear: the liagnosis.	reference standa	ard diagnosis included	consideratio	on of the CSF results	, but the
	Data was only pres	ented as the	e combined results	of the 3 centres f	for the use of combina	tions 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 patients with unknous unclear and a subg	reference st own clinical o roup analys	andard diagnosis in diagnoses or MCI w is was carried out th	cluded considera ere excluded fro nat excluded >10	ation of the CSF result m the study; the timing 0% population (with inc	s; the test c of the refer determinate	ut offs were not pre-s rence and index tests results).)	specified; s is
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Total Tau Total Tau in CSF mea	u asured using an INN	OTEST ELIS	SA kit, optimal cut of	f calculated as 3	89pg/ml			
Results	True positives:	63	False negatives:	10	False positives:	9	True negatives:	42
Additional comme nts	The study descripti CSF was taken 1 n	on of test tir nonth after c	ning is unclear: the liagnosis.	reference standa	ard diagnosis included	consideratio	on of the CSF results	, but the
Risk of bias	Patient selection:	High	Index test:	High	Reference standard:	High	Flow and timing:	Low
Overall risk of bias	Very Serious (The patients with unknounclear.)	reference st own clinical o	andard diagnosis in diagnoses or MCI w	cluded considera ere excluded fro	ation of the CSF result m the study and the ti	s; the test c ming of the r	ut offs were not pre-s reference and index t	specified; ests is

Dumurgier J, Schrae clinical setting of me	en S, Gabelle A, Ver emory centers: a m	cruysse O, ulticentric s	Bombois S, Lapla study. Alzheimer's	nche J-L, Peoc' Research & Th	h K et al. Cerebrospi erapy 2015; 7:30-38.	inal fluid an	nyloid-β 42/40 ratio	in
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: p-tau 18' p-tau 181 in CSF mea	l Isured using an INN	OTEST ELIS	SA kit, optimal cut of	f calculated as 6	4pg/ml			
Results	True positives:	62	False negatives:	11	False positives:	7	True negatives:	44
Additional comme nts	The study descripti CSF was taken 1 n	on of test tir nonth after c	ning is unclear: the l liagnosis.	reference standa	rd diagnosis included	consideratio	on of the CSF results	s, but the
Risk of bias	Patient selection:	High	Index test:	High	Reference standard:	High	Flow and timing:	Low
Overall risk of bias	Very Serious (The patients with unknounclear.)	reference st own clinical o	andard diagnosis in diagnoses or MCI w	cluded considera ere excluded fro	ation of the CSF result m the study and the ti	s; the test c ming of the r	ut offs were not pre-s reference and index	specified; tests is
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Amyloid	Beta 1-42	a an INNOT	EST ELISA kit opti	mal cut off calcu	lated as 836ng/ml			
Results	True positives:	66	False negatives:	7	False positives:	15	True negatives:	36
Additional comme nts	The study descripti CSF was taken 1 n	on of test tir nonth after c	ning is unclear: the l liagnosis.	reference standa	rd diagnosis included	consideratio	on of the CSF results	s, but the
Risk of bias	Patient selection:	High	Index test:	High	Reference standard:	High	Flow and timing:	Low
Overall risk of bias	Very Serious (The patients with unknounclear.)	reference st own clinical o	andard diagnosis in diagnoses or MCI we	cluded considera ere excluded fro	ation of the CSF result m the study and the ti	s; the test c ming of the r	ut offs were not pre- reference and index	specified; tests is

Dumurgier J, Schrae clinical setting of me	en S, Gabelle A, Ver emory centers: a m	cruysse O, ulticentric s	Bombois S, Lapla study. Alzheimer's	nche J-L, Peoc' Research & Th	h K et al. Cerebrospi erapy 2015; 7:30-38.	inal fluid an	nyloid-β 42/40 ratio	in
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Amyloid Amyloid Beta 1-42/1-4	Beta 42/40 10 in CSF measured	using an IN	NOTEST ELISA kit,	optimal cut off of	alculated as 0.082.			
Results	True positives:	66	False negatives:	7	False positives:	17	True negatives:	34
Additional comme nts	The study descripti CSF was taken 1 n	on of test tir nonth after c	ning is unclear: the i liagnosis.	reference standa	rd diagnosis included	consideratio	on of the CSF results	s, but the
Risk of bias	Patient selection:	High	Index test:	High	Reference standard:	High	Flow and timing:	Low
Overall risk of bias	Very Serious (The patients with unknounclear.)	reference st own clinical o	andard diagnosis in diagnoses or MCI we	cluded considera	ation of the CSF result m the study and the ti	s; the test co ming of the r	ut offs were not pre- reference and index	specified; tests is
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Total Tau Total Tau in CSF mea	u sured using an INN	OTEST ELIS	SA kit, optimal cut of	f calculated as 3	43pg/ml			
Results	True positives:	37	False negatives:	13	False positives:	26	True negatives:	85
Additional comme nts	The study descripti CSF was taken 1 n	on of test tir nonth after c	ning is unclear: the i liagnosis.	reference standa	rd diagnosis included	consideratio	on of the CSF results	s, but the
Risk of bias	Patient selection:	High	Index test:	High	Reference standard:	High	Flow and timing:	Low
Overall risk of bias	Very Serious (The patients with unknounclear.)	reference st own clinical o	andard diagnosis in diagnoses or MCI we	cluded considera ere excluded fro	ation of the CSF result m the study and the ti	s; the test co ming of the r	ut offs were not pre- reference and index	specified; tests is

Dumurgier J, Schrae clinical setting of me	en S, Gabelle A, Ver emory centers: a m	cruysse O, ulticentric s	Bombois S, Lapla study. Alzheimer's	nche J-L, Peoc Research & Th	'h K et al. Cerebrospi erapy 2015; 7:30-38.	inal fluid an	nyloid-β 42/40 ratio	in	
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 comme nts	The study descripti CSF was taken 1 m	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 patients with unknounclear.)	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		EST ELISA kit opti	mal cut off calcu	lated as 737ng/ml				
Results	True positives:	35	False negatives:	15	False positives:	22	True negatives:	89	
Additional comme nts	The study descripti CSF was taken 1 m	on of test tir nonth after c	ning is unclear: the l liagnosis.	reference standa	ard diagnosis included	consideratio	on of the CSF results	s, but the	
Risk of bias	Patient selection:	High	Index test:	High	Reference standard:	High	Flow and timing:	Low	
Overall risk of bias	Very Serious (The patients with unknounclear.)	reference st wn clinical o	andard diagnosis in diagnoses or MCI w	cluded considera ere excluded fro	ation of the CSF result m the study and the ti	s; the test controls; the test controls of the r	ut offs were not pre- reference and index	specified; tests is	

Dumurgier J, Schrae clinical setting of me	en S, Gabelle A, Ver emory centers: a m	cruysse O, ulticentric s	Bombois S, Lapla study. Alzheimer's	nche J-L, Peoc Research & Th	'h K et al. Cerebrospi erapy 2015; 7:30-38.	inal fluid an	nyloid-β 42/40 ratio	in		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious	Not serious								
Index Test: Amyloid Beta 42/40										
Results	True positives:	32	False negatives:	18	False positives:	23	True negatives:	88		
Additional comme nts	The study descripti CSF was taken 1 m	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 patients with unknounclear.)	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 Tag	u Beured using an INN(		SA kit ontimal cut of	ff calculated as 3	800pg/ml					
Results	True positives:	35	False negatives:	2	False positives:	2	True negatives:	43		
Additional comme nts										
Risk of bias	Patient selection:	High	Index test:	High	Reference standard:	High	Flow and timing:	Low		
Overall risk of bias	Very Serious (The patients with unknous unclear and it is un	reference st own clinical o clear wheth	andard diagnosis in diagnoses or MCI we er a consecutive or l	cluded considera ere excluded fro random sample	ation of the CSF result m the study and the tir of patients was enrolle	s; the test cu ning of the r ed.)	ut-offs were optimise eference and index t	ed; tests is		

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	l							
p-tau 181 in CSF mea	sured using an INN	OTEST ELIS	SA kit, optimal cut of	f calculated as 5	8pg/ml			
Results	True positives:	32	False negatives:	5	False positives:	4	True negatives:	41
Additional comme nts								
Risk of bias	Patient selection:	High	Index test:	High	Reference standard:	High	Flow and timing:	Low
Overall risk of bias	Very Serious (The patients with unknounclear.)	reference st own clinical o	andard diagnosis in diagnoses or MCI w	cluded considera ere excluded fro	ation of the CSF result m the study and the ti	s; the test cu ming of the r	ut offs were not pre- eference and index	specified; tests is
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 usin	g an INNOT	EST ELISA kit, opti	mal cut off calcu	lated as 814pg/ml			
Results	True positives:	31	False negatives:	6	False positives:	9	True negatives:	36
Additional comme nts								
Risk of bias	Patient selection:	High	Index test:	High	Reference standard:	High	Flow and timing:	Low
Overall risk of bias	Very Serious (The patients with unknounclear.)	reference st own clinical o	andard diagnosis in diagnoses or MCI w	cluded considera ere excluded fro	ation of the CSF result m the study and the tir	s; the test cu ming of the r	ut offs were not pre- eference and index	specified; tests is

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 Bela 1-42/1-2	io in CSF measured	using an in	NUTEST ELISA KIL,	oplimal cut on o	calculated as 0.065.				
Results	True positives:	33	False negatives:	4	False positives:	7	True negatives:	38	
Additional comme nts	The study descripti CSF was taken 1 n	on of test tin nonth after d	ning is unclear: the l liagnosis.	reference standa	ard diagnosis included	consideratio	on of the CSF results	s, but the	
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								

# 1 **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 recognition pattern	J, Hoegh P, Jelic V, Bo Andersen B, Naik M, Wahlund LO, Oeksengaard AR. Quantitative EEG applying the statistical 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 comme nts	We excluded the h population of intere	ealthy indivi est	duals that were recr	uited separately	from our analysis as t	hey do not n	natch the research q	uestion
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-DLI	В							

#### 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 comme nts	We excluded the he population of intere	ealthy individest	duals that were recr	uited separately	from our analysis as t	hey do not n	natch the research q	uestion
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, Camache bodies during life. E	o V, Paredes P, et al. Cardiac (123)I-metaiodobenzylguanidine imaging allows early identification of dementia with Lewy ur 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 (Significan	erious (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								

# 1 P.1.6 F

Ferman TJ, Boeve B Lewy bodies. Neuro	F, Smith GE, Lin S-C, Silber MH, Wszolek Z et al. Inclusion of RBD improves the diagnostic classification of dementia with logy200; 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 comme nts	Features are very s	similar to the	DLB consensus cri	teria, 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	ess Not serious							
Index Test: Two or n	nore of visual hallu	cinations, F	Parkinsonism, fluct	tuating attentio	n and concentration	or RBD		
Two or more of visual	hallucinations, Park	insonism, flu	uctuating attention a	nd concentratior	n or RBD			
Results	True positives:	86	False negatives:	12	False positives:	37	True negatives:	99
Additional comme 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							
Index Test: RBD or t RBD or two or more o	wo or more of visu	al hallucina is, Parkinsor	tions, Parkinsonis	m, and fluctuat	ing attention and con oncentration	ncentration		
Results	True positives:	88	False	10	False positives:	37	True negatives:	99

Ferman TJ, Boeve B Lewy bodies. Neurol	F, Smith GE, Lin S- ogy200; 77: 876-88	C, Silber M 2.	H, Wszolek Z et al.	Inclusion of R	BD improves the dia	gnostic clas	sification of demen	ntia with
			negatives:					
Additional comme 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							
Index Test: Two or n Two or more of visual	<b>hore of visual hallu</b> hallucinations, Park	<b>cinations, F</b> insonism or	<b>Parkinsonism or Rl</b> RBD	BD				
Results	True positives:	81	False negatives:	17	False positives:	21	True negatives:	115
Additional comme 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							

1

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

Flicker L, Logiudice of Geriatric Psychiat	D, Carlin JB, Ames ry 1997; 12: 203–9.	D. The pre	dictive value of de	mentia screenii	ng instruments in cli	nical popula	ations. Internationa	al Journal			
Inclusion criteria	Patients attending tinterpreter.	he memory	clinic who were abl	e to complete the	e 3 assessments (MM	se, Iqcodi	E and AMT) without	an			
Exclusion criteria	Not stated	lot stated									
Sex	37.8% male										
Age	Mean age 73.4 yea	rs (SD 9.3)									
Presentation	Memory problems										
Reference standard	Clinician diagnosis	linician diagnosis based on DSM -III-R criteria.									
Dementia versus no	dementia										
Index Test: Informar	nt Questionnaire on	Cognitive	Decline, IQCODE (	26 item, >3.5)							
Informant Questionna	ire on Cognitive Dec	line, IQCOD	0E (26 item, 3.6)								
Results	True positives:	188	False negatives:	28	False positives:	35	True negatives:	48			
Additional comme nts	The random group suspected dementi	of patients r a at baseline	eferred to the aged	care assessmer	nt team were excluded	from analys	sis as they did not ha	ave			
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High			
Overall risk of bias	Very serious (Due t patient groups inclu results of the index	o non-pre-s Ided in the a test.)	pecification of test t analysis and whethe	hresholds; large or the reference s	number of patients ex standard results were i	cluded from nterpreted v	study; lack of clarity vithout knowledge of	/ about f the			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										
Index Test: Informar IQCODE (26 item, 3.7	it Questionnaire on	Cognitive	Decline, IQCODE (	26 item, >3.6)							
Results	True positives:	176	False negatives:	40	False positives:	32	True negatives:	51			
Additional comme	The random group	of patients r	eferred to the aged	care assessmer	nt team were excluded	from analys	is as they did not ha	ave			

Flicker L, Logiudice of Geriatric Psychiat	D, Carlin JB, Ames ry 1997; 12: 203–9.	D. The pre	dictive value of de	mentia screeni	ng instruments in cli	nical popul	ations. Internationa	al Journal
nts	suspected dementi	a at baselin	е.					
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Very serious (Due patient groups inclu results of the index	to non-pre-s uded in the a test.)	pecification of test the analysis and whethe	hresholds; large r the reference s	number of patients ex standard results were i	cluded from	study; lack of clarity vithout knowledge of	about the
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Informan IQCODE (26 item, 3.8	t Questionnaire on	Cognitive	Decline, IQCODE (	26 item, >3.7)				
Results	True positives:	168	False negatives:	48	False positives:	29	True negatives:	54
Additional comme nts	The random group suspected dementi	of patients r a at baseline	eferred to the aged	care assessme	nt team were excluded	from analys	sis as they did not ha	ive
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Very serious (Due patient groups inclu results of the index	to non-pre-s uded in the a test.)	pecification of test the analysis and whethe	hresholds; large r the reference s	number of patients ex standard results were i	cluded from	study; lack of clarity vithout knowledge of	about the
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Informan IQCODE (26 item, 3.9	t Questionnaire on	Cognitive	Decline, IQCODE (	26 item, >3.8)				
Results	True positives:	161	False negatives:	55	False positives:	24	True negatives:	59
Additional comme	The random group	of patients r	referred to the aged	care assessmen	nt team were excluded	from analys	sis as they did not ha	ive

Flicker L, Logiudice of Geriatric Psychiat	D, Carlin JB, Ames ry 1997; 12: 203–9.	D. The pre	dictive value of de	mentia screeni	ng instruments in cli	nical popu	lations. Internationa	ıl Journal
nts	suspected dement	a at baselin	e.					
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Very serious (Due patient groups inclu results of the index	to non-pre-s uded in the a test.)	pecification of test t analysis and whethe	hresholds; large or the reference s	number of patients ex standard results were i	cluded from	n study; lack of clarity without knowledge of	about the
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Informan IQCODE (26 item, 4.0	t Questionnaire on	Cognitive	Decline, IQCODE (	26 item, >3.9)				
Results	True positives:	152	False negatives:	64	False positives:	21	True negatives:	62
Additional comme nts	The random group suspected dement	of patients r a at baseline	referred to the aged e.	care assessme	nt team were excluded	from analy	sis as they did not ha	ive
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Very serious (Due patient groups inclu results of the index	to non-pre-s uded in the a test.)	pecification of test t analysis and whethe	hresholds; large or the reference s	number of patients ex standard results were i	cluded from	n study; lack of clarity without knowledge of	about the
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Informan IQCODE (26 item, 4.1	t Questionnaire on	Cognitive	Decline, IQCODE (	26 item, >4.0)				
Results	True positives:	140	False negatives:	76	False positives:	17	True negatives:	66
Additional comme	The random group	of patients r	referred to the aged	care assessme	nt team were excluded	from analy	sis as they did not ha	ave

Flicker L, Logiudice of Geriatric Psychiat	D, Carlin JB, Ames ry 1997; 12: 203–9.	D. The pre	dictive value of de	mentia screenii	ng instruments in cli	nical popu	lations. Internationa	al Journal
nts	suspected dementi	a at baseline	е.					
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Very serious (Due patient groups inclu results of the index	to non-pre-s uded in the a test.)	pecification of test the analysis and whethe	hresholds; large r the reference s	number of patients ex tandard results were	cluded fror interpreted	n study; lack of clarity without knowledge of	about the
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Informan IQCODE (26 item, 4.2	t Questionnaire on	Cognitive	Decline, IQCODE (	26 item, >4.1)				
Results	True positives:	126	False negatives:	90	False positives:	14	True negatives:	69
Additional comme nts	The random group suspected dementi	of patients r a at baseline	eferred to the aged	care assessmer	t team were excluded	I from analy	sis as they did not ha	ave
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Very serious (Due patient groups inclu results of the index	to non-pre-s uded in the a test.)	pecification of test the analysis and whethe	hresholds; large r the reference s	number of patients ex tandard results were	cluded fror interpreted	n study; lack of clarity without knowledge of	about the
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE (17/18)	18)							
Results	True positives:	108	False negatives:	108	False positives:	8	True negatives:	75
Additional comme	The random group	of patients r	referred to the aged	care assessmer	nt team were excluded	I from analy	sis as they did not ha	ave

Flicker L, Logiudice of Geriatric Psychiat	D, Carlin JB, Ames ry 1997; 12: 203–9.	D. The pre	dictive value of de	mentia screenii	ng instruments in cli	nical popu	lations. Internationa	al Journal
nts	suspected dementi	a at baseline	е.					
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Very serious (Due patient groups inclu results of the index	to non-pre-s uded in the a test.)	pecification of test the analysis and whethe	hresholds; large r the reference s	number of patients ex tandard results were	cluded from	n study; lack of clarity without knowledge of	about the
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE (18/19)	19)							
Results	True positives:	120	False negatives:	96	False positives:	11	True negatives:	72
Additional comme nts	The random group suspected dementi	of patients r a at baseline	eferred to the aged	care assessmer	t team were excluded	from analy	sis as they did not ha	ave
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Very serious (Due patient groups inclu results of the index	to non-pre-s uded in the a test.)	pecification of test the analysis and whethe	hresholds; large r the reference s	number of patients ex tandard results were i	cluded from	n study; lack of clarity without knowledge of	about the
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE (19/20)	20)							
Results	True positives:	134	False negatives:	82	False positives:	13	True negatives:	70
Additional comme	The random group	of patients r	referred to the aged	care assessmer	t team were excluded	from analy	sis as they did not ha	ave

Flicker L, Logiudice of Geriatric Psychiat	D, Carlin JB, Ames ry 1997; 12: 203–9.	D. The pre	dictive value of de	mentia screenii	ng instruments in cli	nical popu	lations. Internationa	al Journal
nts	suspected dementi	a at baseline	е.					
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Very serious (Due patient groups inclu results of the index	to non-pre-s uded in the a test.)	pecification of test the analysis and whethe	hresholds; large r the reference s	number of patients ex tandard results were	cluded fron	n study; lack of clarity without knowledge of	about the
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE (20/21)	21)							
Results	True positives:	149	False negatives:	67	False positives:	20	True negatives:	63
Additional comme nts	The random group suspected dementi	of patients r a at baseline	eferred to the aged	care assessmer	t team were excluded	l from analy	sis as they did not ha	ave
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Very serious (Due patient groups inclu results of the index	to non-pre-s uded in the a test.)	pecification of test the analysis and whethe	nresholds; large r the reference s	number of patients ex tandard results were i	cluded fron interpreted	n study; lack of clarity without knowledge of	about the
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE (21/22)	22)							
Results	True positives:	162	False negatives:	54	False positives:	24	True negatives:	59
Additional comme	The random group	of patients r	referred to the aged	care assessmer	t team were excluded	I from analy	sis as they did not ha	ave

Flicker L, Logiudice of Geriatric Psychiat	D, Carlin JB, Ames ry 1997; 12: 203–9.	D. The pre	dictive value of de	mentia screenii	ng instruments in cli	nical popul	ations. Internationa	al Journal
nts	suspected dementi	a at baseline	е.					
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Very serious (Due patient groups inclu results of the index	to non-pre-s uded in the a test.)	pecification of test the analysis and whethe	nresholds; large r the reference s	number of patients ex tandard results were	cluded from	n study; lack of clarity without knowledge of	about the
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE (22/23)	:23)							
Results	True positives:	172	False negatives:	44	False positives:	26	True negatives:	57
Additional comme nts	The random group suspected dementi	of patients r a at baseline	eferred to the aged	care assessmer	t team were excluded	I from analy	sis as they did not ha	ive
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Very serious (Due patient groups inclu results of the index	to non-pre-s uded in the a test.)	pecification of test the analysis and whethe	hresholds; large r the reference s	number of patients ex tandard results were i	cluded from	n study; lack of clarity without knowledge of	about the
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE (23/24)	:24)							
Results	True positives:	183	False negatives:	33	False positives:	33	True negatives:	50
Additional comme	The random group	of patients r	referred to the aged	care assessmer	it team were excluded	I from analy	sis as they did not ha	ive

Flicker L, Logiudice of Geriatric Psychiat	D, Carlin JB, Ames ry 1997; 12: 203–9.	D. The pre	dictive value of de	mentia screenii	ng instruments in cli	nical popu	llations. Internationa	al Journal
nts	suspected dementi	a at baseline	е.					
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Very serious (Due patient groups inclures of the index	to non-pre-s uded in the a test.)	pecification of test thanalysis and whethe	hresholds; large r the reference s	number of patients ex tandard results were	cluded from interpreted	n study; lack of clarity without knowledge of	about the
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE (24/25)	:25)							
Results	True positives:	194	False negatives:	22	False positives:	39	True negatives:	44
Additional comme nts	The random group suspected dementi	of patients r a at baseline	referred to the aged e.	care assessmer	t team were excluded	from analy	ysis as they did not ha	ive
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Very serious (Due patient groups inclures of the index	to non-pre-s uded in the a test.)	pecification of test the analysis and whethe	hresholds; large r the reference s	number of patients ex tandard results were i	cluded from interpreted	n study; lack of clarity without knowledge of	about the
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE (25/26)	26)							
Results	True positives:	199	False negatives:	17	False positives:	45	True negatives:	38
Additional comme	The random group	of patients r	referred to the aged	care assessmer	t team were excluded	from analy	sis as they did not ha	ive

Flicker L, Logiudice of Geriatric Psychiat	D, Carlin JB, Ames try 1997; 12: 203–9.	D. The pre	dictive value of de	mentia screeni	ng instruments in cli	nical popul	ations. Internationa	al Journal
nts	suspected dementi	a at baseline	е.					
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Very serious (Due patient groups inclu results of the index	to non-pre-s uded in the a test.)	pecification of test the analysis and whethe	hresholds; large r the reference s	number of patients ex standard results were	cluded from	n study; lack of clarity without knowledge of	about the
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Abbrevia AMT (6/7)	ated Mental Test, A	MT (<7)						
Results	True positives:	126	False negatives:	90	False positives:	11	True negatives:	72
Additional comme nts	The random group suspected dementi	of patients r a at baseline	eferred to the aged	care assessme	nt team were excluded	from analy	sis as they did not ha	ave
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Very serious (Due patient groups inclure results of the index	to non-pre-s uded in the a test.)	pecification of test the analysis and whethe	hresholds; large r the reference s	number of patients ex standard results were i	cluded from	n study; lack of clarity without knowledge of	about the
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Abbrevia AMT (7/8)	ated Mental Test, A	MT (<8)						
Results	True positives:	157	False negatives:	59	False positives:	24	True negatives:	59
Additional comme	The random group	of patients r	referred to the aged	care assessmen	nt team were excluded	from analy	sis as they did not ha	ave

Flicker L, Logiudice of Geriatric Psychiat	D, Carlin JB, Ames try 1997; 12: 203–9.	D. The pre	dictive value of de	mentia screeni	ng instruments in cli	nical popul	ations. Internationa	al Journal
nts	suspected dementi	a at baseline	е.					
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Very serious (Due patient groups inclu results of the index	to non-pre-s uded in the a test.)	pecification of test the analysis and whethe	hresholds; large r the reference s	number of patients ex standard results were i	cluded from	n study; lack of clarity without knowledge of	about the
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Abbrevia AMT (8/9)	ated Mental Test, A	MT (<9)						
Results	True positives:	189	False negatives:	27	False positives:	39	True negatives:	44
Additional comme nts	The random group suspected dementi	of patients r a at baseline	eferred to the aged	care assessme	nt team were excluded	I from analy	sis as they did not ha	ave
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Very serious (Due patient groups inclure results of the index	to non-pre-s uded in the a test.)	pecification of test the analysis and whethe	hresholds; large r the reference s	number of patients ex standard results were i	cluded from	n study; lack of clarity without knowledge of	about f the
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Abbrevia Abbreviated Mental T	ated Mental Test, A est, AMT (9/10)	MT (<10)						
Results	True positives:	210	False negatives:	6	False positives:	60	True negatives:	23
Additional comme	The random group	of patients r	referred to the aged	care assessmer	nt team were excluded	I from analy	sis as they did not ha	ave

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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 dementi	uspected 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.
C.ID versus not C.ID	

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	Index Test: CSF 14-3-3 immunoblotting										
14-3-3 detected by important characterization as ne	munoblotting. The 1- gative or positive sa	4-3-3 proteir mple	n band in CSF samp	oles was optically	observed and compa	ared to knov	vn specimen to perm	it a			
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<br/>cerebrospinal fluid. J Neurol 2017; 81: 79-92.Study typeProspective cohortCountryUSASettingNational Prion disease pathology surveillance centreInclusion criteriaWHO diagnosis of CJD or non-CJD, methionine or valine at codon 129 or hPrP gene, unequivocal classification of pathologyExclusion criteriaNone stated

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Foutz A, Appleby BS cerebrospinal fluid.	6, Hamlin C, Liu X, Y Ann Neurol 2017; 8	Ƴang S, Col 1: 79-92.	nen Y, Chen W, Ble	evins J et al. Dia	agnostic and prognos	stic value o	f human prion dete	ection in		
Sex	Not stated									
Age	Nor stated									
Presentation	Suspected CJD									
Reference standard	Neuropathology									
CJD versus not CJD										
Index Test: Real-tim	e quaking-induced	prion conv	ersion, RT-QuIC.							
Real-time quaking-inc total (in first and repea	luced prion conversion at rounds) were posi	on (RT-Qul0 tive and exc	<ol> <li>c), (second generati eeded the diagnosti</li> </ol>	on assay). Samp c cut-off stated.	ples considered positiv	/e if >1 well i	in the first round or >	> 2 wells		
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 14-3-3 detected by im	<b>3-3 immunoblotting</b> imunoblotting.									
Results	True positives:	53	False negatives:	12	False positives:	8	True negatives:	6		
Additional comme 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				

Foutz A, Appleby BS cerebrospinal fluid.	6, Hamlin C, Liu X, Y Ann Neurol 2017; 8	Ƴang S, Coł 1: 79-92.	nen Y, Chen W, Ble	evins J et al. Dia	agnostic and progno	stic value o	of human prion dete	ection in
Overall indirectness	Not serious							
Index Test: Total Tau	h							
Total tau, ELISA, cut-	off > 1150 pg/ml.							
Results	True positives:	62	False negatives:	3	False positives:	4	True negatives:	10
Additional comme 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							

 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

 Lalv
 Italv

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 depressed with sec without knowledge	Serious (Subgroup analysis with >10% population excluded; patients whose cognitive deficit reverted (regarded as primarily lepressed with secondary cognitive impairment) were excluded from the study; unclear whether reference test was interpreted vithout 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 w excluded from the s results of index tes	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 (Subg depressed with sec without knowledge	/ery serious (Subgroup analysis with >10% population excluded; patients whose cognitive deficit reverted (regarded as primarily lepressed 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										
	and the strength of the second strength of the strength of the second strength of the strength										

# 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			
Ovorall risk of bias	Sorious (Patients y	origue (Detients where cognitive deficit reverted (regarded as primarily depressed with secondary cognitive imperment) were									

erall 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 incl	uded)							
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 w excluded from the s results of index tes	/hose cognit study; uncle t interpreted	tive deficit reverted ( ar whether reference without knowledge	regarded as prir e test was interp of reference tes	narily depressed with s reted without knowled t.)	secondary c ge of index t	ognitive impairment) est and unclear whe	) were ether	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								
AD versus non-AD c	lementias (excludin	ng 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 L, Ghidoni R, Gerolo 317.	A, Zanetti O, Galluz li C. Markers of Alz	zi S, Roma heimer's di	no M, Cotelli M, Ge sease in a populat	nnarelli M, Bine ion attending a	etti G, Bocchio L, Pag memory clinic. Alzho	ghera B, An eimers Derr	nicucci G,Bonetti M lent 2009; 5: 307-	l,Benussi		
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 der	nentias and	d 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	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									

# 1 **P.1.7 G**

 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 borners 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, Dumurgie cerebrospinal fluid b	er J, Vercruysse O, biomarkers in resea	Paquet C, E	Bombois S, Laplan y center: the PLM	che J-L., et al.lı Study. J. Alzhe	npact of the 2008-20 imers Dis. 2013; 34: ˈ	12 French / 7–305.	Alzheimer plan on t	he use of	
Inclusion criteria	People with cogniti	ve or behavi	ioural disorders atte	nding the partici	pating clinics.				
Exclusion criteria	People with unclea	r, unknown	or postponed clinica	I diagnosis					
Sex	44.2% male								
Age	Median age varies	from 61-73	years across diagno	stic 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 thres random or consecu was excluded the s	holds were itive people itudy was no	not pre-specified, bu or avoided inapprop ot downgraded for th	ut optimised base priate exclusions is.)	ed on the data; it was A subgroup analysis	unclear whe was carried	ther the study enroll out but as < 10% pc	ed opulation	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								
Index Test: Total Ta	u								
Total tau, INNOTEST	hTau-Ag ELISA, cut	off >301pg/	/ml						
Results	True positives:	283	False negatives:	66	False positives:	48	True negatives:	161	
Additional comme nts									
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 thres random or consecu was excluded the s	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	l										
p-tau, INNOTEST tau	181, cut off >59pg/n	nl									
Results	True positives:	293	False negatives:	56	False positives:	40	True negatives:	169			
Additional comme nts											
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	Low			
Overall risk of bias	Serious (Test thres random or consecu was excluded the s	holds were i itive people study was no	not pre-specified, bu or avoided inapprop ot downgraded for th	It optimised base riate exclusions is.)	ed on the data; it was . A subgroup analysis	unclear whe was carried	ther the study enroll out but as < 10% pc	ed opulation			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										
Index Test: Amyloid Amyloid Beta 1-42/tot	<b>Beta 1-42/Total Ta</b> aLtau ≤ 1 43	u									
Results	True positives:	292	False negatives:	57	False positives:	51	True negatives:	158			
Additional comme nts											
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 187	1								
Amyloid Beta 1-42/p-	tau, cut off ≤ 6.53									
Results	True positives:	282	False negatives:	67	False positives:	41	True negatives:	168		
Additional comme nts										
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	Low		
Overall risk of bias	Serious (Test thres random or consecu was excluded the s	holds were utive people study was no	not pre-specified, bu or avoided inapprop ot downgraded for th	ut optimised base priate exclusions iis.)	ed on the data; it was . A subgroup analysis	unclear whe was carried	ther the study enroll out but as < 10% pc	ed opulation		
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	INOTEST Amyloid B	eta 1-42 EL	ISA, cut off <519pg/	′ml						
Results	True positives:	222	False negatives:	50	False positives:	106	True negatives:	264		
Additional comme nts										
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 Ta	u									
Total tau, INNOTEST	hTau-Ag ELISA, cut	t off >362pg/	/ml							
Results	True positives:	221	False negatives:	51	False positives:	80	True negatives:	290		
Additional comme nts										
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	Low		
Overall risk of bias	Serious (Test thres random or consecu was excluded the s	holds were i itive people study was no	not pre-specified, bu or avoided inapprop ot downgraded for th	ut optimised base riate exclusions is.)	ed on the data; it was . A subgroup analysis	unclear whe was carried	ther the study enroll out but as < 10% pc	ed opulation		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									
Index Test: p-tau 18	1									
p-tau 181, INNOTEST	FELISA, cut off >61p	og/ml								
Results	True positives:	209	False negatives:	63	False positives:	43	True negatives:	327		
Additional comme nts										
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 thres random or consecu was excluded the s	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 Tai	u									
Amyloid Beta 1-42/tot	al tau, ≤ 2.48										
Results	True positives:	236	False negatives:	36	False positives:	79	True negatives:	291			
Additional comme nts											
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	Low			
Overall risk of bias	Serious (Test thres random or consecu was excluded the s	holds were itive people study was no	not pre-specified, bu or avoided inapprop ot downgraded for th	ut optimised bas priate exclusions is.)	ed on the data; it was . A subgroup analysis	unclear whe was carried	ther the study enroll out but as < 10% pc	ed opulation			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										
Index Test: Amyloid	Beta 1-42/p-tau 187	1									
Amyloid Beta 1-42/ p-	tau 181, cut off $\leq 15$	5.10									
Results	True positives:	232	False negatives:	40	False positives:	59	True negatives:	311			
Additional comme nts											
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 thres random or consecu was excluded the s	sholds were utive people study was no	not pre-specified, bu or avoided inapprop t downgraded for th	ut optimised base priate exclusions his.)	ed on the data; it was . A subgroup analysis	unclear whe was carried	ther the study enrolled out but as < 10% population			
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  $\geq$ 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 wa	as carried out exclud	ling >30% study	population.)					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Overall Not serious Indirectness									
DLB versus non-DLI	B dementias									
Index Test: Lewy body composite risk score, LBCRS, $\geq$ 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 $\geq$ 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 wa	as carried out exclud	ling >30% study	population.)					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious	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 fa	acility							
Inclusion criteria	People referred to	the facility d	ue to memory loss,	behavioural disc	order and/or cognitive of	deterioration			
Exclusion criteria	People with previou the patient selection	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 Coch	rane Review	,						
Age	Not stated in Coch	lot stated in Cochrane Review							
Presentation	Memory loss, beha	vioural disor	der and/or cognitive	e deterioration.					
Reference standard	Clinician diagnosis based on DSM -III-R								
Dementia versus no	Dementia versus no dementia								
Index Test: Informar	t Questionnaire on item, 3.6 primary th	Cognitive	Decline, IQCODE( study	16 item, >3.5)					
Results	True positives:	83	False negatives:	7	False positives:	4	True negatives:	19	
Additional comme nts	The random group suspected demention	of patients r a at baseline	eferred to the aged e.	care assessmer	nt team were excluded	from analys	is as they did not ha	ive	
Risk of bias	Patient selection:	High	Index test:	Unclear	Reference standard:	Unclear	Flow and timing:	Unclear	
Overall risk of bias	Serious (Inappropr	iate exclusio	ns at patient selecti	on 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, C of Four Sets of Clini	anuto A, Bergallo M cal Criteria for Vaso	/I, Herrman cular Deme	n FR, Hof PR, Mayo ntia. Am J Psychia	or P-A, Michel J try 2002; 159:8	I-P, Giannakopoulos 2–87.	P. Clinicop	athological Validat	ion Study	
Country	Switzerland								
Setting	University of Genev	va Hospitals	Belle-Idée						
Inclusion criteria	Diagnosis of demenerations and h	ntia and sub nead compu	sequent autopsy ex terized tomography	amination; clinic (CT) or magneti	ally evaluated, includin c resonance imaging (	ng neurologi (MRI), within	cal and mental statu 6 months of their de	.s eath.	
Exclusion criteria	Patients with major	neuropsych	niatric illness, alcoho	olism, or Parkins	on's disease were exc	luded.			
Sex	61.8% male								
Age	Mean age 84.7 yea	lean age 84.7 years (SD 6.4)							
Presentation	Dementia								
Reference standard	Cases of Alzheime on the presence of AD and the study a	ases of Alzheimer's disease were confirmed by using the National Institute on Aging-Reagan criteria. VaD was assessed based n the presence of both macroscopic and microscopic vascular pathology. Cases that satisfied both neuropathological criteria for D 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-A NINDS-AIREN, possil	NINDS-AIREN (possible) EN, possible diagnosis								
Results	True positives:	11	False negatives:	9	False positives:	11	True negatives:	58	
Additional comme nts	The data for the IC	D-10 and D	SM-IV was not extra	icted as updated	I versions of these crite	eria 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-A	IREN (probable)								
NINDS-AIREN, proba	ble 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 comme nts	The data for the IC	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	Not serious							
Index Test: ADDTC	(possible)								
ADDTC, possible diag	gnosis								
Results	True positives:	14	False negatives:	6	False positives:	15	True negatives:	54	
Additional comme nts	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 dia	gnosis								
Results	True positives:	5	False negatives:	15	False positives:	6	True negatives:	63	
Additional comme nts	The data for the IC	D-10 and D	SM-IV was not extra	icted as updated	versions of these crite	eria exist.			
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	Low	

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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 Ashle	v A Miller F Alexee	eva O Zano	lers I King V Vali	dity of the Mon	treal Cognitive Asse	ssment 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	USA							
Setting	Memory disorders	Memory disorders clinic at Grady memorial Hospital, Atlanta.							
Inclusion criteria	African American,	African American, $\geq$ 50 years old, cognitive assessment at the clinic.							
Exclusion criteria	Pre-existing condit affect their perform	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 (SI	0 9.5)							
Presentation	Suspected dement	Suspected dementia							
Reference standard	Clinician diagnosis based on neuropsychological battery								
Dementia versus no	dementia (MCI inc	luded							
Index Test: Montrea MoCA ≤23	I Cognitive Assess	ment, MoC/	A (<24)						
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:	Patient     High     Index test:     Low     Reference     Low       selection:							

Goldstein FC, Ashle impairment and dem	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	Serious (Study only recruited African Americans ≥ 50 years old.)						
Index Test: Montreal MoCA ≤24	Il Cognitive Assessment, MoCA (<25)							
Results	True positives:	27	False negatives:	0	False positives:	42	True negatives:	12
Additional comme 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:	High	Index test:	Low	Reference standard:	Low		
Overall indirectness	Serious (Study only	y recruited A	frican 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	Clinician diagnosis based on DSM-IV-TR criteria plus all available information (including index tests)
standard	
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: Informan	t Questionnaire on	Cognitive	Decline, IQCODE (	16 item, >4.1)				
IQCODE (16 item), op	timised threshold fo	r 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 refere	ence diagnos	sis was not indepen	dent of the index	tests; optimised test	thresholds w	vere used.)	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall Not serious								
Index Test: MMSE (<24)								
SMMSE (Molloy, 1991	I version of MMSE).	Optimised t	hreshold for study <	24				
Results	True positives:	126	False negatives:	26	False positives:	14	True negatives:	38
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	High	Flow and timing:	Low
Overall risk of bias	Serious (The refere	ence diagnos	sis was not indepen	dent of the index	tests; optimised test	thresholds w	vere used.)	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

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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 r	eferred by th	neir primary care phy	ysicians.					
Exclusion criteria	Patients lacking an	informant to	complete the IQCO	DDE for them.					
Sex	44.0% male	.0% male							
Age	Mean age 76.9 yea	ean age 76.9 years (SD 8.9)							
Presentation	Memory problems								
Reference standard	DSM-IV-TR criteria	DSM-IV-TR criteria plus all available information (including index tests)							
Dementia verus no dementia (incluídes MCI)									
Index Test: Rowland Universal Dementia Assessment Scale, RUDAS (<21)									
Rowland Universal De	ementia Assessment	t Scale, RUE	DAS (<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 refere	ence diagno	sis was not indepen	dent of the index	tests; optimised test	thresholds w	vere used.)		
Indirectness	Patient selection:	Patient     Low     Index test:     Low     Reference     Low       selection:							
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<br/>blinded prospective study of urine neural thread protein measurements in patients with suspected Alzheimer's disease. J Am Med Dir Assoc<br/>2007; 8: 21-30.Study typeImage: Study type

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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 morning urine).	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 yea	Mean age 69.6 years (SD 11.7)						
Presentation	People had cogniti	ve impairme	nt, memory impairm	nent or suspecte	d dementia			
Reference standard	AD diagnosed usin	g the NINCI	DS-ARDRA criteria,	MCI using the C	auality Standards Subo	committee of	the AAN (AAN MCI	criteria).
AD (probable and po	ossible) versus non	-AD (includ	ling MCI)					
Index Test: Urinary AD7c-NTP (2)	: Urinary AD7c-NTP (22ug/ml) 7c-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	verall 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 comme nts	The probable AD g	roup was ex	cluded from this su	bgroup analysis	(n= 35).			
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	High

Goodman I, Golden ( blinded prospective 2007; 8: 21-30.	G,Flitman S, Xie K, study of urine neu	McConville ral thread p	M, Levy S ,Zimme rotein measureme	erman E, Lebed nts in patients	eva Z, Richter R, Min with suspected Alzhe	agar A, Ave eimer's dise	erback P. A multi-ce ease. J Am Med Dir	enter Assoc
Overall risk of bias	s 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 A Urinary AD7c-NTP (22	AD7c-NTP (22ug/ml 2ug/ml)	)						
Results	True positives:	20	False negatives:	33	False positives:	22	True negatives:	58
Additional comme nts	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	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, Englur Neuropathologically	nd E, Brunnstrom H, Brun A, Erikson C, Warkentin S, Passant U. The Accuracy of Short Clinical Rating Scales in / Diagnosed Dementia. The American Journal of Geriatric Psychiatry 2010; 18: 810- 820.								
Exclusion criteria	Chronic psychosis neurological sympt	and epileps oms and a c	y, severe somatic di condition that did no	isease, severe h t allow the applic	ead injury, addiction, s ation of the three clini	stroke with re cal rating sc	emaining gross focal ales.		
Sex	41.1% male	1.1% male							
Age	Mean age at onset	64.0 years	(no SD stated)						
Presentation	Dementia with subl	Dementia with subtype diagnosis required							
Reference standard	Neuoropathology u Diseases (Wallin, 1 and Manchester gr	ising standa 1994) and in oups criteria	rdised procedures c accordance with cr n, 1994; Neary, 1998	ptimised over tir iteria for AD (Bra 3).	ne with reference to th aak, 1991; CERAD), D	ne Swedish ( LB (McKeith	Consensus on Deme , 2005) and FTD (Th	entia ne Lund	
AD (including mixed	VaD and AD) versu	us FTD and	VaD alone						
Index Test: AD scale AD scale, cut-off $\geq 6$	e (≥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 st	tudy was not	t downgraded for su	bgroup analysis	as <10% population v	vas excludeo	J.)		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								
FTD versus AD and	VaD								
Index Test: FTD scale FTD scale, cut- off $\geq 6$	<b>le (≥6)</b> ∂.								
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 st	udy was not	t downgraded for su	bgroup analysis	as <10% population v	vas excludeo	d.)		
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 mixe	d VaD and AD) vers	sus AD alor	ne and FTD					
Index Test: Hachins	ki Ischemic score, I	HIS (≥7)						
Hachinski Ischemic so	core (HIS), cut-off ≥ 7	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							

# 1 **P.1.8 H**

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 specifie	ed						
Prion disease versu	s 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 Ta Tau, >1150 pg/ml (Inv	<b>u</b> <i>v</i> itrogen ELISA)							
Results	True positives:	213	False negatives:	32	False positives:	57	True negatives:	118
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (Multiple th test was interpreted	resholds we d without kno	ere tested and uncle owledge of index test	ar whether resea st.)	archers were blind to r	eference tes	st results or that the	reference
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: CSF 14-3	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, Immunoblottin	g with ambiguous re	sults ignore	d					
Results	True positives:	183	False negatives:	10	False positives:	76	True negatives:	30
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Very serious (> 28% researchers were b	% population lind to reference	excluded as 14-3-3 ence test results or	3 results were an that the reference	nbiguous; multiple three test was interpreted	esholds wer without kno	e tested and unclear wledge of index test.	whether )
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	rall 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 centre	psychiatric	hospital and cogniti	ve function clinic	based in a regional n	euroscienco	9	
Inclusion criteria	Patients attending r	memory/cog	nitive function clinic	s with an inform	ant.			
Exclusion criteria	Patients lacking an	informant to	complete the IQC	ODE 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: Informan	t Questionnaire on	Cognitive	Decline, IQCODE (	26 item, >3.5)				

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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.								
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 optimis	sed test thre	shold was used.)					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

Hancock P and Larn	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	Prospective cohort						
Country	UK							
Setting	A memory clinic in	a psychiatri	c hospital and a cog	nitive functional	clinic in a regional neu	uroscience c	entre.	
Inclusion criteria	People referred to	the memory	clinics over a 23- m	onth period (Fe	bruary 2008- Decembe	er 2009).		
Exclusion criteria	Not stated							
Sex	58.0% male							
Age	Mean age 63.3 yea	Mean age 63.3 years (SD 12.6)						
Presentation	Suspected dement	Suspected dementia						
Reference standard	Clinician diagnosis 1993; McKeith 199	using DSM 6, 1999; Ne	-IV for dementia and ary, 1998 and Peter	d established crit sen 1999.)	teria for dementia subt	ypes (McKha	ann, 1984, 2001; Ro	oman,
Dementia versus no	t dementia (includii	ng MCI)						
Index Test: Test You	ır Memory, TYM (≤4	2)						
Test your memory (T)	/M), 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 Larn	er L. Test your mer	nory test: d	liagnostic utility in	a memory clini	ic population. Int. Joi	urnal Geriat	r Psych 2011; 25: 9	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 You Test your memory (TY	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 comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (Optimised	l test thresho	old.)					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE, ≤ 23/30 (Folst	<b>24)</b> ein version)							
Results	True positives:	56	False negatives:	15	False positives:	7	True negatives:	132
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (Optimised	I test thresho	old.)					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		

Hancock P and Larn	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: Addenbr	ooke's Cognitive E	xamination	-Revised, ACE-R (	<74)				
Addenbrooke's Cognit	ive Examination-Re	vised, ACE-	R (<74)					
Results	True positives:	35	False negatives:	4	False positives:	7	True negatives:	94
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (Optimised	I test thresho	old.)					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

1

Hanyu H, Shimizu S scintigraphy in the c 384.	, Hirao K, Sakurai H, Iwamoto T, Chikamori T, Hida S et al. The role of 123-I Metaiodobenzylguanidine myocardial Jiagnosis of Lew Body Disease in patients with dementia in a memory clinic. Dementia Geriatr Cogn Disord 2006; 22: 379-
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 scintigraphy in the o 384.	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 versu	s other dementias							
Index Test: 123I-MIB	BG cardiac scintigra	phy						
and SPECT were per After scatter correctio dividing the count der controls obtained at th	Inderstanding approximate 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	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							

1

Harris JM, Gall C, Th dementia. Neurolog	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, Th dementia. Neurology	ompson JC, Richa / 2013; 20: 1881-18	rdson AMT 87.	, Neary D et al. Ser	nsitivity and spe	ecificity of FTDC crite	eria for beha	avioural frontotem	poral	
Sex	58.2% male	58.2% male							
Age	Mean age 60.7 yea	Vlean age 60.7 years (SD not calculable)							
Presentation	Early onset demen	Early onset dementia							
Reference standard	Neuropathology - c	Neuropathology - criteria not stated							
Probable by FTD ver	rsus not bv FTD (in	cluding pos	ssible)						
Index Test: FTDC criteria for bvF	i <b>teria for bv FTD</b> ΓD (Rascovsky, 201 <sup>-</sup>	1)							
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 exc	ludes third c	of sample at initial so	creening)					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								
Possible by FTD ver	sus not bv FTD								
Index Test: FTDC criteria for bvF	i <b>teria for bv FTD</b> ID (Rascovsky, 201 <sup>-</sup>	1)							
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 exc	ludes third o	of sample at initial so	creening)					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								

1

Heath CA, Cooper S Annals of Neurology	A, Murray K, Lowm / 2010; 6: 761-770.	an A, Henr	y C, MacLeod MA e	et al. Validation	of diagnostic criteria	a for variant	Creutzfeldt-Jakob	Disease.	
Study type	Retrospective coho	Retrospective cohort							
Country	UK	UK							
Setting	National CJD Surve	eillance Unit	t						
Inclusion criteria	Cases of suspecter vCJD or an alterna	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 b	iopsy							
CJD (probable and p	oossible) versus no	t CJD							
Index Test: WHO CJ	D 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 und consecutive or rand	lear whethe	r the index test was of patients was enr	interpreted with olled or inapprop	out knowledge of the r priate exclusions were	esults of the avoided.)	reference test; whe	ther a	
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low			
Overall indirectness	Serious (Mean age	e at onset< 4	0 years old)						
CJD (probable) vers	us not CJD (includi	ing possibl	e CJD)						
Index Test: WHO CJ Diagnostic criteria for	D criteria CJD (WHO, 2002)								
Results	True positives:	88	False	18	False positives:	0	True negatives:	45	

1

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 und consecutive or rand	erious (It was unclear whether the index test was interpreted without knowledge of the results of the reference test; whether a onsecutive 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< 4	0 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	Sermany						
Setting	Memory clinic of the	e Central In	stitute for Mental He	ealth, University	of Heidelberg			
Inclusion criteria	People referred to t	he memory	clinic with cognitive	disturbances				
Exclusion criteria	Not stated							
Sex	Not stated							
Age	Mean age 68.6 yea	rs (SD8.6)						
Presentation	Suspected dement	ia						
Reference standard	AD diagnosed acco specified. No deme available to clinicia	ording to the entia group i ns during di	NINCDS-ADRDA on ncluded people with agnosis.	criteria; VD accor MCI and no coo	rding to NINDS-AIREN gnitive disturbances. T	I criteria; crit he MRI and	eria for DLB and FT CERAD battery resu	D not ults were
Dementia versus no	dementia							
Index Test: MRI MRI using T1. double echo and FLAIR sequence.								
Results	True positives:	ue positives: 46 False 4 False positives: 23 True negatives: 28 negatives:						
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 i thresholds were us	'ery serious (The index tests were carried out with knowledge of the primary care diagnosis and it is unclear whether pre-specified presholds 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 b CERAD battery. It cons MMSE; Word List Test them after a delay).	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 comme nts									
Risk of bias	Patient selection:	Low	Index test:	Unclear	Reference standard:	High	Flow and timing:	Low	
Overall risk of bias	Very serious (The i thresholds were us	ndex tests v ed; the refer	vere carried out with rence standard diag	knowledge of th nosis used all av	ne primary care diagno vailable data including	osis and it is the index te	unclear whether pre st results)	-specified	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								

1

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- Nucl Med. 2000; 41:	Bohmer KA ,Hanson M, Krain B, Hulette C, Earl N etal. FDG PET imaging in patients with pathologically verified dementia. J 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.
	lomenting.

#### 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 comme nts	Data was not extra neuropathology as	cted to exan a newer ver	nine the diagnostic f	est accuracy of RDA is now in ι	the NINCDS-ADRDA ( use (2011).	clinical criter	ia compared to	
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	n KA, Gerada B, Carvalho PA, Satlin A.The scintigraphic appearance of Alzheimer's disease: a prospective study using
technetium-99m-HM	PAO SPECT. J Nucl Med 1992; 33: 181–185.
Study type	Prospective cohort

Country

USA

Holman BL, Johnson technetium-99m-HM	n KA, Gerada B, Carvalho PA, Satlin A.The scintigraphic appearance of Alzheimer's disease: a prospective study using PAO 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.

### 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 comme nts	In the absence of in having pattern A (n disorders including	nformation a lormal). The depression.	bout which pattern i non-AD group cons	s considered dia sisted of patients	agnostic for AD we onl diagnosed with other	y analysed A dementias a	AD versus non-AD fo and other non-demen	or not ntia
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Serious (People wi	th uncertain	clinical diagnoses (	> 10% population	on) were excluded fror	n analysis)		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

# 1 **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, D controls and an age-	ragon M, Poljansky -matched random s	ν S, Haen E, ample. Νει	, Schmitz E, et al. 0 Irobiol Aging 2006	Cerebrospinal fl ; 27: 1202–11.	uid tau and beta-am	yloid in Alzh	eimer patients, die	sease
Study type	Prospective cohort	Prospective cohort						
Country	Germany							
Setting	In-patient service a Regensburg, Germ	nd/or memo any.	ory disorders outpati	ent clinic at State	e Hospital for Psychia	try and Psycl	notherapy, Bezirksk	linikum
Inclusion criteria	Participants undergoing the Stste Hospital.	oing diagno	ostic procedure for s	uspected demer	ntia or cognitive declin	e in a memo	ry clinic or in-patient	t clinic at
Exclusion criteria	Not stated							
Sex	43.0% male							
Age	Mean age 65.5 yea	ars (SD 10.2	)					
Presentation	Suspected cognitiv	e decline or	dementia.					
Reference standard	DSM-III-R, DSM-IV according to NINCI	′ criteria for DS-ADRDA;	dementia with all oth Newcastle criteria	ner available test was used for DL	t information apart fror B.	n CSF index	test results. AD dia	gnosed
AD versus other den	nentias							
Index Test: Amyloid	Beta 1-42							
Beta Amyloid 1-42 in	CSF, INNOTEST EL	_ISA, 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 u were avoided; the t of the reference dia	inclear whet est threshol agnosis; a si	her a consecutive o ds were not pre-spe ubgroup analysis wa	r random sample ecified and it is u as used where >	e of patients was enro nclear whether the ind 10% study population	lled and whe ex test was i was exclude	ther inappropriate e nterpreted without k d.)	xclusions (nowledge
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Total Tau		cut off 400p	a/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 comme nts								
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 comme nts								
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 comme nts									
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 comme nts									
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								

# 1 **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 T.I. Arlt S. Kellmn M. Mullen W. Fichenlaub M. Mischak H. Wiedmann K. Pentide Fingerprinting of

1

Alzheimer's Disease	in Cerebrospinal F	luid: Identi	fication and Prosp	ective Evaluati	on of New Synaptic E	Biomarkers.	PLoS ONE 2011; 6	5: e26540.
Study type	Prospective cohort	Prospective cohort						
Country	Germany	Germany						
Setting	University Hospital	Hamburg- I	Eppendorf memory	clinic				
Inclusion criteria	People referred to	the memory	clinic of the Univers	sity Hospital Har	nburg- Eppendorf.			
Exclusion criteria	Not stated							
Sex	49.0% male							
Age	Mean age 65.3 yea	ars (12.3)						
Presentation	Memory problems							
Reference standard	ICD-10 and the Na Disorders Associat to the criteria of Pe	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 ETD was diagnosed according to the Lund–Manchester criteria						
AD versus non-AD (	AD versus non-AD (excluding MCI)							
Index Test: Mass sp	ec(trometry)							
CE-MS analysis was Daltonic).	performed as descril	bed using a	P/ACEMDQ (Beckn	nan Coulter, Ful	lerton, USA) system or	n-line couple	d to a Micro- TOF M	IS (Bruker
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	<i>verall risk of bias</i> 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 A&42, 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 comme nts								
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							

1

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. Clinic Patients Aged	An Investigation of over 75 Years. De	the Utility nent Geriat	of the Addenbrook r Cogn Disord 201	ce's Cognitive E 5; 40:222–232.	Examination III in the	Early Deteo	tion of Dementia in	n Memory
Sex	61.0% male	61.0% male						
Age	Mean age 80.0 yea	ars (2.7)						
Presentation	Memory or other co	ognitive prob	olems					
Reference standard	Dementia was diag MCI.	nosed base	d on DSM-IV; AD a	ccording to NIN	CDS-ADRDA; NINCDS	S-AIREN for	VaD; Peterson crite	ria for
Dementia versus no	dementia							
Index Test: Addenbr	ooke's Cognitive E	xamination	-III, ACE- III (<88)					
Addenbrooke's Cogni		40E- III (<88	5) 			47		47
Results	I rue 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 pop	oulation was	confined to >75 yea	ars)				
Index Test: Addenbr Addenbrooke's Cogni	ooke's Cognitive E tive ExaminationIII, A	xamination	-III, ACE- III (<84) <sup>4</sup> )					
Results	True positives:	24	False negatives:	2	False positives:	13	True negatives:	20
Additional comme nts								
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (Optimised	I threshold u	ised for analysis.)					
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low		
Overall	Serious (Study pop	ulation was	confined to >75 year	ars)				

Jubb MT, Evand JJ. Clinic Patients Aged	An Investigation of l over 75 Years. Der	the Utility nent Geriat	of the Addenbrook r Coan Disord 201		xamination III in the	Early Detec	ction of Dementia ir	n Memory
indirectness				-,				
Index Test: Addenbr Addenbrooke's Cogni	<b>ooke's Cognitive E</b> tive ExaminationIII, A	xamination	<b>-III, ACE- III (&lt;81)</b> 1)					
Results	True positives:	21	False negatives:	5	False positives:	10	True negatives:	23
Additional comme nts								
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	rall   Serious (Study population was confined to >75 years )     rectness   Serious (Study population was confined to >75 years )							
Index Test: Addenbr Addenbrooke's Cogni	rooke's Cognitive E tive ExaminationIII, A	xamination	<b>-III, ACE- III (&lt;82)</b> 2)					
Results	True positives:	21	False negatives:	5	False positives:	1	True negatives:	32
Additional comme nts								
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (Optimised	I threshold u	sed for analysis.)					
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low		
Overall indirectness	Serious (Study pop	oulation was	confined to >75 yea	ars)				

# 1 **P.1.11 K**

Kaneta T, Nakatsuka detection of hot spo Medicine 2016; 41: e	۱ M, Nakamura K, S ts at the primary se ۱1-6.	eki T, Yama ensorimoto	aguchi S et al. Impi r area for the diagr	roved diagnosti losis of Alzhein	ic accuracy of SPEC ner disease in a com	T through s munity-bas	tatistical analysis a ed study. Clinical N	Ind the luclear
Study type	Prospective cohort							
Country	Japan							
Setting	Memory clinic at O	saki-Tajiri S	KIP Centre					
Inclusion criteria	Patients visiting the of dementia subtyp Screening instrume	e clinic with be; medical t ent and Weo	a previous diagnosis reatment for demen chsler Memory Scale	s of dementia ba tia for > 3 month e-Revised Neuro	sed on DSM-IV, a CD is and additional evide psychological Tests.	R of 1+ and ence of deme	who received a final entia on the Cognitiv	diagnosis e Abilities
Exclusion criteria	Patients with depre	ession accor	ding to the Geriatric	Depression Sca	ale.			
Sex	23.6% male							
Age	Mean age 81.6 yea	ars (SD 5.0)						
Presentation	Dementia with sub	type to be d	etermined					
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) verse	us not AD						
Index Test: 99mTc-E 99mTc-ECD SPECT images by specialist.	CD SPECT, visual was carried out using	assessmen g a triple-he	nt method aded gamma camer	a (Prism Irix) wit	th high-resolution fan t	peam collima	ators. Visual assessr	ment of
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	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 comme nts								
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-E	CD SPECT, automa	ated and vis	sual method		h high recelution for h		tore Automated dia	~~~`~
based on visual asses of 14.2%.	ss ment and Easy Z-	score imag	ing system with a cu	a (Prism inx) will it-off value for di	scriminating between	healthy cont	rols and patients wit	h early AD
Results	True positives:	20	False negatives:	28	False positives:	6	True negatives:	35
Additional comme nts								
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-E	CD SPECT, positiv	e SMG sigr	า					

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 comme nts								
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-E 99mTc-ECD SPECT v sensorimotor hotspot	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 botspot sign and visual assessment							
Results	True positives:	31	False negatives:	17	False positives:	15	True negatives:	26
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Unclear	Flow and timing:	Low
Overall risk of bias	<b>rall risk of bias</b> 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 comme nts								
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							

1

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, I bodies: a retrospect	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	of DLB						
Reference standard	Clinician diagnosis	- not suppor	rted by any specific	set of diagnostic	c criteria, but using the	results of th	e imaging	
DLB vs no-DLB								
Index Test: 123I-FP-								
MEDISO Nucline X-R photopeak window at	ing/4R SPECT came 159keV and 6% upp	era dedicate	d for brain imaging v r scatter windows	with low-energy	high-resolution collima	ators. 128 pro	ojections acquired w	ith a
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 par	rt of the reference s	tandard)				
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall Not serious Indirectness								

1

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 in the cerebrospinal	C, Takahashi H, Ku fluid of suspected	rohara K, A Creutzfeldt	nderson P, Gibbs -Jakob disease pa	CJ Jr. An enzyr tients. Ann Neu	ne-linked immunoso Irol 2000; 48: 395–39	rbent assay 8.	y to quantify 14-3-3	proteins
CJD (definite and pr	obable) versus not	CJD						
Index Test: CSF 14-3	3-3 ELISA							
CSF 14-3-3 protein de	etected by ELISA wit	h 8.3ng/ml o	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 tl enrolled or inappro reference standard	nreshold wa priate exclus or the refer	s not pre-specified a sions avoided; the ir ence standard resul	and it was uncleandex test results ts were interpret	ar whether: a consecut were interpreted witho ed without knowledge	tive or rando out knowled of the resul	om sample of patient ge of the results of th ts of the index test.)	s was ie
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
CJD (definite) versu	s not CJD							
Index Test: CSF 14-3 CSF 14-3-3 protein de	<b>3-3 ELISA</b> etected by ELISA wit	h 8.3ng/ml c	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 (Subg whether: a consect interpreted without knowledge of the re	roup analys utive or rand knowledge esults of the	is with >10% popula om sample of patien of the results of the index test.)	ation excluded, ti nts was enrolled reference standa	he test threshold was or inappropriate exclu ard or the reference st	not pre-spec sions avoide andard resu	sified and it was uncl ed; the index test res Its were interpreted	ear sults were without
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall	Not corious							
indirectness	Not senous							

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 unc index test results w were interpreted wi	lear whethe ere interpre thout knowle	r: a consecutive or r ted without knowled edge of the results o	random sample o ge of the results of the index test.	of patients was enrolle of the reference stand )	d or inappro dard or the r	priate exclusions av eference standard re	oided; the esults		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									
CJD (definite) versus	s not CJD									
Index Test: CSF 14-3	3-3 immunoblotting									
CSF 14-3-3 protein de	etected by immunobl	otting								
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 patients was enrolle of the reference sta	analysis wit ed or inappr andard or the	th >10% population opriate exclusions a e reference standard	excluded and it v voided; the inde d results were in	was unclear whether: x test results were inte terpreted without know	a consecutiverpreted with	ve or random sample hout knowledge of th e results of the index	e of e results test.)		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									

1

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 Be tomography in the d	rckel BNM, Herholz iagnosis of the beh	x K, Dols A, avioural va	van der Flier WM o riant of Frontotem	et al. The added poral Dementia	l value of 18-Fluorod ı.	eoxyglucos	e-positron Emissio	on
Study type	Retrospective coho	ort						
Country	The Netherlands							
Setting	VU Medical centre	Alzheimer's	Centre					
Inclusion criteria	Clinical suspicion c the scan.	Inical suspicion of bvFTD; no MRI abnormalities characteristic of a neurodegenerative disorder; 2 years of clinical follow up after ne scan.						
Exclusion criteria	None							
Sex	81.0% male	1.0% male						
Age	Mean age 65.0 (SE	ean age 65.0 (SD 8.1)						
Presentation	Suspected bvFTD	uspected bvFTD						
Reference standard	FTD diagnosed acc	TD diagnosed according to Neary (1998) plus functional decline at 2 years.						
bvFTD/fd+ versus no	t bvFTD/fd+							
Index Test: FDG-PE								
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 comme nts	bvFTD/fd+ refers to	bvFTD with	n 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 of Parkinson's disea	J-B, Godot J, Voge se dementia: their	el T, Schwei usefulness	iger L, Chayer S, K and limitations in	althenbach G. elderly patients	The Movement disor 6. J. Neurol 2013; 260	ders Societ ): 2569-2579	y criteria for the dia 9.	agnosis		
Country	France	France								
Setting	Strasbourg geriatri	c centre								
Inclusion criteria	≥ 65 years old; PD	diagnosed v	with the UK PDS Bra	ain bank criteria;	stable motor function;	; CDR. 0.5 a	nd MMSE> 16.			
Exclusion criteria	Dementia due to a stroke, anticholiner	mentia due to a cause other than PD; delirium < 3 months before study inclusion; severe depressive syndrome; previous major oke, anticholinergic treatment and unable to consent.								
Sex	40.0% male	).0% male								
Age	Mean age 80.5 yea	ean age 80.5 years (SD 4.9)								
Presentation	Suspected PDD									
Reference standard	Clinician diagnosis	iician diagnosis								
PDD versus not PDD	)									
Index Test: Moveme Movement disorders of	ent disorders criteria for PDD (≤120) criteria for PDD, cut-off ≤ 120									
Results	True positives:	ue positives: 25 False of negatives: 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 thres	hold was no	ot pre-specified.)							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									
Index Test: Moveme Movement disorders of	nt disorders criteria	a for PDD (s -off ≤ 123	≦123)							
Results	True positives:	29	False negatives:	2	False positives:	2	True negatives:	7		
Additional comme nts										
Risk of bias	Patient	Low	Index test:	High	Reference	Low	Flow and	Low		

Kiesman M, Canson of Parkinson's disea	J-B, Godot J, Voge se dementia: their	el T, Schwei usefulness	iger L, Chayer S, K and limitations in	althenbach G. elderly patients	The Movement disord s. J. Neurol 2013; 260	ders Society ): 2569-2579	v criteria for the dia	agnosis
	selection:				standard:		timing:	
Overall risk of bias	Serious (Test thres	hold was no	ot pre-specified.)					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Moveme Movement disorders of	nt disorders criteria criteria for PDD, Cut-	a for PDD (: off ≤ 132	≤132)					
Results	True positives:	31	False negatives:	0	False positives:	5	True negatives:	4
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (Test thres	hold was no	ot pre-specified.)					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: FCSRT-I	R 3- FR (≤22)							
The Grober and Busc	hke's 3 and cued sel	lective remir	nding test with imme	diate recall (Fre	nch version) 3 Free re	calls. Cut-off	≦ 22	
Results	True positives:	26	False negatives:	5	False positives:	2	True negatives:	7
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (Test thres	hold was no	ot pre-specified.)					
Indirectness	Patient	Low	Index test:	Low	Reference	Low		

Kiesman M, Canson of Parkinson's disea	J-B, Godot J, Voge se dementia: their	el T, Schwei usefulness	ger L, Chayer S, K and limitations in	althenbach G. <sup>-</sup> elderly patients	The Movement disord 5. J. Neurol 2013; 260	ders Society ): 2569-2579	y criteria for the dia ).	agnosis
	selection:				standard:			
Overall indirectness	Not serious							
Index Test: Rey-Oster The Rey-Osterrieth co	errieth complex figure test, cu	u <b>re test, RO</b> ut-off ≤ 21	CF (≤21)					
Results	True positives:	28	False negatives:	3	False positives:	2	True negatives:	7
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (Test thres	hold was no	t pre-specified.)					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

1

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 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 w pre-specified thres	hether all pa hold.)	atients were included	d in the analysis	; unclear interval betw	een index a	nd reference tests; la	ack of a			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										
Index Test: MMSE (< MMSE carried out as	: <b>24)</b> part of the CAMDEX	test, cut-off	< 24.								
Results	True positives:	192	False negatives:	37	False positives:	25	True negatives:	69			
Additional comme nts											
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Unclear			
Overall risk of bias	Serious (Unclear w pre-specified thres	hether all pa hold.)	atients were included	d in the analysis	; unclear interval betw	een index a	nd reference tests; la	ack of a			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										

1

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, Enge Alzheimer disease a	edal K, Braekhus A nd associate disord	. Performar ders 2016: <i>'</i>	nce of cerebrospina 1: 8-14.	al fluid biomark	ers in Alzheimer dis	ease in a m	emory clinic in Nor	way.		
Study type	Retrospective coho	ort								
Country	Norway	orway								
Setting	Oslo University Hos	slo University Hospital								
Inclusion criteria	Patients undergoin	atients undergoing lumbar puncture for the study of amyloid beta and tau.								
Exclusion criteria	None									
Sex	53.7% male									
Age	Mean age 61 (SD 6	6.4)								
Presentation	Suspected dement	ia								
Reference standard	ICD-10 for dementi	a								
AD versus not AD										
Index Test: Amyloid Amyloid Beta 1-42 IN	<b>Beta 1-42</b> NOTEST ELISA, cut	-off < 550 p	g/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 Ta	J									
Total-tau, INNOTEST	ELISA with cut-offs	> 300 pg/ml	for people under 50	), > 450 pg/ml fo	r people 50-69, > 500	pg/ml for 70	or older			
Results	True positives:	90	False negatives:	48	False positives:	15	True negatives:	52		
Additional comme nts										

Knapsgog A-B, Enge Alzheimer disease a	edal K, Braekhus A nd associate disore	. Performar ders 2016: 1	nce of cerebrospina 1: 8-14.	al fluid biomark	ers in Alzheimer dis	ease in a m	emory clinic in Nor	way.
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 18 <sup>4</sup> p-tau, INNOTEST ELI	<b>l</b> SA, cut-off > 80 pg/r	nl						
Results	True positives:	65	False negatives:	73	False positives:	7	True negatives:	60
Additional comme 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							

1

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

Koikkalainena J, Rh D, Soininene H, Ren 11: 435–449.	odius-Meesterb H, nese AM et al. Diffe	Tolonena A rential diag	A, Barkhofc F, Tijms Inosis of neurodeg	sb B, Lemstrat enerative disea	o AW, Tongd T, Guerr ases using structural	erod R, Sch MRI data. N	uhd A, Ledigd C, R leurolmage: Clinica	lueckertd 1, 2016;	
Exclusion criteria	Not stated								
Sex	66.0% male								
Age	Mean age 64.0 yea	ars (8.0)							
Presentation	Cognitive complain	its							
Reference standard	Patients were diag Alzheimer's Diseas Aging-Alzheimer's Neary criteria; patie diagnosed using th l'Enseignement en et al., 2005)	atients were diagnosed with probable AD using the criteria of the National Institute for Neurological and Communicative Diseases zheimer's Disease and Related Disorders Association; all patients also met the core clinical criteria of the National Institute on ging-Alzheimer's Association guidelines for AD (McKhann et al., 1984; McKhann et al., 2011). FTD was diagnosed using the eary criteria; patients also met the core criteria from Rasckovsky (Neary et al., 1998; Rascovsky et al., 2011). VaD was agnosed using the National Institute of Neurological Disorders and Stroke and Association Internationale pour la Recherché et 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. Imaging data were as changes.	0 T, 1.5 T or 3.0 T M sessed visually for a	RI devices. trophy and	All scans include a 3 vascular	3-dimensional T	-1-weighted gradient e	cho sequenc	e and a fast FLAIR s	sequence.	
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	

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Koikkalainena J, Rh D, Soininene H, Ren 11: 435–449.	odius-Meesterb H, nese AM et al. Differ -	Tolonena A ential diag	, Barkhofc F, Tijms nosis of neurodeg	sb B, Lemstrab enerative diseas	AW, Tongd T, Guerro ses using structural	erod R, Sch MRI data. N	uhd A, Ledigd C, R leurolmage: Clinica	lueckertd al, 2016;
Overall risk of bias	Serious (Subgroup patients was enroll reference standard	analysis wh ed and inap or the refer	nere >10% population propriate exclusions rence test was interp	on excluded and were avoided; the preted independe	unclear whether: a col he index test was inte ently of the index test.)	nsecutive or rpreted witho	random sample of e out knowledge of the	eligible
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. Imaging data were as changes.	0 T, 1.5 T or 3.0 T M sessed visually for a	RI devices. trophy and v	All scans include a vascular	3-dimensional T1	I-weighted gradient ec	cho sequenc	e and a fast FLAIR s	sequence.
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 patients was enroll reference standard	analysis wh ed and inap or the refer	nere >10% population propriate exclusions ence test was interp	on excluded and were avoided; the preted independe	unclear whether: a col he index test was inte ently of the index test.)	nsecutive or rpreted witho	random sample of e out knowledge of the	eligible
Indirectness	Patient	Low	Index test:	Low	Reference	Low		
	selection:				standard:			
Overall indirectness	Selection: Not serious				standard:			

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	erall 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 Imaging data were as changes.	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	erall 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	Il 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 Imaging data were as changes.	0 T, 1.5 T or 3.0 T M sessed visually for a	RI devices trophy and v	All scans include a : /ascular	3-dimensional T	1-weighted gradient eo	cho sequenc	e and a fast FLAIR s	sequence.		
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				

Koikkalainena J, Rh D, Soininene H, Ren 11: 435–449.	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:				
Overall indirectness	Not serious								
FTD versus AD									
Index Test: MRI									
MRI imaging using 1. Imaging data were as changes.	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 patients was enroll reference standard	analysis wl ed and inap or the refe	here >10% population propriate exclusions rence test was interp	on excluded and s were avoided; f preted independe	unclear whether: a column the index test was interently of the index test.)	nsecutive or rpreted with	random sample of e out knowledge of the	eligible e	
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	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 enroll reference standard	ed and inapp or the refer	propriate exclusions ence test was interp	were avoided; to were avoided; to were avoided; to were avoid the second s	he index test was interently of the index test.)	rpreted with	out knowledge of the	;		
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 patients was enrolle reference standard	analysis wh ed and inapp or the refer	ere >10% populatio propriate exclusions ence test was interp	n excluded and were avoided; t preted independe	unclear whether: a con he index test was inte ently of the index test.)	nsecutive or rpreted with	random sample of e out knowledge of the	eligible e		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									
DLB versus non-DLE	3									
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		

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:	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	arall Not serious irectness									
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 patients was enroll reference standard	analysis wh ed and inap or the refer	ere >10% populatio propriate exclusions ence test was interp	n excluded and were avoided; t reted independe	unclear whether: a co he index test was inte ently of the index test.)	nsecutive or rpreted with	random sample of e out knowledge of the	ligible		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									
DLB versus AD										
Index Test: MRI MRI imaging using 1. Imaging data were as changes.	0 T, 1.5 T or 3.0 T M sessed visually for a	RI devices. trophy and v	All scans include a 3 /ascular	3-dimensional T	1-weighted gradient eo	cho sequenc	e 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.									
			negatives:						
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Unclear	Flow and timing:	High	
<b>Dverall risk of bias</b> 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 patients was enroll reference standard	analysis wh ed and inapp or the refer	ere >10% populatio propriate exclusions ence test was interp	n excluded and were avoided; t reted independe	unclear whether: a co the index test was inte ently of the index test.)	nsecutive or rpreted with	random sample of e out knowledge of the	eligible e	
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 as	sessed visually for a	trophy 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 Not serious								
VaD versus non-VaD	) dementias							
Index Test: MRI MRI imaging using 1.0 Imaging data were as changes.	0 T, 1.5 T or 3.0 T M sessed visually for a	RI devices. trophy and	All scans include a 3 vascular	3-dimensional T	1-weighted gradient eo	cho sequen	ce and a fast FLAIR s	sequence.
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 comme nts									
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 Imaging data were as changes.	0 T, 1.5 T or 3.0 T M sessed visually for a	RI devices. trophy and v	All scans include a 3 /ascular	3-dimensional T <sup>-</sup>	I-weighted gradient eo	cho sequenc	e and a fast FLAIR s	sequence	
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	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. Neurolmage: Clinical, 2016; 11: 435–449.								
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	Il 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 refer	ence test was interp	reted independe	ently of the index test.)	1			
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	Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								
AD versus non-AD d	lementias								
Index Test: MRI MRI imaging using 1.0 Imaging data were as	0 T, 1.5 T or 3.0 T M sessed using an aut	RI devices. <i>i</i> omatic imag	All scans include a 3 e quantification met	3-dimensional T <sup>^</sup> hod.	I-weighted gradient ec	cho sequenc	e and a fast FLAIR	sequence.	
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 test was interpreted independently of the index test.)								

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. Neurolmage: Clinical, 2016; 11: 435–449.									
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	Prall 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 Imaging data were as	0 T, 1.5 T or 3.0 T M sessed using an aut	RI devices. omatic imag	All scans include a a le quantification met	3-dimensional T hod.	1-weighted gradient ec	cho sequenc	e and a fast FLAIR	sequence.	
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 refer	ence test was interp	reted independe	ently 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 patients was enrolle reference standard	analysis wh ed and inapp or the refer	ere >10% populatio propriate exclusions ence test was interp	n excluded and were avoided; t reted independe	unclear whether: a con he index test was inte ently of the index test.)	nsecutive or rpreted with	random sample of e out knowledge of the	eligible e	
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	Not serious									
FTD versus DLB	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	s 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										

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 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-DLI	B 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									

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	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	as 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, Rh D, Soininene H, Rem 11: 435–449.	odius-Meesterb H, nese AM et al. Diffe	Tolonena A rential diag	, Barkhofc F, Tijms nosis of neurodege	sb B, Lemstrab enerative disea	AW, Tongd T, Guerre ses using structural	erod R, Sch MRI data. N	uhd A, Ledigd C, R leurolmage: Clinica	Rueckertd al, 2016;				
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	patients was enroll reference standard	tients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the ierence 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	ot serious										
DLB versus VaD												
Index Test: MRI												
MRI imaging using 1.0 Imaging data were as	0 T, 1.5 T or 3.0 T M sessed using an aut	RI devices.	All scans include a e quantification met	3-dimensional T <sup>r</sup> hod.	-weighted gradient ec	cho sequenc	e and a fast FLAIR s	sequence.				
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 patients was enroll reference standard	analysis wh ed and inap or the refer	ere >10% population propriate exclusions ence test was interp	n excluded and were avoided; t preted independe	unclear whether: a counce index test was international index test was international index test.)	nsecutive or rpreted with	random sample of e out knowledge of the	eligible e				
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low						
Overall indirectness	Not serious											
VaD versus non-Va	)											
Index Test: MRI MRI imaging using 1.0 Imaging data were as	0 T, 1.5 T or 3.0 T M sessed using an aut	RI devices. A	All scans include a 3	3-dimensional T <sup>2</sup> hod.	-weighted gradient ec	cho sequenc	e and a fast FLAIR s	sequence.				
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, Rho D, Soininene H, Rem 11: 435–449.	odius-Meesterb H, <sup>*</sup> ese AM et al. Diffe	Tolonena A rential diagi	, Barkhofc F, Tijms nosis of neurodege	sb B, Lemstrab enerative diseas	AW, Tongd T, Guerro ses using structural	erod R, Sch MRI data. N	uhd A, Ledigd C, R leurolmage: Clinica	Rueckertd al, 2016;
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 Imaging data were as	) T, 1.5 T or 3.0 T M sessed using an aut	RI devices. / omatic imag	All scans include a 3 e quantification met	3-dimensional T´ hod.	I-weighted gradient ec	cho sequenc	e and a fast FLAIR s	sequence.
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 patients was enroll reference standard	analysis wh ed and inapp or the refer	ere >10% populatio propriate exclusions ence test was interp	n excluded and were avoided; t reted independe	unclear whether: a con he index test was inte ently of the index test.)	nsecutive or rpreted with	random sample of e out knowledge of the	eligible e
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 Imaging data were as	RI sing 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. ere 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 wh	ere >10% populatio	n excluded and	unclear whether: a co	nsecutive or	random sample of e	ligible

Koikkalainena J, Rho D, Soininene H, Rem 11: 435–449.	odius-Meesterb H, lese AM et al. Diffe	Tolonena A rential diag	, Barkhofc F, Tijms nosis of neurodege	sb B, Lemstrab enerative disea	AW, Tongd T, Guerre ses using structural	erod R, Sch MRI data. N	uhd A, Ledigd C, R Ieurolmage: Clinica	Rueckertd al, 2016;			
	patients was enroll reference standard	itients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the ference 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	ot serious									
VaD versus FTD											
Index Test: MRI MRI imaging using 1.0 Imaging data were as	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 patients was enroll reference standard	analysis wh ed and inap or the refer	ere >10% populatio propriate exclusions ence test was interp	n excluded and were avoided; t reted independe	unclear whether: a con he index test was inten ently of the index test.)	nsecutive or preted with	random sample of e out knowledge of the	eligible e			
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 Imaging data were as	ex Test: MRI I 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. ging 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, Rho D, Soininene H, Rem 11: 435–449.	odius-Meesterb H, <sup>-</sup> nese AM et al. Diffei	Tolonena A rential diag	, Barkhofc F, Tijms nosis of neurodeg	sb B, Lemstrab enerative disea	AW, Tongd T, Guerro ses using structural	erod R, Sch MRI data. N	uuhd A, Ledigd C, R leurolmage: Clinica	Rueckertd al, 2016;		
Overall risk of bias	Serious (Subgroup patients was enroll reference standard	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible batients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the eference 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 E dementia. J Clin Epi	B, Teri L, Bowen J demiol 1994; 47: 10	, McCormic 61-1067.	k W, Pfanschmidt	ML. The mini m	ental state examinat	ion score a	nd the clinical diag	nosis of		
Study type	Prospective Cohort	t								
Country	USA									
Setting	Not stated									
Inclusion criteria	People with suspect primary care, neuro	cted dement plogy and ot	ia who had medical her speciality clinics	insurance cover	with a particular healt	h maintenar	nce organisation. Ide	ntified by		
Exclusion criteria	Previous diagnosis	of dementia	3							
Sex	45.9% male									
Age	Mean age 71.6 yea	ars (SD 8.8)								
Presentation	Suspected dement	ia								
Reference standard	DSM-IIIR criteria w	as used to c	liagnose dementia.							
Dementia versus no	dementia									
Index Test: MMSE (< MMSE, 25	:25)									
Results	True positives:	56	False negatives:	24	False positives:	7	True negatives:	46		
Additional comme nts	The data for cut off	s above 25	was not extracted a	s these values a	re not commonly used	l.				
Risk of bias	Patient	Low	Index test:	High	Reference	Low	Flow and	Low		

Koikkalainena J, Rho D, Soininene H, Rem 11: 435–449.	odius-Meesterb H, <sup>*</sup> lese AM et al. Diffe	Tolonena A rential diag	, Barkhofc F, Tijms nosis of neurodege	sb B, Lemstrab enerative disea	AW, Tongd T, Guerro ses using structural	erod R, Sch MRI data. N	uhd A, Ledigd C, R leurolmage: Clinica	Rueckertd al, 2016;
	selection:				standard:		timing:	
Overall risk of bias	Serious (It is unclear multiple pre-specifi standard diagnosis	ar whether the the the cut-offs v	he index test results vere used to determ	were interpreted ine the optimal of	d without knowledge o aut-off; the index test re	f the results esult was kn	of the reference sta own during the refer	ndard; ence
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE, 24	:24)							
Results	True positives:	50	False negatives:	30	False positives:	2	True negatives:	51
Additional comme nts	The data for cut off	s above 25	was not extracted as	s these values a	re not commonly used	l.		
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (It is unclear multiple pre-specifi standard diagnosis	ar whether the	he index test results vere used to determ	were interpreted ine the optimal o	d without knowledge o ut off; the index test re	f the results esult was kn	of the reference sta own during the refer	ndard; ence
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE, 23	:23)							
Results	True positives:	45	False negatives:	35	False positives:	0	True negatives:	53
Additional comme nts	The data for cut off	s above 25	was not extracted as	s these values a	re not commonly used	l.		

Koikkalainena J, Rho D, Soininene H, Rem 11: 435–449.	odius-Meesterb H, <sup>-</sup> nese AM et al. Differ	Tolonena A rential diag	, Barkhofc F, Tijms nosis of neurodege	sb B, Lemstrab enerative disea	AW, Tongd T, Guerro ses using structural	erod R, Sch MRI data. N	uhd A, Ledigd C, R eurolmage: Clinica	lueckertd II, 2016;		
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low		
Overall risk of bias	Serious (It is unclea multiple pre-specifi standard diagnosis	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 (< MMSE, 22	:22)									
Results	True positives:	45	False negatives:	35	False positives:	0	True negatives:	53		
Additional comme nts	The data for cut off	s above 25	was not extracted a	s these values a	re not commonly used	l.				
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low		
Overall risk of bias	Serious (It is unclea multiple pre-specifi standard diagnosis	ar whether the	he index test results vere used to determ	were interpreted ine the optimal c	d without knowledge o out off; the index test re	f the results esult was kn	of the reference sta own during the refer	ndard; ence		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									

# 1 **P.1.12** L

 Larner AJ. Addenbroke'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. Addenbro Neurosurgery 2007;	ooke's Cognitive Ex 109 : 491–494	camination	(ACE) for the diag	nosis and differ	rential diagnosis of d	lementia. Cl	inical Neurology a	nd		
Country	UK									
Setting	Cognitive function	ognitive function clinic								
Inclusion criteria	Consecutive new re	eferrals to th	ne memory clinic							
Exclusion criteria	No exclusion criteri	а								
Sex	52.0% male									
Age	Not stated.									
Presentation	Suspected dement	ia								
Reference standard	Dementia was diag	nosed using	g DSM-IV criteria.							
Dementia versus no	dementia									
Index Test: Addenbr Addenbrooke's Cogni	<b>ooke's Cognitive E</b> tive Examination (AC	o <b>ke's Cognitive Examination, ACE (&lt;88)</b> ve Examination (ACE) <88/100								
Results	True positives:	140	False negatives:	0	False positives:	83	True negatives:	62		
Additional comme nts	The data on using in practice for this p	VLOM ratios ourpose.	s to differentiate bet	ween dementia s	subtypes was not extra	acted here as	s this test would not	be used		
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: Addenbr	ooke's Cognitive E	xamination	, ACE (<83)							
Addenbrooke's Cogni	ognitive Examination (ACE) <83/100									
Results	True positives:	134	False negatives:	6	False positives:	54	True negatives:	91		
Additional comme nts	The data on using in practice for this p	VLOM ratios ourpose.	s to differentiate bet	ween dementia s	subtypes was not extra	acted here as	s this test would not	be used		

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: Addenbr Addenbrooke's Cogni	<b>ooke's Cognitive E</b> tive Examination (AC	<b>xamination</b> CE) <75/100	, ACE (<75)						
Results	True positives:	119	False negatives:	21	False positives:	25	True negatives:	120	
Additional comme nts	The data on using in practice for this p	VLOM ratios ourpose.	to differentiate betw	ween dementia s	subtypes was not extra	acted here a	s this test would not	be used	
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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Larner AJ. AD8 Info	rmant 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 Infor	mant questionnair	e: pragmati	ce diagnostic test	accuracy study	. Journal of Geriatr.	Psychiatry,	2015; 28: 198-202.			
Age	Median age 64.4 ye	ears (range	16-92)							
Presentation	Cognitive complain	gnitive complaints								
Reference standard	Dementia diagnose	ed according	to DSM-IV criteria.							
Dementia versus not	t dementia									
Index Test: AD8 (≥2)										
AD8, $\geq$ 2/8 defined as	cognitive impairmer	nt								
Results	True positives:	67	False negatives:	2	False positives:	127	True negatives:	16		
Additional comme nts	Data for 6CIT could	d not be ana	lysed as it was pres	ented for cogniti	ve impairment (demer	ntia plus MC	I) 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 (< MMSE, ≤24/30	25)									
Results	True positives:	21	False negatives:	7	False positives:	30	True negatives:	67		
Additional comme nts	Data for 6CIT could	d not be ana	lysed as it was pres	ented for cogniti	ve impairment (demer	ntia plus MC	I) 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									

Dementia

Appendix P: Diagnosis evidence tables & GRADE

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

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Larner AJ. MACE ve	ersus MoCA: equiva	llence or su	periority? Pragma	tic diagnostic t	est accuracy study.	nt. Psych. C	Geriatr. 2017; 29: 9	31-7.	
Study type	Prospective cohort								
Country	UK								
Setting	Cognitive functiona	gnitive functional clinic at a regional neuroscience centre							
Inclusion criteria	New patient referra	w patient referrals from a cognitive function clinic.							
Exclusion criteria	Pre-existing diagno	e-existing diagnosis of dementia							
Sex	65.0% male	0% male							
Age	Median 69 years (r	lian 69 years (range 31-89 years)							
Presentation	Not specified.	specified.							
Reference standard	DSM-IV diagnosis	of dementia							
Dementia versus no	dementia (includin	g MCI and	SMC)						
<b>Index Test: Mini-AC</b> Mini-ACE, ≤ 25/30	E (<26)								
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: Montrea MoCA (<26)	I Cognitive Assess	ment, MoC	A (<26)						
Results	True positives:	43	False	0	False positives:	150	True negatives:	67	

Larner AJ. MACE ver	arner 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										

1

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  $450 \pm 10$  nm (excitation) and  $480 \pm 10$  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  $450 \pm 10$  nm (excitation) and  $480 \pm 10$  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. False positives: 118 Results True positives: 298 False 61 True negatives: 585 negatives: Patient Low Index test: Reference Flow and **Risk of bias** Low Low Low selection: standard: timing: **Overall risk of bias** Not serious Indirectness Patient Low Index test: Low Reference Low selection: standard: Overall Not serious indirectness 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. True positives: 194 False 39 False positives: 79 True negatives: 133 Results negatives: **Risk of bias** Patient Index test: Reference Flow and Low Low Low Low selection: standard: timing: **Overall risk of bias** Not serious Indirectness Patient Low Index test: Low Reference Low selection: standard: Overall Not serious indirectness 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 optimis	sed threshol	d was used for the a	assay.)				
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
CJD (definite) versus	s not CJD (definite)							
Index Test: Total Tau	ı							
Total-tau, > 1250pm/n	nl. INNOTEST ELIS	A.						
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 optimis	sed threshol	d was used for the a	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	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	13	False positives:	5	True negatives:	28
			negatives:					
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 us	ed with >10% study	population exclu	uded.)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
VaD versus non-VaD	)							
Index Test: 99mTc-H	IMPAO SPECT							
99mTc-HMPAO SPEC without knowledge of performed. VaD patter	CT; threshold pre-sp the clinical diagnosis rn used to determine	ecified at 25 s. BUT single e positive res	% for lower thresho e head camera used sults.	ld value; rCBF p d - less accurate	atterns on the SPECT and not in clinical use	scans were today. Imag	interpreted visually ge analysis was not	and
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 us	ed with >10% study	population exclu	ided.)			
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	Unclear	Index test:	Low	Reference	Low	Flow and	High

Overall risk of bias	Serious (Subgroup	analysis us	ed with >10% study	population exclu	uded.)

Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low
Overall indirectness	Not serious					

standard:

timing:

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selection:

# 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 us	ed with >10% study	population exclu	uded.)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
FTD versus VaD								
Index Test: 99mTc-H	IMPAO 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 us	ed with >10% study	population exclu	uded.)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

1

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	8.3% male								
Age	Mean age 64.6 (SD 12.1)								
Presentation	Suspected CJD								
Reference standard	Neuropathology								
CJD versus not CJD									
Index Test: CSF 14-3	Index Test: CSF 14-3-3 ELISA								
14-33, Circulex 14-3	3-3γ ELISA. Cut-off >14552 arbitrary units/ml								
Results	True positives:70False2False positives:4True 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 und exclusions; test thr	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	Not serious									
Index Test: Total Ta	u										
Total tau, INNOTEST	ELISA, cut-off > 103	35 pg/ml									
Results	True positives:	70	False negatives:	2	False positives:	5	True negatives:	66			
Additional comme nts											
Risk of bias	Patient selection:	Unclear	Index test:	Unclear	Reference standard:	Low	Flow and timing:	Low			
Overall risk of bias	Serious (It was und exclusions; test thr	clear whethe esholds wer	r: a consecutive or r e pre-specified.)	andom sample o	of patients was enrolle	d; the study	avoided inappropria	ite			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										
Index Test: p-tau/tot	al tau										
ratio of p-tau/t-tau, IN	NOTEST ELISA, cut	-off < 45.56									
Results	True positives:	70	False negatives:	2	False positives:	9	True negatives:	64			
Additional comme nts											
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 und exclusions; test thr	lear whethe esholds wer	r: a consecutive or ı e pre-specified.)	random sample o	of patients was enrolle	d; the study	avoided inappropriate			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									

Lemstra AW, van Me Jakob disease: A pre	egen MT, Vreyling ospective study in	JP, Meijerir 112 patients	nk PH, Jansen GH, s.Neurology 2000;	Bulk S, Baas F 55: 514-6	, van Gool WA. 14-3-	3 testing in	diagnosing Creutz	feldt-		
Study type	Prospective cohort	Prospective cohort								
Country	Netherlands									
Setting	The only specialist	laboratory fa	acility used to test for	or 14-3-3 in CSF	in Netherlands.					
Inclusion criteria	Samples from patie	ents with sus	pected CJD that we	ere sent to the la	boratory for testing.					
Exclusion criteria	Not stated									
Sex	Not stated									
Age	Not stated									
Presentation	Rapidly progressive	Rapidly progressive dementia leading to suspected CJD								
Reference standard	Diagnosis based of cases. The criteria	n criteria usi used are no	ng information from t specified.	referring physici	ans, with pathology co	onfirmation o	f CJD in 25/33 CJD	positive		
CJD versus not CJD										
Index Test: CSF 14-3 Detection of presence	<b>3-3 immunoblotting</b> of 14-3-3 protein in	CSF by imm	nunoblotting, thresh	old of detection r	not stated.					
Results	True positives:	32	False negatives:	1	False positives:	10	True negatives:	67		
Risk of bias	Patient selection:	Patient selection:     Low     Index test:     High     Reference standard:     Unclear     Flow and Low								
Overall risk of bias	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	Not serious								

# 1 **P.1.13 M**

Maddalena A, Papas fluid ratio of phosph	sotiropoulos A, Mu orylated tau protei	iller-Tillmar n to beta-ar	nns B, et al. Bioche nyloid peptide(42)	emical diagnosi . Arch Neurol 20	s of Alzheimer disea 003; 60: 1202–6.	se by meas	uring the cerebros	pinal	
Study type	Prospective cohort								
Country	Switzerland								
Setting	Memory disorders	unit							
Inclusion criteria	Outpatients at a me	emory disord	ders unit who were	referred for diagr	nostic workup.				
Exclusion criteria	Not stated								
Sex	54.0% male								
Age	Mean age 68.4 yea	rs (SD9.4)							
Presentation	Suspected dement	ia							
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 d	lementia								
Index Test: Amyloid	Beta 1-42	oid FLISA (	cut off 0 49ma/ml						
Results	True positives:	40	False	11	False positives:	9	True negatives:	21	
		-	negatives:				J. J		
Additional comme	We excluded health	ny controls a	as they did not have	suspected dem	entia at baseline.				
nts	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, Papas fluid ratio of phosph	sotiropoulos A, Mu orylated tau protei	il <mark>ler-Tillma</mark> r n to beta-ar	nns B, et al. Bioche nyloid peptide(42).	emical diagnosi Arch Neurol 20	s of Alzheimer disea 003; 60: 1202–6.	se by meas	uring the cerebros	pinal		
Overall risk of bias	Serious (It was und each test for differe other.)	lear whethe ent analyses	r inappropriate exclu ; it was unclear whe	usions had been ther the index a	made; an optimised t nd reference tests wer	hreshold was e interpreted	s used for each test I independently of ea	and within ach		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious	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 comme nts	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 und each test for differe other.)	lear whethe ent analyses	r inappropriate exclu ; it was unclear whe	usions had been ther the index a	made; an optimised t nd reference tests wer	hreshold was e interpreted	s used for each test I independently of ea	and within ach		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									
Index Test: p-tau/Am p-tau/Amyloid Beta 1-	<b>yloid Beta 1-42</b> 42, cut off 83									
Results	True positives:	41	False negatives:	10	False positives:	8	True negatives:	22		
Additional comme nts	We excluded health We were unable to analyses and we ca	ny controls a compare de annot obtain	as they did not have ementia versus no d a 2x2 table of the c	suspected demo ementia as the a complete data se	entia at baseline. authors used different t as a result.	cut offs withi	n the same test for o	different		

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	ot serious									
AD versus no demer	ntia										
Index Test: Amyloid	Beta 1-42										
Amyloid Beta 1-42, IN	NOTEST Beta Amyl	oid ELISA, o	cut off 0.58ng/ml								
Results	True positives:	43	False negatives:	8	False positives:	3	True negatives:	16			
Additional comme nts	We excluded health We were unable to analyses and we ca	hy controls a compare de annot obtain	as they did not have ementia versus no d a a 2x2 table of the c	suspected deme ementia as the a complete data se	entia at baseline. authors used different et as a result.	cut offs with	in the same test for	different			
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low			
Overall risk of bias	Serious (It was und each test for differe other.)	lear whethe ent analyses	r inappropriate exclu ; it was unclear whe	usions had been ther the index a	made; an optimised t nd reference tests wer	hreshold was e interpreted	s used for each test d independently of e	and within ach			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										
Index Test: p-tau 181 p-tau, INNOTEST p-ta	l au 181 ELISA, cut of	f 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 comme nts	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 und each test for differe other.)	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/Am p-tau/Amyloid Beta 1-	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 comme nts	We excluded health We were unable to analyses and we ca	hy controls a compare de annot obtain	as they did not have ementia versus no d a 2x2 table of the c	suspected demo ementia as the a complete data se	entia at baseline. authors used different t as a result.	cut offs with	in the same test for o	different		
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low		
Overall risk of bias	Serious (It was und each test for differe other.)	clear whethe ent analyses	r inappropriate exclı ; it was unclear whe	usions had been ther the index ar	made; an optimised the reference tests wer	hreshold wa e interpreteo	s used for each test d independently of ea	and within ach		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									

1

Malhotra C, Chan A, Dementia Among Pa	Matcher D, Seow D tients Attending Co	), Chuo A, I ognitive As	Do YK. Diagnostic sessment Clinics i	Performance of n	f Short Portable Ment	tal Status Q	uestionnaire for So	creening	
Singapore. Ann Aca	d Med Singapore 2	013; 42: 315	5-9.						
Study type	Prospective cohort								
Country	Singapore								
Setting	Cognitive assessm	ent clinics a	t Singapore Genera	l Hospital, Chan	gi General Hospital an	d Tan Tock	Seng Hospital		
Inclusion criteria	Patients attending	cognitive as	sessment clinics.						
Exclusion criteria	None stated								
Sex	30.7% male								
Age	Ages ranged from	60-94 years							
Presentation	Suspected dement	ia							
Reference standard	Clinician diagnosis	Clinician diagnosis -criteria not stated							
Dementia versus no dementia (including MCI)									
Index Test: Short Po	ortable Mental Statu	is Question	naire, SPMSQ (≥5)						
Short Portable Menta	Status Questionnai	re (SPMSQ)	, cut-off $\geq$ 5, in Engl	ish 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 und population groups.	clear whethe )	r the study avoided	inappropriate ex	clusions and optimise	d test cut-off	s were used for diffe	erent	
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low			
Overall indirectness	Serious (60% parti	cipants had	< 6 years education	)					
Index Test: Short Po	ortable Mental Statu	is Question	naire, SPMSQ (≥6)						
Short Portable Menta	Status Questionnai	re (SPMSQ)	, cut-off ≥ 6, in Engl	ish or Chinese					
Results	True positives:	74	False negatives:	29	False positives:	14	True negatives:	10	

Malhotra C, Chan A, Dementia Among Pa Singapore. Ann Aca	Matcher D, Seow D Itients Attending Co d Med Singapore 20	), Chuo A, E ognitive As: 013; 42: 315	Do YK. Diagnostic l sessment Clinics i 5-9.	Performance of n	Short Portable Ment	al Status Q	uestionnaire for So	creening
Additional comme nts								
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Yes	Flow and timing:	High
Overall risk of bias	Very serious (It was population group a	s unclear wh nd a subgrou	nether the study avo up analysis was use	ided inappropria d which exclude	te exclusions; optimise d 40% study population	ed test cut-c on.)	ffs were used for dif	ferent
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low		
Overall indirectness	Serious (Participants had < 6 years education )							
Index Test: Short Po Short Portable Mental	rtable Mental Statu	re (SPMSQ)	naire, SPMSQ (≥4) , cut-off ≥ 4, in Engli	sh or Chinese				
Results	True positives:	81	False negatives:	22	False positives:	6	True negatives:	18
Additional comme nts								
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Yes	Flow and timing:	High
Overall risk of bias	Very serious (It was population group a	s unclear wh nd a subgrou	nether the study avo up analysis was use	ided inappropria d which exclude	te exclusions; optimise d 60% study population	ed test cut-c on.)	ffs were used for dif	ferent
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious (Partici	pants had ≥	6 years education )					

1

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

Manabe Y, Inui Y, To differential diagnosis	yama H and Kosaka K. 123I-metaiodobenzylguanidine myocardial scintigraphy with early images alone is useful for the s 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 knowledge of the re	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, To differential diagnosi	oyama H and Kosak s of dementia with	a K. 123I-m Lewy bodie	etaiodobenzylgua s. Psychiatry Reso	nidine myocard earch: Neuroim	lial scintigraphy with aging, 2017; 261: 75-	early imag -79.	es alone is useful f	or the
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 comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Unclear	Flow and timing:	Low
Overall risk of bias	Serious (Optimised knowledge of the re	test cut-offs	s were calculated ar index test or the inc	nd it was unclear dex test was inte	whether the reference	e standard w edge of the r	vas interpreted witho	ut ce test.)
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

1

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 wh	nere >10% study po	pulation exclude	d)			
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, Men in discriminating Alz	dez MF, Fairbanks I zheimer's disease f	A, Cummi rom other c	ngs JL. Sensitivity lementias. J Geria	, specificity, an tr Psychiatry Ne	d positive predictive eurol 1997; 10: 15–21	value of tee	chnetium 99-HMPA	O SPECT
Overall risk of bias	Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
possible AD versus	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 wh	ere >10% study por	pulation exclude	d)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Mathuranath PS, Ne	stor PJ, Berrios GE	, Rakowicz	W and Hodges JR	. A biref cognit	ive test battery to dif	ferentiate A	lzheimer's disease	and

frontotemporal demutia. Neurology 2000; 55: 1613-1620.Study typeProspective cohortCountryUKSettingCambridge memory clinicInclusion criteriaNew patients attending the memory clinic between June 1996 and October 1998 who met the following criteria: follow up of at least<br/>12 months; able to complete the full assessment; and CDR and neuropsychological tests completed within 90 days of ACE.Exclusion criteriaEvidence of two or more pathologies, either of which could independently be the main cause of dementia; major depression by the<br/>DSM-IV or other psychiatric illness; causes of cognitive impairment other than vascular or degenerative pathology (eg. head<br/>injuries, alcoholism).

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Mathuranath PS, Net frontotemporal demo	stor PJ, Berrios GE entia. Neurology 20	, Rakowicz 00; 55: 161	W and Hodges JR 3-1620.	. A biref cognit	ive test battery to dif	ferentiate A	Izheimer's disease	e and			
Sex	57.6% male	57.6% male									
Age	Mean age 66.1 yea	Mean age 66.1 years (SD 8.6)									
Presentation	Suspected dement	ia									
Reference standard	Dementia was diag	nosed acco	rding to the DSM-IV	<b>'</b> .							
Dementia versus no	dementia										
Index Test: Addenbr	ooke's Cognitive E	xamination	, ACE (<88)								
Addenbrooke's Cogni	tive Exam (ACE), cu	t-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: Addenbr Addenbrooke's Cogni	<b>ooke's Cognitive E</b> tive Exam (ACE), cu	xamination t-off 83.	, ACE (<83)								
Results	True positives:	94	False negatives:	21	False positives:	1	True negatives:	23			
Additional comme nts											
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low			
Overall risk of bias	Serious (Optimised results of the reference	l test-threshe	old used and it was rd.)	unclear whether	the index test results	were interpro	eted without knowle	dge of the			
Indirectness	Patient	Low	Index test:	Low	Reference	Low					

Mathuranath PS, Nes frontotemporal demo	stor PJ, Berrios GE entia. Neurology 20	, Rakowicz 00; 55: 161	W and Hodges JR 3-1620.	. A biref cognit	ive test battery to dif	ferentiate A	Izheimer's disease	and
	selection:				standard:			
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE, cut-off 27.	:27)							
Results	True positives:	85	False negatives:	30	False positives:	1	True negatives:	23
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (Optimised results of the reference	l test-thresho ence standa	old used and it was rd.)	unclear whether	the index test results	were interpre	eted without knowled	dge of the
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE, conventional of	<b>:24)</b> cut-off 24.							
Results	True positives:	60	False negatives:	55	False positives:	1	True negatives:	23
Additional comme 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							

Mayeux R, Saunders Alzheimer's disease	s A, Shea S, Mirra S . NEJM 1998; 338: {	5, Evans D, 506-511.	Roses AD, Hyman	BT et al. Utility	of the Apolipoprotei	n E genotyj	pe in the diagnosis	of
Study type	Retrospective cohort							
Country	USA							
Setting	Twenty-six Alzheim	ner's diseas	e centres across US	SA.				
Inclusion criteria	People referred to	26 Alzheime	er's disease centres	for the evaluatio	on of dementia.			
Exclusion criteria	Not stated							
Sex	49.0% male							
Age	Mean age 72.0 yea	ars (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 (≥ Apo E, ≥ 1 allele as d	<b>1 allele)</b> etermined by PCR u	sing DNA fr	om tissue or blood s	samples; if this w	vas not available frozei	n tissue was	assayed.	
Results	True positives:	1142	False negatives:	628	False positives:	133	True negatives:	285
Additional comme nts	Data on the diagno one clinical criteria	stic test acc was used a	curacy of the initial c cross the 26 study s	linical diagnosis sites.	was not compared to	the patholog	jical diagnosis as mo	ore than
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							

1

McMurdo ME, Grant Alzheimer's disease	DJ, Kennedy NS, Gilchrist J,Findlay D, McLennan JM. The value of HMPAO SPECT scanning in the diagnosis of early 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 Alzheimer's disease	DJ, Kennedy NS, G in patients attendi	Silchrist J,F ng a memo	indlay D, McLenna ry clinic. Nucl Med	n JM. The value Commun 1994	e of HMPAO SPECT : ; 15: 405-409.	scanning in	the diagnosis of e	arly
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 us	ed with >10% study	population disca	arded.)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
VaD versus non-VaD	)							
99mTc-HMPAO SPEC collected using a 128 normal; AD pattern; is	CT imaging was carr x128 matrix, around chemic pattern (VaE	ied out using an elliptical ); abnormal	g a single-headed ca orbit off 360 degrees I other. Here the dat	amera with a hig s. Images were r a is analysed for	h-resolution parallel-h reconstructed and class the AD pattern.	ole collimato ssified into o	or. Sixty-four 35s vie ne of four SPECT pa	ws were atterns:
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-H 99mTc-HMPAO SPEC collected using a 1282 normal: AD pattern: is	IMPAO SPECT CT imaging was carr x128 matrix, around schemic pattern (VaE	ied out using an elliptical )): abnormal	g a single-headed ca orbit off 360 degrees other. Here the dat	amera with a hig s. Images were r a is analysed for	h-resolution parallel-h econstructed and clast the AD pattern.	ole collimato ssified into o	or. Sixty-four 35s vie ne of four SPECT pa	ws were atterns:
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.								
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Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Unclear	Flow and timing:	High
Overall risk of bias	Serious (Subgroup	analysis us	ed with >10% study	population disca	arded.)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

1

Mendez MF, Shapira 830-835.	JS, McMurtray A, I	₋icht E, Mil	ler BL. Accuracy o	f the clinical ev	aluation of Frontoten	nporal dem	entia. Arch Neurol	2007; 64:	
Study type	Retrospective coho	ort							
Country	USA								
Setting	Neurology clinic at	UCLA.							
Inclusion criteria	People with suspect	cted FTD re	ferred to the clinic fo	or diagnosis.					
Exclusion criteria	Patients with langu	age-predon	ninant variants (PA o	or semantic dem	entia) and frontotempo	oral lobar de	generation.		
Sex	43.3% male								
Age	Mean age 63.4 yea	lean age 63.4 years (SD 7.5)							
Presentation	Suspected FTD	Suspected FTD							
Reference standard	Clinician diagnosis	after 2 year	rs follow up.						
FTD versus not FTD									
Index Test: FTD con FTD consensus criter	<b>sensus criteria</b> ia (Neary, 1998)								
Results	True positives:	True positives: 23 False of the positives: 0 True negatives: 71   Inegatives: 1							
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 830-835.	JS, McMurtray A, I	∟icht E, Mill	er BL. Accuracy of	f the clinical ev	aluation of Frontoter	nporal dem	entia. Arch Neurol	2007; 64:
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MRI								
MRI. Details of machi	nes used not stated,	as existing	scans were re-analy	ysed by the rese	archers.			
Results	True positives:	40	False negatives:	23	False positives:	21	True negatives:	50
Additional comme 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							
Index Test: SPECT/F SPECT/PET. Details rated for atrophy, hyp	PET of machines used no ometabolism or hypo	ot stated, so operfusion o	me patients had SPI n a 4 point scale.	ECT and others	PET results which we	re re-analyse	ed by the researcher	s. Results
Results	True positives:	57	False negatives:	6	False positives:	18	True negatives:	53
Additional comme 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	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

1

Milian M, Leiherr AM Drawing Test in dail	l, Straten G, Muller y clinical practice: s	S, Leyhe T, screening v	Eschweiler GW. T alue in a German l	he Mini-Cog ve Memory Clinic.	rsus the Mini-Mental International Psycho	State Exam geriatrics 2	nination and the Cl 012; 24: 766-74	ock
Study type	Retrospective Cohe	ort						
Country	Germany							
Setting	Memory clinic of the	e Departme	nt of Psychiatry and	Psychotherapy	at the University Hosp	ital of Tubin	gen.	
Inclusion criteria	People admitted to	the memory	y clinic between 200	4 and 2009.				
Exclusion criteria	Not stated	stated						
Sex	38.6% male	b male						
Age	Mean age 74.8 yea	ge 74.8 years (SD 8.1)						
Presentation	Suspected dement	ia						
Reference standard	Diagnosis of deme	iagnosis of dementia based on the DSM-IV criteria and the NINCDS-ADRDA criteria for AD.						
Dementia versus no	sus no dementia							
Index Test: Mini-Cog	g (Scanlan and Bors	son algorith	ım)					
Mini-Cog, Scanlan an	d Borson algorithm							
Results	True positives:	380	False negatives:	58	False positives:	0	True negatives:	64
Additional comme nts	Diagnostic test acc groups were used f	uracy data v for the analy	was not extracted fo vsis and no raw data	r detecting AD o is presented.	r non-AD dementia be	cause it is u	nclear which compa	rator
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Unclear	Flow and timing:	Low
Overall risk of bias	Serious (Unclear w whether the referer	hether inap	propriate exclusions d result was interpre	were avoided; weted without know	whether the patients w	ere a randor f the index te	n or consecutive sai est.)	mple and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

Milian M, Leiherr AM Drawing Test in daily	, Straten G, Muller y clinical practice:	S, Leyhe T, screening v	Eschweiler GW. T alue in a German l	<sup>°</sup> he Mini-Cog ve Memory Clinic.	rsus the Mini-Mental International Psycho	State Exan	nination and the Cle 2012; 24: 766-74	ock
Index Test: Clock Dr	awing Test, CDT, S	hulman sco	oring method (>2)					
Clock Drawing Test, C	CDT, cut-off >2, mod	ified version	of Shulman and Go	old (1 perfect, 6	no reasonable represe	entation of a	clock)	
Results	True positives:	342	False negatives:	96	False positives:	2	True negatives:	62
Additional comme nts	Diagnostic test acc groups were used t	uracy data v for the analy	vas not extracted fo sis and no raw data	r detecting AD o i is presented.	r non-AD dementia be	ecause it is u	nclear which compa	rator
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Unclear	Flow and timing:	Low
Overall risk of bias	Serious (Unclear w whether the referen	hether inapp nce standard	propriate exclusions result was interpre	were avoided; were avoided; were avoided; were avoided; without know	vhether the patients w vledge of the results o	ere a randor f the index te	n or consecutive sar est.)	mple and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE, ≤ 24	:25)							
Results	True positives:	318	False negatives:	120	False positives:	0	True negatives:	64
Additional comme nts	Diagnostic test acc groups were used t	uracy data v for the analy	vas not extracted fo sis and no raw data	r detecting AD o i is presented.	r non-AD dementia be	ecause it is u	nclear which compa	rator
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Unclear	Flow and timing:	Low
Overall risk of bias	Serious (Unclear w whether the referen	hether inapp nce standard	propriate exclusions result was interpre	were avoided; weted without know	vhether the patients w vledge of the results o	ere a randor f the index te	n or consecutive sar est.)	mple and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE, ≤ 25	:26)							

Milian M, Leiherr AM Drawing Test in daily	, Straten G, Muller / clinical practice: s	S, Leyhe T, screening v	Eschweiler GW. T alue in a German I	he Mini-Cog ve Nemory Clinic.	rsus the Mini-Mental International Psycho	State Examogeriatrics 2	nination and the Cl 2012; 24: 766-74	ock
Results	True positives:	347	False negatives:	91	False positives:	0	True negatives:	64
Additional comme nts	Diagnostic test acc groups were used t	agnostic test accuracy data was not extracted for detecting AD or non-AD dementia because it is unclear which comparator oups 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 w whether the referen	hether inapp nce standard	propriate exclusions result was interpre	were avoided; were avoided; were avoided; were avoid the second structure without know the second structure	vhether the patients we vledge of the results of	ere a randor f the index te	n or consecutive sar est.)	nple and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

1

Mormont E, Jamart , setting. Journal of G	J, Robaye L. Validity of the Five -word testfor the evaluation of verbal episodic memory and dementia in a memory clinic Beriatr 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 SM	IC (MCI excluded)
Index Test: MMSE (< MMSE, ≤ 27	<28)

Mormont E, Jamart . setting. Journal of G	I, Robaye L. Validit eriatr Psych and N	y of the Five eurol 2012;	e -word testfor the 25: 78-84.	evaluation of v	erbal episodic memo	ory and der	mentia in a memory	clinic
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 (Exclu	usion of >35°	% population at ana	lysis and use of	optimised test thresho	olds.)		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Free reca	all score of 5- word	test, ≤ 6 fo	r all dementia					
Free recall score of 5-	word test, $\leq 6$ for al	l dementia						
Results	True positives:	75	False negatives:	21	False positives:	5	True negatives:	44
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Very serious (Exclu	usion of >35°	% population at ana	lysis and use of	optimised test thresho	olds.)		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Total rec	all 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 comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	High

Mormont E, Jamart S setting. Journal of G	J, Robaye L. Validit eriatr Psych and N	y of the Fiv eurol 2012;	e -word testfor the 25: 78-84.	evaluation of v	verbal episodic memo	ory and den	nentia in a memory	clinic
Overall risk of bias	Very serious (Exclu	usion of >35	% population at ana	lysis and use of	optimised test thresho	lds.)		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Total we	ighted score of 5-w	vord test, ≤	15					
Total weighted score	of 5-word test, $\leq 16$							
Results	True positives:	72	False negatives:	24	False positives:	2	True negatives:	47
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Very serious (Exclu	usion of >35	% population at ana	lysis and use of	optimised test thresho	olds.)		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus SMC (MC	l excluded)							
Index Test: MMSE (< MMSE, ≤ 28	: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 (Exclu	usion of >35	% population at ana	lysis and use of	optimised test thresho	lds.)		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall	Not serious							

Mormont E, Jamart J setting. Journal of G	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 reca	all score of 5- word	test, ≤ 5 fo	r AD					
Free recall score of 5-	word test, ≤ 5 for A	D						
Results	True positives:	50	False negatives:	11	False positives:	0	True negatives:	49
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Very serious (Exclu	usion of >35°	% population at ana	lysis and use of	optimised test thresho	olds.)		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Total rec	all 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 comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Very serious (Exclu	usion of >35°	% population at ana	lysis and use of	optimised test thresho	olds.)		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Total we Total weighted score	<b>ighted score of 5-w</b> of 5-word test, ≤ 16	vord test, ≤	15					

Mormont E, Jamart S setting. Journal of G	J, Robaye L. Validit eriatr Psych and N	y of the Fiv eurol 2012;	e -word testfor the 25: 78-84.	evaluation of v	verbal episodic memo	ory and den	nentia in a memory	clinic
Results	True positives:	55	False negatives:	6	False positives:	2	True negatives:	47
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Very serious (Exclu	usion of >35°	% population at ana	lysis and use of	optimised test thresho	lds.)		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

1

Motara H, Olusoga T deoxy-D-glucose po brain imaging in pat	, Russell G, Jamieson S, Ahmed S, Brindle N, Pillai A et al. Clinical impact and diagnostic accuracy of 2-[18F]- fluoro-2- sitron-emission tomography/computed tomography (PET/CT) ients 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-2deoxy-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 comme nts	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 N Phosphorylated Tau Cerebrospinal Fluid	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										
<b>Cerebrospinal Fluid</b>	Biomarkers for the	Diagnosis	of Alzheimer Disea	ase. Clinical Ch	emistry 2010; 56: 24	8-253.				
Exclusion criteria	Not stated									
Sex	50.4% male									
Age	Mean age 64.9 yea	ars (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 CSF Beta Amyloid 42	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	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 Ta Tau, 375ng/ml	u									
Results	True positives:	211	False negatives:	37	False positives:	29	True negatives:	102		
Additional comme nts										
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	Low		

Mulder C, Verway NA Phosphorylated Tau	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									
<b>Cerebrospinal Fluid</b>	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 18 p-Tau, 52ng/ml	1									
Results	True positives:	211	False negatives:	37	False positives:	42	True negatives:	89		
Additional comme nts										
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	Low		
Overall risk of bias	Very Serious (It is the but selected to obtain index test was interested to be a selected t	unclear whe ain 85% sei rpreted inde	ether participants we nsitivity; the timing be ependently of the refe	re consecutively etween the refer erence test resu	or randomly recruited ence and index tests is lts )	; the test cu s unclear an	t offs were not pre-s d it is unclear wheth	pecified er the		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									

# 1 **P.1.14 N**

Nielsen TR, Anderse Disord 2013; 36: 354	n BB, Gottrup H, e -62.	t al. Validati	ion of the RUDAS f	or multicultura	I screening in Danisł	n memory c	linics. Dement Ger	iatr Cogn			
Inclusion criteria	People referred to with suspected der	the memory nentia occur	clinics for the evalu red.	ation of possible	dementia. After Marc	h 2012 seleo	ctive inclusion of imr	nigrants			
Exclusion criteria	After a March 2012	fter a March 2012 people from a non-immigrant background with suspected dementia were excluded.									
Sex	52.6% male	2.6% male									
Age	Dementia median a	age 77 years	s (Q1-Q3= 71.5-81);	non-dementia 6	1 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	Index Test: Rowland Universal Dementia Assessment Scale, RUDAS (<22)										
RUDAS (Rowland Un	iversal Dementia As	sessment So	cale), <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 s time period; the pe thresholds are repo	study selecte ople with im orted.)	ed some participants migrant background	s on the basis of s were significar	immigrant backgroun htly younger than Dani	d and exclud ish-born part	ded non-immigrants ticipants; a variety o	during this f test			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										
Index Test: Rowland	<b>Universal Dement</b>	ia Assessm	ent Scale, RUDAS	(<23)							
RUDAS (Rowland Un	iversal Dementia As	sessment So	cale), <23/30								
Results	True positives:	46	False negatives:	26	False positives:	11	True negatives:	54			
Additional comme nts											
Risk of bias	Patient	High	Index test:	High	Reference	Low	Flow and	Low			

Nielsen TR, Anderse Disord 2013; 36: 354	n BB, Gottrup H, et -62.	t al. Validati	ion of the RUDAS f	or multicultura	I screening in Danisł	n memory c	linics. Dement Ger	iatr Cogn		
	selection:				standard:		timing:			
Overall risk of bias	Very serious (The s time period; the per thresholds are repo	study selecte ople with imported.)	ed some participants migrant background	s on the basis of s were significar	immigrant backgroun tly younger than Dani	d and excluc sh-born part	led non-immigrants icipants; a variety of	during this f test		
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 comme nts										
Risk of bias	Patient selection:	High	Index test:	High	Reference standard:	Low	Flow and timing:	Low		
Overall risk of bias	Very serious (The s time period; the per thresholds are repo	study selecte ople with im orted.)	ed some participants migrant background	s on the basis of s were significar	immigrant backgroun htly younger than Dani	d and excluc sh-born part	led non-immigrants icipants; a variety of	during this f test		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									
Index Test: Rowland RUDAS (Rowland Uni	Universal Dementia	<b>ia Assessm</b> sessment So	ent Scale, RUDAS cale), <25/30	(<25)						
Results	True positives:	55	False negatives:	17	False positives:	22	True negatives:	43		
Additional comme nts										
Risk of bias	Patient	High	Index test:	High	Reference	Low	Flow and	Low		

Nielsen TR, Anderse Disord 2013; 36: 354	en BB, Gottrup H, et I-62.	t al. Validati	ion of the RUDAS f	or multicultura	I screening in Danisł	n memory c	linics. Dement Ger	iatr Cogn			
	selection:				standard:		timing:				
Overall risk of bias	Very serious (The s time period; the pe thresholds are repo	study selecte ople with im orted.)	ed some participants migrant background	s on the basis of s were significar	immigrant background htly younger than Dani	d and exclud ish-born par	ded non-immigrants ticipants; ; a variety	during this of test			
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 comme nts											
Risk of bias	Patient selection:	High	Index test:	High	Reference standard:	Low	Flow and timing:	Low			
Overall risk of bias	Very serious (The s time period; the pe thresholds are repo	study selecte ople with im orted.)	ed some participants migrant background	s on the basis of s were significar	immigrant background htly younger than Dani	d and exclud ish-born par	ded non-immigrants ticipants; ; a variety	during this of test			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										
Index Test: MMSE (< MMSE, <23/30	<23)										
Results	True positives:	38	False negatives:	33	False positives:	8	True negatives:	52			
Additional comme nts	6 participants lacke	ed MMSE da	ta and so were excl	uded from the a	nalysis by the authors						
Risk of bias	Patient	High	Index test:	High	Reference	Low	Flow and	Low			

Nielsen TR, Anderse Disord 2013; 36: 354	en BB, Gottrup H, et I-62.	t al. Validati	ion of the RUDAS f	or multicultura	I screening in Danish	n memory c	linics. Dement Ger	iatr Cogn				
	selection:				standard:		timing:					
Overall risk of bias	Very serious (The s time period; the per was not pre-specifi	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 (< MMSE, <24/30	<24)											
Results	True positives:	46	False negatives:	25	False positives:	8	True negatives:	52				
Additional comme nts	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 s time period; the per was not pre-specifi	study selecte ople with im ed.)	ed some participants migrant background	s on the basis of s were significar	immigrant background htly younger than Dani	d and excluc sh-born part	led non-immigrants licipants; the test thr	during this eshold				
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low						
Overall indirectness	Not serious											
Index Test: MMSE (< MMSE, <25/30	<25)											
Results	True positives:	54	False negatives:	17	False positives:	10	True negatives:	50				
Additional comme nts	6 participants lacke	ed MMSE da	ata and so were excl	uded from the a	nalysis by the authors							
Risk of bias	Patient	High	Index test:	High	Reference	Low	Flow and	Low				

Nielsen TR, Anderse Disord 2013; 36: 354	en BB, Gottrup H, et I-62.	t al. Validati	ion of the RUDAS f	or multicultura	I screening in Danish	n memory c	linics. Dement Ger	iatr Cogn			
	selection:				standard:		timing:				
Overall risk of bias	Very serious (The s time period; the per was not pre-specifi	study selecte ople with im ed.)	ed some participants migrant background	s on the basis of s were significar	immigrant background htly younger than Dani	d and exclud sh-born par	led non-immigrants ticipants; the test thr	during this eshold			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious	Not serious									
Index Test: MMSE (< MMSE, <26/30	<26)										
Results	True positives:	54	False negatives:	17	False positives:	16	True negatives:	44			
Additional comme nts	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 s time period; the per was not pre-specifi	study selecte ople with im ed.)	ed some participants migrant background	s on the basis of s were significar	immigrant background htly younger than Dani	d and exclud sh-born par	ded non-immigrants ticipants; the test thr	during this eshold			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										
Index Test: MMSE (< MMSE, <27/30	<b>2</b> 7)										
Results	True positives:	63	False negatives:	8	False positives:	22	True negatives:	38			
Additional comme nts	6 participants lacke	ed MMSE da	ta and so were excl	uded from the a	nalysis 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 s time period; the peo was not pre-specifio	study select ople with im ed.)	ed some participant migrant background	s on the basis of Is were significa	immigrant backgroun ntly younger than Dani	d and exclud ish-born part	led non-immigrants during this ticipants; the test threshold				
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										

# 1 **P.1.15 O**

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	D was diagnosed using the NINCDS-ADRDA criteria; VaD using NINDS-AIREN; DLB using the consensus criteria (McKeith) and epression using DSM-IV.						
Dementia versus no	dementia						
Index Test: CT							
CT scans were carried degrees C caudal to t the section that correst anterior and posterior	d out using an IGE CT 9800 head scanner. Angled scans 5mm through the temporal lobes were acquired approximately 20-25 he orbito-meatal line. The medium width of the medial temporal line (MTL) was measured from hard copies using callipers, through sponded most closely to that passing through the mid-point of the temporal lobes. The medium width of the MTL on either side of the margins of the brain stem was chosen for analysis. Cut off < 11.5mm.						

Results	True positives: 56	False	47 <b>F</b> a	alse positives:	3	True negatives:	10
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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.											
			negatives:								
Additional comme nts	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 comme nts	Subgroup analysis	was not car	ried out for DLB as	the numbers of p	patients was very smal	ll (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 wi	th >10% population	excluded)							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										
AD versus other der	nentias										
Index Test: CT											
CT scans were carrie	d out using an IGE C	T 9800 hea	d scanner. Angled s	scans 5mm throu	ugh the temporal lobes	were acquir	red 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 comme nts	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 wi	th >10% population	excluded)						
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									
O'Brien JT, McKeith The British Journal of	IG, Walker Z, Tatso of Psychiatry 2009;	ch K, Booij 194: 34-39	J et al. Diagnostic	accuracy of 12	3I-FP-CIT SPECT in p	ossible der	nentia with Lewy b	odies.		
Study type	Prospective cohort									
Country	UK									
Setting	Not stated									
Inclusion criteria	People aged 55-90 more.	) years with	a DSM-IV diagnosis	s of dementia an	d possible dementia w	ith Lewy boo	dies ; an MMSE scor	e of 10 or		
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 ye	ears (mean	age not stated)							
Presentation	possible DLB									
Reference standard	Clinician diagnosis DLB.	after 12 mo	onths follow-up using	9 NINCDS-ADRI	DA for AD, NINDS-AIR	EN for VaD,	, DLB consensus crit	eria for		

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	AD diagnosed using the NINCDS-ARDRA criteria; supranuclear palsy using NINDS-SPS workshop criteria; FTD using the criteria
standard	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 comme nts	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 d	ementias									
Index Test: FDG-PE	r									

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 comme nts	The study population consisted of 2 groups that could not be separated during the analysis.										
	The data for [11C]	Pittsburgh c	ompound B ([11C] F	PIB) imaging was	s not extracted as this	test is only i	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 unclea	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.										
Results	True positives:	38	False negatives:	27	False positives:	4	True negatives:	14		
Additional comme nts	The study population	on consisted	of 2 groups that co	uld not be separ	ated during the analys	sis.	used for records in			
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 unclea	ar whether tl	ne LeARN cohort co	onsisted of peopl	e with suspected cogr	nitive impairi	ment.)			
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 basel gapglia).										
Results	True positives:	38	False negatives:	27	False positives:	4	True negatives:	1		
Additional comme nts	The study population	on consisted	of 2 groups that co	uld not be separ	ated during the analys	sis.	used for recently in			
Risk of bias	Patient	Unclear	Index test:	High	Reference	Low	Flow and	Hiah		

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 unclea	ar whether tl	he LeARN cohort co	nsisted of peopl	e with suspected cogr	nitive impairr	nent.)			
FTD versus non- FTI	D									
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										
Results	True positives:	6	False negatives:	12	False positives:	12	True negatives:	123		
Additional comme nts	The study population	on consisted	ompound B ([11C] E	uld not be separ	ated during the analys	is. test is only i	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 avoided; the index	ar whether a test was inte	consecutive or rand erpreted with knowle	dom sample of p edge of the refere	atients was enrolled a ence diagnosis.)	ind whether	inappropriate exclus	ions were		
Indirectness	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low				
Overall	Serious (It is unclea	ar whether th	he LeARN cohort co	nsisted of peopl	e with suspected cogr	nitive impairr	nent.)			

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 comme nts	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.

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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 comme nts	The study population consisted of 2 groups that could not be separated during the analysis.										
	The data for [11C]	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-DLE	3										

#### 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	4	False positives:	6	True negatives:	142
			negatives:					

Ossenkoppele R, Pri Verhey FR, Verbeek diagnostic process i Alzheimers Dement	ins ND, Pijnenburg MM, van Buchem M n a memory clinic. 2013; 9: 414–421.	YA, Lemstr MA, Hoekstr	ra AW, van der Flie ra OS, Lammertsm	r WM, Adriaans a AA, Scheltens	e SF, Windhorst AD, s P, van Berckel BN:	, Handels R Impact of r	L, Wolfs CA, Aalter nolecular imaging o	י P, on the
Additional comme nts	The study population	on consisted	l of 2 groups that co	uld not be separ	ated during the analys	sis.		
	The data for [11C]	Pittsburgh c	compound B ([11C] F	PIB) imaging was	s 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 avoided; the index	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	Dverall   Serious (It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.)     ndirectness   Indirectness							
DLB versus non-DLB	3 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 comme nts	The study population	on consisted	l of 2 groups that co	uld not be separ	ated during the analys	sis.		

The data for [11C] Pittsburgh compound B ([11C] PIB) imaging was not extracted as this test is	only used for research in the UK.
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Risk of bias	Patient	Unclear	Index test:	High	Reference	Low	Flow and	High
	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							

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 popula	>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.)						

# 1 P.1.16 P

Panegyres PK, Roge of early-onset demen	ers JM, McCarthy M, Campbell A, Wu JS. Fluorodeoxyglucose-Positron Emission Tomography in the differential diagnosis ntia: 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	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	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 recruite	ed 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   Serious (The study only recruited people with early onset dementia (<65 years old).)						

1

Postel-Vinay N, Han Population. The Clir	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	o 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  $\leq$  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 langua	age, cut-off 24/30							
Results	True positives:	60	False negatives:	8	False positives:	23	True negatives:	110
Additional comme nts								
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							

# 1 **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-H	IMPAO 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							

1

Rohan Z, Smetakova autopsy-confirmed p	a M, Kukal J, Rusina prion diseases and	a R, Matej F other neuro	R. Proteinase-active odegenerative dise	ated receptor 2 eases. BMC Neu	and disease biomarl irology, 2015; 15: 50-	kers in cere ∙ 54.	brospinal fluid in c	ases with
Study type	Retrospective coho	Retrospective cohort						
Country	Czech Republic	Czech Republic						
Setting	National Reference	e Laboratory	for Diagnostics of H	luman Prion Dis	eases, Thomayer Hos	pital, Prague	9	
Inclusion criteria	Patients referred for diagnosis of neuroo the study.	or dementia ( degenerative	(including possible/ e disease and an an	probable Creutz te mortem CSF	feldt-Jakob disease; C analysis of T-tau, P-ta	JD) with a n u, Aβ, and p	europathologically c rotein 14-3-3 were i	confirmed ncluded in
Exclusion criteria	Not stated							
Sex	45.7% male							
Age	Mean age at death	66.3 years	(SD 9.1)					
Presentation	Suspected dement	ia, including	possible/probable (	CJD)				
Reference standard	A definite diagnosis resistant form of pr disease-associated	s of CJD was ion protein. I mutations.	s confirmed through In positive cases, th	neuropathologic e prion protein g	cal examination and w ene (PRNP) was anal	estern blot d ysed for cod	letection of the prote on 129 polymorphis	einase K ms and
CJD versus not CJD								
Index Test: Total Ta	u							
Total tau analysed us	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 comme nts								
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							

1

Rollin-Silliare A, Bor tomography to the d	nbois S, Deramecourt V, Steinert- Emptaz A, Salleron J, Morvan J, et al. Contribution of single photon emission computed lifferential 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 comme nts	Data was presente neuropathology in f	ata was presented for SPECT alone versus final neuropathological diagnosis and for SPECT with clincal data versus europathology 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 comme nts	Data was presente neuropathology in f	d for SPECT he paper. O	Γ alone versus final our analysis uses the	neuropathologic e SPECT alone r	al diagnosis and for S esults.	PECT with c	lincal data versus	
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-H	IMPAO 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 comme nts	Data was presente neuropathology in t	d for SPEC <sup>-</sup> he paper. C	T alone versus final Our analysis uses the	neuropathologic e SPECT alone i	al diagnosis and for Sl results.	PECT with c	lincal data versus	
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Serious (Subgroup	analysis wh	nere >10% study pop	pulation exclude	d)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

## 1 **P.1.18 S**

Sager MA, Hermann 2006; 105: 25–29.	BP, LaRue A and Woodard JL. Screening for dementia in community-based memory clinics. Wisconsin Medical Journal,
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 2006; 105: 25–29.	BP, LaRue A and V	Voodard JL	. Screening for de	mentia in comn	nunity-based memor	y clinics. W	isconsin Medical J	ournal,
Presentation	Suspected dement	ia						
Reference standard	DSM-IV with Clinic	al Dementia	Rating, neuropsych	nological tests ar	nd research diagnostic	criteria for N	ICI, DLB and FTD.	
Dementia versus no	n-dementia (includi	ing MCI)						
Index Test: Clock Dr Clock Drawing Test, C	awing Test, CDT, s CDT <8 out of 10 (fre	coring met e- hand- dra	h <b>od unclear (&lt;8)</b> aw 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 (< MMSE <24	:24)							
Results	True positives:	157	False negatives:	104	False positives:	1	True negatives:	102
Additional comme nts								
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 ca	ategory fluency (an	imal namin	g), 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 comme nts								
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							

1

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

<b>6</b> 11.	
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 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, Shirais diagnostic performa 211.	hi S, Yoshida M, Tomiguchi S, Hirai T, Namimoto T, Hashimoto M, Ikeda M et al.Diagnosis of dementia with Lewy bodies: nce of combined 123I-IMP brain perfusion SPECT and 123I-MIBG myocardial scintigraphy. Ann Nucl Med, 2014; 28:203–
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.

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 und interpreted without	lear whethe knowledge	er the study avoided of the results of the	inappropriate ex index test .)	clusions or whether th	ne reference	standard results we	re
Indirectness	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
DLB versus not DLB	3							

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

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

akamoto F, Shiraishi S, Yoshida M, Tomiguchi S, Hirai T, Namimoto T, Hashimoto M, Ikeda M et al.Diagnosis of dementia with Lewy bod	ies:
agnostic performance of combined 123I-IMP brain perfusion SPECT and 123I-MIBG myocardial scintigraphy. Ann Nucl Med, 2014; 28:20	)3–
11.	

mediastinum area. Th	e early H/M ratio use	ed for analys	sis 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 und interpreted without	lear whethe knowledge	r the study avoided of the results of the	inappropriate ex index test.)	clusions or whether th	e reference	standard results we	re
Indirectness	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

#### Index Test: 123I-IMP SPECT

1

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 comme nts								
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	High	Flow and timing:	Low
Overall risk of bias	Serious (It was und interpreted without	clear whethe knowledge	r the study avoided of the results of the	inappropriate ex index test.)	clusions or whether th	e reference	standard results we	re
Indirectness	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

Sakamoto F, Shirais can 123I-IMP and 12	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	Japan						
Setting	Kumamoto Univers	ity Hospital.						
Inclusion criteria	People with suspect Kumamoto University	ted DLB wh ity Hospital	no had undergone b between January 2	oth 123I-IMP bra 008 and March 2	ain perfusion SPECT a 2014.	ind 123I-MIE	3G myocardial scinti	graphy at
Exclusion criteria	Congestive heart fat the resulst of the M	ailure, ischao IBG scintigr	emic heart disease, aphy.	cardiomyopathy	and diabetes, and pa	tients taking	antipsychotic drugs	that affect
Sex	41.6% male							
Age	Mean age 76.0 yea	rs (SD 8.3)						
Presentation	Suspected DLB							
Reference standard	Clinician diagnosis	using the C	onsortium on DLB i	nternational Wor	kshop criteria (McKeit	h, 2006)		
DLB versus not DLB								
Index Test: 123I-MIB	Index Test: 123I-MIBG cardiac scintigraphy							
123-I MIBG cardiac se equipped with a medi	cintigraphy, early hea um-energy general p	art-to-media urpose colli	statinum (H/M) ration mator. Early and de	<ul> <li>Images were a layed imaging w</li> </ul>	cquired with a dual-he as performed at 15 mi	ad gamma on and 3 hrs	camera (Symbia T16 after injection. Cut-c	6), off <2.0.
Results	True positives:	76	False negatives:	16	False positives:	9	True negatives:	231
Additional comme nts	Study also looked a	at 123-I-IMP	SPECT but did not	present DTA da	ta for this or for other	MIBG variat	oles.	
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.)					est results			
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 coho	Retrospective cohort						
Country	Germany							
Setting	Magnetic Resonan	ce/Compute	d Tomography Insti	tute Hamburg				
Inclusion criteria	All cases reported	to the Germ	an CJD surveillance	e unit				
Exclusion criteria	Not stated							
Sex	For the CJD positiv	e group 31.	5% male, not stated	I for CJD negtive	e group			
Age	Mean age 65.5 yea	rs (range 38	8-86) for the CJD po	ositive group, CJ	D negative not stated			
Presentation	Rapidly progressive	e dementia l	leading to suspected	d 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-CJI	ט							
Index Test: MRI								
MRI scans were made proton density- weigh	e with either 1.0-T or ted and fluid attenua	1.5-T magr tion inversio	netic resonance imagon recovery.	gers. The followi	ing MRI scans were pe	erformed: T1	-weighted, T2 weigh	nted,
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							

1

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 Prospecti

Prospective cohort

Sikkes SA, Van den between Alzheimer's 2010; 30: 411–6.	Berg MT, Knol DL, s disease, mild cog	De-Lange-c nitive impa	te Klerk ES, Schelt irment and subject	ens P, Uitdehaa tive memory co	ag BM, et al. How use mplaints?. Dementia	eful is IQCC a and Geriat	DE for discriminat ric Cognitive Disor	ing ders
Country	The Netherlands	ne Netherlands						
Setting	Alzheimer Centre a	Izheimer Centre at a University Hospital						
Inclusion criteria	Patients visiting the	e Alzheimer	Centre at the VU Ur	niversity Medical	Centre between 2004	1 and 2007		
Exclusion criteria	Not stated							
Sex	56.4% male							
Age	mean age 68.4 yea	ars (SD 8.8)						
Presentation	Suspected dement	ia						
Reference standard	Petersen criteria fo complaints.	Petersen criteria for MCI, NINCDS-ADRDA for dementia. All remaining patients were classified as having subjective memory complaints.						
AD versus subjectiv	e memory complai	nts (no dem	nentia 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 comme nts	Data for 2x2 table of	obtained from	m Harrison et al. (20	015) Cochrane R	eview. Not is an acces	ssible forma	t 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 unclear that index a	of subgroup and reference	analysis where >10 ce tests are interpret	% study populat ted without know	ion excluded (MCI gro rledge of each other.)	oup); lack of	a pre-specified test	threshold;
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 between Alzheimer's 2010; 30: 411–6.	Berg MT, Knol DL, s disease, mild cog	De-Lange-c nitive impa	le Klerk ES, Schelt irment and subject	ens P, Uitdehaa tive memory co	ag BM, et al. How use mplaints?. Dementia	eful is IQCO and Geriat	DE for discriminat ric Cognitive Disor	ing ders
Additional comme nts	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 unclear that index a	of subgroup and referenc	analysis where >10 e tests are interpret	% study populat ed without know	tion excluded (MCI gro /ledge of each other.)	oup); lack of	a pre-specified test	threshold;
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 comme nts	Additional comme 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 unclear that index a	of subgroup and referenc	analysis where >10 e tests are interpret	% study populat ed without know	tion excluded (MCI gro vledge of each other.)	oup); lack of	a pre-specified test	threshold;
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 of	obtained from	m Harrison et al. (20	)15) Cochrane F	Review. Not is an acces	ssible forma	t in original paper.	

Sikkes SA, Van den between Alzheimer's 2010; 30: 411–6.	Berg MT, Knol DL, s disease, mild cog	De-Lange-c nitive impa	le Klerk ES, Schelt irment and subject	ens P, Uitdehaa ive memory co	ag BM, et al. How use mplaints?. Dementia	eful is IQCO and Geriat	DE for discriminat ric Cognitive Disor	ing ders
nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Unclear	Flow and timing:	High
Overall risk of bias	ias 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 comme nts	Data for 2x2 table of	obtained froi	m Harrison et al. (20	15) Cochrane R	eview. Not is an acces	sible format	t 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 unclear that index a	of subgroup and referenc	analysis where >10 e tests were interpre	% study populat eted without kno	ion excluded (MCI gro wledge of each other.	up); lack of ; )	a pre-specified test	hreshold;
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

1

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	eople presenting with symptoms of dementia at one of the academic centres						
Exclusion criteria	Not stated							
Sex	51.4% male							
Age	Mean age 67.0 yea	ars (10.0)						
Presentation	Suspected dement	ia						
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							

1

Silverman DHS, Sma regional brain metal	all GW, Chang CY, I polism and long-ter	Lu CS,Kung m outcome	g De Abarto MA, Cl 9. JAMA. 2001; 286	nen W,et al. Pos : 2120-7.	sitron emission tomo	graphy in e	valuation of demen	ntia;	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious	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 Si	riraj Hospita	l, Mahidol Universit	y.					
Inclusion criteria	People with DSM-I	V diagnosed	d dementia						
Exclusion criteria	Not stated	Not stated							
Sex	30.3% male	30.3% male							
Age	Mean age 71.2 yea	ars (SD 10.2	.)						
Presentation	Diagnosed dement	ia, but subty	/pe to be determine	d.					
Reference standard	Clinician diagnosis	using stand	lard tests and neuro	imaging as need	led.				
VaD and mixed dem	entia (VaD with AD)	) versus AD	)						
Index Test: Hachins	ki Ischemic Score,	HIS (≥5)							
Hachinski Ischemic S	core (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 (Subg the index test resul was interpreted wit	roup analys ts were inte hout knowle	is excluded >45% s rpreted without know edge of the results o	tudy population; wledge of the res f the index test.)	optimised test-thresho sults of the reference s	old was used tandard or v	d and it was unclear whether the referenc	whether e standard	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			

1

Siritho S, Senanaron experience. J Med A	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 exposed to antiretro	AJ, DeBlock L, Gill viral therapy. HIV N	MJ, Power /ledicine, 20	C. Neurocognitive	screening tool	s in HIV/AIDS: comp	arative perf	ormance among pa	atients
Study type	Prospective cohort							
Country	Canada							
Setting	Northern and Sout	hern Alberta	a neurology clinics					
Inclusion criteria	HIV+ people under	going evalu	ation for neuropsych	nological deficits	as part of a neurologi	cal consultat	ion.	
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 Academ	y of Neurolo	gy algorithm for HI∖	/-1 associated co	ognitive/motor disorde	r		
HAND versus other	neurological disord	ler in HIV+	people					
Index Test: HIV dem HIV dementia scale (I	<b>entia scale, HDS (&lt;</b> HDS) (<10)	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 dem	entia 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 comme nts								
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 th	nreshold.)					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Internati	onal HIV Dementia	scale (IHDS	S) (<10)					
International HIV Dem	nentia scale (IHDS) (	<10)						
Results	True positives:	10	False negatives:	3	False positives:	7	True negatives:	13
Additional comme nts								
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							

1

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

### 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 comme nts								
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 t	threshold to the star	ndard one and th	at was not pre-specifie	ed.)		
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. 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  $\geq$  7.

Results	True positives:	49	False negatives:	20	False positives:	12	True negatives:	14
Additional comme nts								
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 t	threshold to the star	ndard one and th	at was not pre-specifie	ed.)		
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. 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  $\geq$  8.

Results	True positives:	45	False negatives:	24	False positives:	9	True negatives:	17
Additional comme nts								
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. 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  $\geq$  9.

Results	True positives:	40	False negatives:	29	False positives:	8	True negatives:	18
Additional comme nts								
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 $\leq$ 1 and 2013 only DLE	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	None stated							
Sex	48% male								
Age	Mean age 74.0 yea	ars (SD 8.2)							
Presentation	People have previo	ously been d	iagnosed with deme	entia					
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: Internation	onal Consensus DI	B diagnost	tic criteria (McKeit	h 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 groups.)	7 the study s	electivey recruited p	participants with	a DLB or PDD diagno	sis to increa	se the sample size f	or these	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Overall 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

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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 confi	rmation of th	ne clinical diagnosis					
Exclusion criteria	Not stated, but peo hyperlipidemia, iscl	ple were no nemic heart	t excluded for conco disease, and heart	omitant diseases failure as well as	and conditions like dia pharmacological trea	abetes mellit tments at the	tus, arterial hyperten e time of MIBG scan	ision, ning.
Sex	61.0% male							
Age	Mean age 76.0 yea	rs (SD 8.0)						
Presentation	Clinically ambiguou	is 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 scintigra (GE) scanner, both wi head camera) and the	aphy data for 67 pati th a low-energy, higl same settings of ac	ents was ac n-resolution quisition pa	equired with a Philips collimator. Both car rameters. MIBG upt	s XCT scanner, v neras had simila ake was determi	whereas for 18 patient ir hardware characteris ined by calculating the	s, the data v stics (LEHR heart-to-me	vas acquired with a v collimator, large field ediastinum-uptake (H	Varicam d double- I/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 diagn	osing physic	cians were not blind	to the index test	t results.)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

1

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, Palmo-Mental Reflex	, Zeller A, Burge M. Detecting dementia in patients with normal neuropsychological screening by Short Smell Test and 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 h	ad to have	cognitive complaints	, but normal MM	ISE and CDT tests at I	baseline.)		
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low		
Overall indirectness	Serious (Patients h	ad to have	cognitive complaints	, but score as no	ormal on the MMSE ar	nd CDT tests	5.)	
Index Test: Palmo-M	lental Reflex							
Palmo-Mental Reflex unilateral chin muscle	(PMR). Considered twitch.	positive if br	ushing the thumb ur	nder the thenar (	the region of the palm	at the base	of the thumb) elicite	d a
Results	True positives:	7	False negatives:	10	False positives:	25	True negatives:	112

Streit S, Limacher A, Palmo-Mental Reflex	Zeller A, Burge M. Test: an observati	Detecting onal study.	dementia in patient BMC Geriatrics. 2	ts with normal   015; 15:90-95.	neuropsychological	screening b	by Short Smell Test	and
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (Patients h	ad to have o	cognitive complaints	, but normal MM	ISE and CDT tests at	baseline.)		
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Palmo-M	ental Reflex and SI	hort smell t	est, 1 positive					
Palmo-Mental Reflex ( palm at the base of the instant coffee powder	(PMR) and Short sm e thumb) elicited a u in a can when it was	ell test (SST nilateral chin held 5–10	Γ), 1 positive. PMR c n muscle twitch. SS <sup>-</sup> cm under their nose	considered posit T was considere	ive if brushing the thur d abnormal if patients	nb under the closed their	e thenar (the region of eyes and could not	of the identify
Results	True positives:	12	False negatives:	5	False positives:	50	True negatives:	87
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (Patients h	ad to have o	cognitive complaints	, but normal MM	ISE and CDT tests at I	baseline.)		
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Palmo-M	ental Reflex and SI	hort smell t	est, both positive					
Palmo-Mental Reflex ( palm at the base of the instant coffee powder	(PMR) and Short sm e thumb) elicited a u in a can when it was	ell test (SST inilateral chi s held 5–10	Γ), 1 positive. PMR c n muscle twitch. SS <sup>-</sup> cm under their nose	considered positi T was considere	ive if brushing the thur d abnormal if patients	nb under the closed their	e thenar (the region eyes and could not	of the identify
Results	True positives:	4	False negatives:	13	False positives:	9	True negatives:	128

1

Streit S, Limacher A Palmo-Mental Reflex	, Zeller A, Burge M. c Test: an observati	Detecting onal study.	dementia in patien . BMC Geriatrics. 2	ts with normal 015; 15:90-95.	neuropsychological	screening I	by Short Smell Test	and
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (Patients h	ad to have o	cognitive complaints	, but normal MM	ISE 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) versu	s 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 und assay cut-offs were	clear whethe	r the index test resu d using ROC analys	Ilts were interpre	ted without knowledge	e of the resu	Its of the reference s	tandard;
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Lesier Test MDLUC				0 70				

#### 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 T1weighted 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 comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (It was und assay cut-offs were	clear whethe	r the index test resu I using ROC analys	Ilts were interpre is.)	ted without knowledge	e of the resu	Its of the reference s	standard;
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		

Suppa P, Anker U, S for Detection of Alzh	pies L, Bopp I, Rue eimer's Disease in	gger-Frey, a Memory (	Klaghofer R, Gock Clinic Setting. Jou	e C, Hampel H o rnal of Alzheim	et al. Fully Automate er's Disease, 2015; 4	d Atlas-Bas 4: 183–193	sed Hippocampal V	olumetry
Overall indirectness	Not serious							
Index Test: MRI Tota MRI Total Hippocamp weighted magnetizatio Neurological Institute multiplying the subject Masks for the left and HV was obtained by s	Il Hippocampal gre al grey matter volum on prepared rapid gr (MNI) space using a t's GM component ir the right hemisphere umming the GM volu	y matter vo ne, Hv. MRI adient echo combined s nage with a e were used ume within b	lume, Hv. Cut off 4 was carried out usin (MPRAGE). MR ima regmentation and re predefined binary m separately yielding oth masks. Cut off	. <b>95ml.</b> g Siemens Avar ages were segm gistration approa lask from a freel two sub-volume 4.95ml.	nto 1.5 T (Siemens Erl ented and stereotactio ach. Hippocampal GM y available atlas and t s for each brain hemis	langen, Gerr cally normali l volume (H\ hen summir sphere, HVL	many) deploying 3D ized to the Montreal /) was calculated by ig over all voxel inter and HVR, respectiv	T1- nsities. ely. Total
Results	True positives:	27	False negatives:	17	False positives:	8	True negatives:	48
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (It was und assay cut-offs were	lear whethe determined	r the index test resu I using ROC analysi	Its were interpre	ted without knowledge	e of the resu	Its of the reference s	standard;
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MRI Hipp MRI Hippocampal gre Germany) deploying 3 normalized to the Mor was calculated by mu voxel intensities. Mast respectively. Total HV Results	y matter volume left boot T1-weighted mag ntreal Neurological In tiplying the subject's s for the left and the was obtained by su True positives:	ter volume f / total grey m netization pr nstitute (MNI GM compo e right hemis mming the C 35	left/ total grey math natter volume, (HVL repared rapid gradie ) space using a con nent image with a p sphere were used se GM volume within bo False	ter volume (HVI /GMV). MRI was ent echo (MPRA hbined segmenta redefined binary eparately yielding oth masks. Cut-o 9	J/GMV). Cut-off 4.69 carried out using Sie GE). MR images were ation and registration a mask from a freely av two sub-volumes for off 4.69 per mille False positives:	per mille. mens Avant segmented approach. H vailable atlas each brain	o 1.5 T (Siemens Er and stereotactically ippocampal GM volu s and then summing hemisphere, HVL an <b>True negatives:</b>	langen, me (HV) over all d HVR, 37
Noonio		00	negatives:	0		13	nue negatives.	57

Additional comme

Suppa P, Anker U, S for Detection of Alzh	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		
<b>Dverall risk of bias</b> 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 comme										

nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (It was und assay cut-offs were	lear whethe	er the index test resu d using ROC analys	Ilts were interpre	eted without knowledge	e of the resu	Its of the reference s	tandard;
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 comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (It was und assay cut-offs were	clear whethe e determined	r the index test resu I using ROC analysi	ilts were interpre is.)	ted without knowledge	e of the resu	Its of the reference s	standard;
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

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## 2 **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 Italy Country Setting Memory clinic **Inclusion criteria** Diagnosis of rapidly progressive dementia (RPD), 12 month follow up after first neurological assessment Cases of RPD where the aetiology could be easily diagnosed by first line investigations; not possible to make a clinical diagnosis Exclusion criteria according to established criteria; cognitive decline reported before the first clinical symptom of RPD. 48.6% male Sex Mean age 68.7 years (SD 11.2) Age

Textienietye M. Zeny			erentenelle C. Zem		M. Managa C. et al. A		die en optio onitonio	far
sporadic Creutzfeldt	t-Jakob Disease am	ong rapidly	/ progressive demo	entia. Journal o	of Alzheimer's diseas	e 2013; 1: 2	31-238.	IOr
Presentation	Suspected CJD du	e to rapidly	progressive dement	ia				
Reference standard	Clinician diagnosis	using Europ	bean sCJD (EUROC	JD) consortium	criteria (Zerr, 2009) fo	r probable o	r possible CJD	
CJD versus not CJD	)							
Index Test: MRI, DW	1							
MRI DWI and FLAIR i cortical regions, in eit	images were taken. / her DWI or FLAIR im	According to ages, was s	the EUROCJD crite suggestive for sCJD	eria (Zerr 2009)	hyperintensities in both	h caudate ar	nd putamen and /or i	n two
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 i cortical regions, in eitl	images were taken. / her DWI or FLAIR im	According to ages, was s	the EUROCJD crite	eria (Zerr 2009)	hyperintensities in both	h caudate ar	nd putamen and /or i	n two
Results	True positives:	4	False negatives:	6	False positives:	4	True negatives:	16
Additional comme nts								
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 comme nts								
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 14-3-4 detected by im	3-3 immunoblotting munoblotting.							
Results	True positives:	11	False	0	False positives:	13	True negatives:	10
	<b>-</b>		negatives:				i i de negativor	10
Additional comme nts			negatives:					10
Additional comme nts Risk of bias	Patient selection:	Unclear	negatives: Index test:	Unclear	Reference standard:	Low	Flow and timing:	Low
Additional comme nts Risk of bias Overall risk of bias	Patient selection: Not serious	Unclear	negatives: Index test:	Unclear	Reference standard:	Low	Flow and timing:	Low
Additional comme nts Risk of bias Overall risk of bias Indirectness	Patient selection: Not serious Patient selection:	Unclear Low	negatives: Index test: Index test:	Unclear Low	Reference standard: Reference standard:	Low	Flow and timing:	Low
Additional comme nts Risk of bias Overall risk of bias Indirectness Overall indirectness	Patient selection: Not serious Patient selection: Not serious	Unclear Low	negatives: Index test: Index test:	Unclear Low	Reference standard: Reference standard:	Low	Flow and timing:	Low
Additional comme nts Risk of bias Overall risk of bias Indirectness Overall indirectness Index Test: Total tau	Patient selection: Not serious Patient selection: Not serious	Unclear Low	negatives: Index test: Index test:	Unclear Low	Reference standard: Reference standard:	Low	Flow and timing:	Low

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 comme nts								
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							

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Neurology, Neurosu	rgery, 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.

Neurology, Neurosu	rgery, and Psychia	y D, Testa ∣ try 1998;63	HJ. A clinical role f :306-13.	or 99mTc-HMP	AO SPECT in the inv	estigation of	of dementia? Journ	al of			
Results	True positives:	21	False negatives:	37	False positives:	21	True negatives:	235			
Additional comme nts	Data obtained from	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 (Uncle knowledge of the ir index test threshold	ear if avoide idex test an d; subgroup	d inappropriate excl d whether the index analysis used as da	usions; unclear test was carried ta on 'other' clin	whether the reference out without knowledg ical diagnosis group is	standard re e of referend not reporte	sults were interprete ce test result; no pre- d.)	d without -specified			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										
FTD versus VaD											
Index Test: 99mTc-H 99mTc-HMPAO SPE plus unilateral posteri images. SPECT 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 ETD pattern indicative of ETD; bilateral anterior brain by poperfusion.										
	pattern indicative of	FTD: bilater	al anterior brain hyp	operfusion.	n with image analysis;	single- hea	ded camera used to	nterior take			
Results	pattern indicative of <b>True positives:</b>	FTD: bilater	al anterior brain hyp False negatives:	43	n with image analysis; <b>False positives:</b>	single- hea	ded camera used to True negatives:	nterior take 57			
Additional comme nts	pattern indicative of <b>True positives:</b> Data obtained from	FTD: bilater 37 Archer et a	ral anterior brain hyp False negatives: Il, (2015) Cochrane	43 review as not pro	n with image analysis; False positives: esented in a useful for	single- hea 21 mat in origir	ded camera used to True negatives: al paper.	nterior take 57			
Results Additional comme nts Risk of bias	pattern indicative of True positives: Data obtained from Patient selection:	FTD: bilater 37 Archer et a Unclear	al anterior brain hyp False negatives: Il, (2015) Cochrane Index test:	43 review as not pro	n with image analysis; False positives: esented in a useful for Reference standard:	single- hea 21 mat in origir Unclear	ded camera used to True negatives: al paper. Flow and timing:	57 High			
Results Additional comme nts Risk of bias Overall risk of bias	pattern indicative of <b>True positives:</b> Data obtained from <b>Patient</b> <b>selection:</b> Very serious (Uncle knowledge of the ir index test threshold	FTD: bilater 37 Archer et a Unclear ear if avoide idex test an d; subgroup	al anterior brain hyp False negatives: I, (2015) Cochrane Index test: d inappropriate excl d whether the index analysis used with 3	43 review as not pro High usions; unclear >10% study popu	n with image analysis; False positives: esented in a useful for Reference standard: whether the reference out without knowledg ulation excluded.)	single- hea 21 mat in origir Unclear standard re e of reference	ded camera used to True negatives: al paper. Flow and timing: sults were interprete ce test result; no pre-	take 57 High d without -specified			
Results Additional comme nts Risk of bias Overall risk of bias Indirectness	pattern indicative of <b>True positives:</b> Data obtained from <b>Patient</b> <b>selection:</b> Very serious (Uncle knowledge of the ir index test threshold <b>Patient</b> <b>selection:</b>	FTD: bilater 37 Archer et a Unclear ear if avoide idex test an d; subgroup Low	al anterior brain hyp False negatives: I, (2015) Cochrane Index test: Index test: Index test: analysis used with a Index test:	43 review as not pro High usions; unclear test was carried >10% study popu	n with image analysis; False positives: esented in a useful for Reference standard: whether the reference out without knowledg ulation excluded.) Reference standard:	single- hea 21 mat in origin Unclear standard re e of reference Low	ded camera used to True negatives: al paper. Flow and timing: sults were interprete ce test result; no pre-	hterior take 57 High d without -specified			

# 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 comme nts	Data obtained from	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										

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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 dement	Suspected dementia								
Reference standard	DSM-IV for demen consensus criteria	tia, NINCDS for DBL.	ADRDA for AD, NI	NDS-AIREN for	VaD, Neary et al (1998	<ol> <li>criteria for</li> </ol>	FTD, McKeith et al	. (1999)		
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 la	acking a clin	ical diagnosis were	excluded from the	ne analysis)					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not Serious									
Index Test: Addenbr Addenbrooke's Cogni	ooke's Cognitive E tive Examination-Re	xamination	-Revised, ACE-R ( R, 84/100, optimal of	<85) cut off from ROC						
Results	True positives:	70	False negatives:	12	False positives:	8	True negatives:	32		
Additional comme nts										
Risk of bias	Patient selection:	Low	Index test:	Unclear	Reference standard:	Unclear	Flow and timing:	High		
Overall risk of bias	Serious (Patients la	acking a clin	ical diagnosis were	excluded from the	ne analysis)					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not Serious									
Index Test: Addenbr	ooke's Cognitive E	xamination	-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 comme nts									
Risk of bias	Patient selection:	Low	Index test:	Unclear	Reference standard:	Unclear	Flow and timing:	High	
Overall risk of bias	Serious (Patients la	acking a clin	ical diagnosis were	excluded from th	ne analysis)				
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not Serious								

1

Thomas AJ, Attems diagnosis of DLB. N	J, Colloby SJ, O'Brien JT, McKeith I, Walker R et al. Autopsy validation of 123I-FP-CIT dopaminergic neuroimaging for the eurology 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-DL	B

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, Brettsch	neider J, Grossman	M, Arnold	SE, Hu, WT, Xie S	X, Lee VM-Y, S	naw LM, Trojanowski	JQ.			
Study type	Retrospective coho	Retrospective cohort							
Country	USA								
Setting	Penn Centre for Ne	urodegenei	ative Disease Rese	arch Integrated	Neurodegenerative Di	sease datab	ase		
Inclusion criteria	Autopsy confirmation	on of a diag	nosis of AD, DLB, F	TD; available M	MSE and CDR scores	and CSF bio	omarker data.		
Exclusion criteria	Not stated								
Sex	Not reported								
Age	Mean age 68.9 yea	Mean age 68.9 years (9.5)							
Presentation	clinically ambiguous	s dementia							
Reference standard	Autopsy confirmation	Autopsy confirmation of previous clinical diagnosis							
AD versus FTD									
Index Test: Amyloid	Beta 1-42 and Tota	l 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.									
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Risk of bias	Patient selection:	Low	Index test:	Unclear	Reference standard:	Low	Flow and timing:	High	
Overall risk of bias	Serious (>10% pop specified)	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, Brettsch	neider							
Study type	Retrospective coho	Retrospective cohort						
Country	USA							
Setting	Penn Centre for Ne	eurodegenei	rative Disease Rese	arch Integrated	Neurodegenerative Di	sease datab	ase	
Inclusion criteria	Autopsy confirmation	on of a diag	nosis of AD, DLB, F	TD; available M	IMSE and CDR scores	and CSF bio	omarker data.	
Exclusion criteria	Not stated							
Sex	Not reported							
Age	Mean age 68.9 yea	ars (9.5)						
Presentation	clinically ambiguou	s dementia						
Reference standard	Autopsy confirmation	on of previo	us clinical diagnosis	i				
AD versus FTD								
Index Test: p-tau 18 p-tau 181, Luminex	1							
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% pop specified)	oulation excl	uded from analysis;	the index test t	hresholds used are not	stated and	it is unclear if they w	vere pre-

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

1

G.Treglia, E.Cason, Fagioli, lodine-123m body diseases: com	3.Treglia, E.Cason, P.Cortelli, A.Gabellini, R.Liguori, A.Bagnato, A.Giordano, G. <sup>-</sup> agioli, lodine-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 de	mentia					

#### 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	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 comme nts									
Risk of bias	Patient selection:	Low	Index test:	Unclear	Reference standard:	Unclear	Flow and timing:	Low	
Overall risk of bias	Not serious (Specif	ic criteria us	sed as the reference	standard not re	ported)				
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.					

Fripathi 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 pa was interpreted wit	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 pa was interpreted wit	irticipants we	ere lost to follow up dge of the reference	and did not rece e standard.)	vive a reference standa	ard; it is uncl	lear whether the inde	ex test
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

1

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	Not stated						
Age	Not stated	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-	MRI, typical and non-typical MRI patterns listed in paper. Hyperintense grey matter on MRI.							
Results	True positives:86False58False positives:6True 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 comme nts	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 v	vave complexes, sta	indard proce	ess for surveillance ι	unit.				
Results	True positives:	42	False negatives:	91	False positives:	2	True negatives:	30
Additional comme nts	Three independent observers.	observers r	ated the index test of	data. We have u	sed the median sensit	ivity and spe	ecificity data for the 3	3
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	8-3							
14-3-3, standard proc	ess for surveillance	unit						
Results	True positives:	128	False negatives:	12	False positives:	19	True negatives:	15
Additional comme nts	Three independent observers.	observers r	ated the index test of	data. We have u	sed the median sensit	ivity and spe	ecificity data for the 3	3

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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## 2 **P.1.20 V**

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 coho	Retrospective cohort							
Country	Belgium								
Setting	Laboratory of neuro	obiology, Ur	niversity of Antwerp						
Inclusion criteria	Clinical symptoms	compatible	with the diagnosis o	f possible CJD a	t the time of lumbar pu	uncture			
Exclusion criteria	Not stated								
Sex	Not reported								
Age	Mean age 67.0 yea	Mean age 67.0 years (SD 8.0)							
Presentation	suspected CJD								
Reference standard	Clinical diagnosis a	according to	Weber (2000) with	neuropathologica	al confirmation.				
CJD versus not CJD									
Index Test: CSF 14-3	3-3 immunoblotting								
14-3-3, immunoblottir	g. The blot was scor	ed for the p	resence or absence	of an immunore	active 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 comme 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									
Index Test: Total Ta	u									
Tau, INNOTEST ELIS	SA, cut-off 1300pg/m	I								
Results	True positives:	45	False negatives:	7	False positives:	5	True negatives:	193		
Additional comme nts										
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 pg/ml cut-off.	1-42. Tau was dete	cted using I	NNOTEST ELISA, c	ut-off 1300pg/m	I; Amyloid Beta 1-42 v	vas detected	l using an ELISA with	h a 400			
Results	True positives:	45	False negatives:	7	False positives:	4	True negatives:	194			
Additional comme 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										

1

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, D patients.J Neurol. 20	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 im	munocytochemi	stry for CJD.						
CJD versus not CJD											
Index Test: Total Tau	ı										
Tau >1300pg/ml, by INNOTEST ELISA											
Results	True positives:	45	False negatives:	7	False positives:	2	True negatives:	79			
Additional comme nts	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% pop	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	e basal gan	glia and thalamus								
Results	True positives:	19	False negatives:	33	False positives:	2	True negatives:	79			
Additional comme nts	Data for Periodic sl reference diagnosis	narp wave c s.	omplexes (PSWCs)	in EEG and 14-	3-3- protein were not a	analysed as	they formed part of	the			
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	High			
Overall risk of bias	Serious (> 10% pop	pulation exc	luded from analysis)	)							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										

1

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-H	IMPAO SPECT (FTI	D 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 SPE	CT scannir	ng in a neuropsych	iatry unit. Aust	N Z J Psychiatry 19	98; 32: 511-	22.				
resolution estimated t were interpreted visua	o be 9mm. Planar da ally. FTD pattern use	ata was proc d for image	essed to provide tra analysis here.	ansverse slices in	n the orbitomeatal line	and corona	l and sagittal images	. Images			
Results	True positives:	6	False negatives:	27	False positives:	9	True negatives:	14			
Additional comme nts											
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-H	IMPAO SPECT										
99mTc-HMPAO SPE0 resolution estimated t were interpreted visua	CT imaging carried o o be 9mm. Planar da ally. AD pattern used	ut in anothe ata was proc for image a	r specialist departm cessed to provide tra inalysis here.	ent. 72 images o ansverse slices in	of tracer distribution wind the orbitomeatal line	ith 24 image and corona	s per scan with imag I and sagittal images	je 5. Images			
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 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 (Subg interpreted without standard results int	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									

1

Vijverberg EGB, Dol Dementia Consensu	s A, Krudop WA, Peters A, Kerssens CJ, van Berckel BNM, Wattjes MP et al. Diagnostic Accuracy of the Frontotemporal Is 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, Dol Dementia Consensu	s A, Krudop WA, Peters A, Kerssens CJ, van Berckel BNM, Wattjes MP et al. Diagnostic Accuracy of the Frontotemporal Is 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).
byFTD versus not by	VETD

#### 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	
<b>Overall risk of bias</b> 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 by	/FTD								
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	4	False positives:	16	True negatives:	73	

Roounto	rido poolarool	20	1 4100	-	i aloo poolaitool	10	indo nogativoo.	10
			negatives:					
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Unclear	Flow and timing:	High

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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 was enrolled or whe	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	Not serious									
Vijverberg EGB, Wat	tjes MP, Dols A, Kr	udop WA, I	Moller C, Peters A,	Kerssens CJ e	t al. Diagnostic Accu	racy of MRI	and Additional [18	BF]FDG-			
PET for Behavioral V 53: 1287–1297.	ariant Frontotempo	oral Demen	tia in Patients with	n Late Onset Be	havioral Changes. Jo	ournal of Al	zheimer's Disease,	, 2016b;			
Study type	Prospective cohort										
Country	The Netherlands										
Setting	VU medical centre	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 yea	ars (SD 6.6)									
Presentation	suspected bv-FTD										
Reference standard	Reference Diagnoses were based on the published consensus guidelines for dementia (Rascovsky, 2011, for FTD; Gorno-Tempini, 2011, for standard DPA; 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-l	bv-FTD										
Index Test: FDG-PET	r 🔤										
18-F FDG-PET scans experienced nuclear r	were made on an E nedicine physician o	CAT EXACT	FHR+ scanner (Sien d/or anterior tempora	mens/CTI). [18F al hypometabolis	FDG-PET-scans were m based on the summ	e assessed v ned images	visually and interpret of all the frames.	ted by an			
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 High timing:		
Overall risk of bias	Serious (19% study was enrolled or who clinical diagnosis.)	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 comme nts								
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 comme nts								
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							

### 1 **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 yea	ars (SD 9.0)									
Presentation	Suspected dement	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-DLE	3 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										
Juday Teat 4021 ED											

#### 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.

boules. movement b	
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 previo	ously diagno	sed DLB or AD					
Reference standard	The neuropatholog Alzheimer's Diseas diagnosis.	he neuropathological diagnostic criteria employed for AD included the following: CERAD (Consortium to Establish a Registry for Izheimer's Disease) score and diagnosis, Braak stage and NIA-RI (National Institute on Aging and Reagan Institute) AD iagnosis.						
	The neuropatholog	ical diagnos	tic criteria employed	for DLB were th	nose recommended by	y the Third re	eport of the DLB Cor	nsortium.
DLB vs no-DLB								
123I-FP-CIT SPECT s were subject to a sem as having binding > 2	scan using a Strichm i-quantitative analys SDs below that of h	an Medical is, interprete ealthy contro	Equipment 810 carr ed by a specialist in ols in the posterior p	nera. Scanning to nuclear medicino utamen on 1 or	ook place 3 to 4 hours e. An abnormal scan o both sides.	after injectio on semi-quai	on of DaTscanT M. Antitative analysis was	All scans s defined
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 t	he included	individuals had a pr	esumed dement	ia diagnosis at baselir	ne)		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

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### 2 **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 referra	als to the me	emory clinic.					
Exclusion criteria	Not stated							
Sex	60.0% male							
Age	Mean age 67.0 yea	ars (SD 10.9	)					
Presentation	Suspected dement	ia						
Reference standard	Patients were diagonal according to NINDS	nosed with A S-AIREN crit	AD according to NIN teria; frontotempora	CDS-ADRDA cr I dementia accor	iteria; MCI according t ding to Lund-Manches	o Petersen o ster criteria.	criteria; vascular der	nentia
AD versus no demen	ntia (excludes MCI)							
Index Test: Total Tak CSF total tau (INNOT	u EST hTau- Ag ELIS/	A), cut-off >5	520ng/l					
Results	True positives:	11	False negatives:	13	False positives:	1	True negatives:	21
Additional comme nts	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 (Subg	roup analys	is with >10% popula	ation excluded; u	se of optimised thresh	olds for test	.)	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus non-AD d	ementias (excludes	s MCI)						
Index Test: Total Tak CSF total tau (INNOT	<b>u</b> EST hTau- Ag ELIS/	A), cut-off >4	140ng/l					
Results	True positives:	13	False negatives:	11	False positives:	1	True negatives:	12
Additional comme nts	p-tau 181 data not sharing the same to	analysed as est cut-off (>	AD versus non-der 65ng/l)	mentia and AD v	ersus other dementias	do not have	e the same sensitivit	y despite
Risk of bias	Patient	Low	Index test:	High	Reference	Low	Flow and	High

Yakushev I, Bartens F-Fluorodeoxygluco	tein, P, Siessmeier se Positron Emissi	T, Hiemke ( ion Tomogr	C, Scheurich A, Lo aphy in the Differe	tz J, Fellgiebel ntial Diagnosis	A, Muller MJ. Cerebro of Alzheimer's Disea	ospinal Flui ase.	d Tau Protein Leve	els and 18
	selection:				standard:		timing:	
Overall risk of bias	Very serious (Subg	group analys	is with >10% popula	ation excluded; u	ise of optimised thresh	olds for test	)	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus no demen	ntia (excludes MCI)							
Index Test: FDG-PET FDG-PET images take realignment and spati SSP) technique. The	<b>F</b> en using a Siemens al normalization, gre findings were finally	ECAT EXAC y matter act rated as AD	CT scanner in 3-D m ivities were extracte -typical or not AD-ty	node. The PET s d to predefined pical.	cans were processed surface pixels using a	using Neuro 3-D stereota	stat software. After i actic surface projecti	mage on (3D-
Results	True positives:	19	False negatives:	5	False positives:	2	True negatives:	20
Additional comme nts	p-tau 181 data not sharing the same to	analysed as est cut-off (>	AD versus non-der 65ng/l)	mentia and AD v	ersus other dementias	do not have	e the same sensitivit	y despite
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Serious (Subgroup	analysis wit	h >10% population	excluded)				
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus non-AD d	ementias (exclude	s MCI)						
Index Test: FDG-PET FDG-PET images tak realignment and spati SSP) technique. The	<b>F</b> en using a Siemens al normalization, gre findings were finally	ECAT EXAC by matter act rated as AD	CT scanner in 3-D m ivities were extracte -typical or not AD-ty	node. The PET s d to predefined prical.	cans were processed surface pixels using a	using Neuro 3-D stereota	stat software. After i actic surface projecti	mage on (3D-
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-der	mentia and AD v	ersus other dementias	do not have	e the same sensitivit	y 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 to	est 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 wit	h >10% population	excluded)				
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus other gro	ups (non-AD deme	ntias and n	o dementia, excluc	les MCI)				
Index Test: FDG-PET	Г							
FDG-PET images take realignment and spatia SSP) technique. The f	en using a Siemens al normalization, gre findings were finally	ECAT EXAC y matter act rated as AD	CT scanner in 3-D m ivities were extracte -typical or not AD-ty	node. The PET s d to predefined a pical.	cans were processed surface pixels using a	using Neuro 3-D stereot	ostat software. After actic surface projecti	image on (3D-
Results	True positives:	19	False negatives:	5	False positives:	2	True negatives:	33
Additional comme nts	p-tau 181 data not sharing the same to Data presented wit	analysed as est cut-off (> h different c	AD versus non-der 65ng/l) ut-offs for MCI so co	nentia and AD v	ersus other dementias MCI results in AD vers	do not hav us all other	e the same sensitivit groups comparison.	y despite
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Serious (Subgroup	analysis wit	h >10% population	excluded)				
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

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Yeung PY, Wong LL MoCA) in Chinese o	/eung PY, Wong LL, Chan CC, Leung JLM, Yung CY. A validation study of the Hong Kong version of Montreal Cognitive Assessment (HK- NoCA) 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 MoCA) in Chinese of	, Chan CC, Leung J der adults in Hong	LM, Yung C Kong. Hon	CY. A validation stu g Kong Med J 2014	udy of the Hong 4; 20: 504–10.	J Kong version of Mo	ontreal Cogi	nitive Assessment	(HK-
Setting	Cognition clinic and	Cognition clinic and memory clinic of a						
	public hospital in H	ong Kong						
Inclusion criteria	Cantonese-speakir consent, were recru	ng Chinese a uited.	adults aged 60 years	s or above, who	were seen for suspect	ted cognitive	e impairment and gav	/e
Exclusion criteria	Patients were exclu system infection, be major depression of barriers such as de with Global Deterio	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 yea	ars (SD 7.5)						
Presentation	Suspected dement	ia						
Reference standard	The DSM-IV criteria	a was used t	to diagnose dement	ia and the Peters	sen criteria (1999) for	MCI.		
Dementia versus no	dementia (includin	g MCI)						
Index Test: Montreal Hong-Kong version of	Cognitive Assessi MoCA, cut off 21/22	ment, MoCA	A (<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 (excludir	ng MCI)						
Index Test: Montrea	Cognitive Assess	ment, MoCA	A (<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	long-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	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.)							e nd on (MCI)
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious	Not serious						
Index Test: MMSE (< Cantonese MMSE, cu	<b>25)</b> t off 24/25							
Results	True positives:	124	False negatives:	6	False positives:	5	True negatives:	44
Additional comme nts	Cantonese MMSE, calculate dementia and population.	cut off 26/2 versus no d	7 -data for dementia lementia (including l	a plus MCI versu MCI) as the spec	s no dementia and MC ificity is not consistent	CI versus no t between te	rmal control cannot l ests at with the same	cut off
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Unclear	Flow and timing:	High
Overall risk of bias	<b>risk of bias</b> 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							

### 1 **P.1.23 Z**

Zerr I, Bodemer M, C Ann Neurol 1998; 43	Gefeller O, et al. Det : 32– 40.	ection of 14	4-3-3 protein in the	cerebrospinal	fluid supports the di	agnosis of (	Creutzfeldt-Jakob o	disease.
Study type	Prospective cohort							
Country	Germany							
Setting	German National S	urveillance	unit					
Inclusion criteria	People referred for	diagnosis w	vith suspected CJD					
Exclusion criteria	Not stated							
Sex	28.4% male							
Age	Median ages range	from 38 to	67 across the diagn	ostic groups				
Presentation	Rapidly progressive	e dementia l	eading to suspected	d CJD				
Reference standard	Criteria for CJD bas	sed on Mast	ers et al. (1979), W	ill et al. (1998), Z	Zerr (1996) and Steinh	off et al. (19	96)	
CJD (including poss	ible CJD) versus no	ot-CJD						
Index Test: CSF 14-3 CSF 14-3-3 protein de	3-3 immunoblotting etected by immunobl	otting with a	ny ambiguous resul	ts defined as po	sitive			
Results	True positives:	161	False negatives:	24	False positives:	7	True negatives:	97
Additional comme nts	The healthy control	group was	excluded as they di	d not have suspe	ected 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 pos	sible CJD) versus n	ot-CJD						

Zerr I, Bodemer M, G Ann Neurol 1998; 43	Cerr 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 de	etected by immunobl	otting with a	ny ambiguous resul	ts defined as po	sitive			
Results	True positives:	132	False negatives:	13	False positives:	7	True negatives:	97
Additional comme nts	The healthy control	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 a unclear whether: a results were interpr interpreted without	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 index test.)						
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

1

Zerr I, Pocchiari M, ( 2000; 55: 811– 815.	Collins S, et al. Analysis of EEG and CSF 14-3-3 proteins as aids to the diagnosis of Creutzfeldt-Jakob disease. Neurology
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:	e positives: 497 False 114 False positives: 34 True negatives: 358 negatives:											
Risk of bias	Patient selection:	Patient         Unclear         Index test:         Unclear         Reference         Low         Flow and         Low           selection:            standard:          timing:											
Overall risk of bias	Serious (It was unc a consecutive or ra specified.)	lear whethe ndom samp	r the index tests we le of people were ei	re interpreted ind nrolled or inappro	dependently of the refe opriate exclusions avo	erence test r ided; or the	results; it was unclea index test threshold	r whether was pre-					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low							
Overall indirectness	Not serious												

Zerr I, Kallenberg K, Jakob disease. Brain	Summers DM, Romero C, Taraturo A, Heinemann U et al. Updated clinical diagnostic criteria for sporadic Creutzfeldt- n 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 diagonal ware diagonal ware ware ware ware ware ware ware ware	nosed using is of brain pa	brain pathology or l athogenic prion prot	by clinician diagi ein.	nosis using the criteria	for probable	e CJD, codon 129 ge	enotyping				
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       8       False positives:       15       True negatives:         negatives:											
Risk of bias	Patient selection:	Patient     Unclear     Index test:     High     Reference     Low     Flow and     High       selection:        standard:      timing:										
Overall risk of bias	k 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:	Patient     Low     Index test:     Low     Reference     Low       selection:        standard:										
Overall indirectness	Not serious											
Index Test: New crit	eria for sporadic C.	JD										
New criteria for spora were measured. For M positive CJD diagnosi	dic CJD (EEG, 14-3- MRI a standardized p is.	-3 and MRI I protocol was	LAIR and DWI). 14 used which include	-3-3 was detected seven cerebra	ed by immunoblotting a I cortex regions. Curre	and EEG (pe ent criteria po	eriodic sharp wave c ositive & MRI positiv	omplexes) e for				
Results	True positives:	49	False negatives:	1	False positives:	7	True negatives:	17				
Additional comme nts												
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.)											

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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	Not serious										
Zwan MD, Bouwman Alzheimer's Researc	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 (MMSE) score ≥ 18 standardized deme measured by a star	of patients 3) or early-or ntia evaluat ndardised st	visiting a memory c nset dementia (defir ion or persisting dia udy questionnaire).	linic with suspec ned by age at dia ignostic uncertai	ted mild dementia (de ignosis ≤ 70 years), w nty (defined as pre-PE	fined as Mini Mental State Examination ho had no firm diagnosis after the T diagnostic confidence < 90% as						
Exclusion criteria	People with suspect	ted dement	ia and diagnostic co	onfidence after st	andardised work-up >	· 90%.						
Sex	55% male											
Age	Mean age 62 years	s (SD 6)										
Presentation	Suspected dementi	ia										
Reference standard	ce 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] flut	temetamol 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         Not serious										

1

# 2 P.2 GRADE tables

### 3 P.2.1 Dementia versus no dementia

#### 4 P.2.1.1 10-point Cognitive Screener (10-CS) ( $\leq$ 5)



Apolinario 2015: Included patients were selected to be ≥ 60 years old and had on average only 4.7 years of schooling

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Analinania 2015)	Dreamantiva	220	0.04 (0.00, 0.07)		LR+	2.34 (1.88, 2.91)	Serious	n/a	Serious	Serious		VERY LOW
1 study (Apolinario 2015)         Prospective         230         0.94 (0.88, 0.97)         0.60 (0.51, 0.68)           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  $\geq$  60 years old and had on average only 4.7 years of schooling

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Apolipario 2015)	Draanaatiwa	220	0.07 (0.02, 0.00)	0 40 (0 22 0 40)	LR+	1.63 (1.40, 1.89)	Serious	n/a	Serious	Not serious		LOW
T study (Apolinano 2015)	Prospective	230	0.97 (0.92, 0.99)	0.40 (0.32, 0.49)	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

#### 1 P.2.1.4 6 item screener (≥0)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Callahan	Broonostivo	651	1 00 (0 08 1 00)	0.00 (0.00, 0.02)	LR+	1.00 (0.99, 1.01)	Serious	n/a	Not serious	Not serious		MODERATE
2002)	FIOSPECTIVE	051	1.00 (0.96, 1.00)	0.00 (0.00, 0.03)	LR-	0.89 (0.02, 44.58)	Serious	n/a	Not serious	V. serious	-	VERY LOW
Notes on risk of higs												

#### 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.

#### 2 P.2.1.5 6 item screener (≥1)



#### 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.

#### 6 item screener (≥2) 1 **P.2.1.6**

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Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAP	RE											
1 study (Callahan	Dreenestive	054		0.70 (0.75, 0.04)	LR+	4.35 (3.48, 5.44)	Serious	n/a	Not serious	Not serious		MODERATE
2002)	Prospective	100	0.90 (0.66, 0.92)	0.79 (0.75, 0.84)	LR-	0.13 (0.10, 0.18)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of higs												

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.

#### 2 **P.2.1.7** 6 item screener (≥3)



#### 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.

#### 6 item screener (≥4) 1 **P.2.1.8**

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAP	RE											
1 study (Callahan	Dreanactive	651	0.69 (0.62, 0.72)	0.06 (0.02, 0.08)	LR+	17.22 (9.84, 30.13)	Serious	n/a	Not serious	Not serious		MODERATE
2002)	Prospective	001	0.00 (0.02, 0.72)	0.96 (0.93, 0.98)	LR-	0.34 (0.29, 0.39)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of higs												

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.

#### 2 **P.2.1.9** 6 item screener (≥5)



#### 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.
# 1 P.2.1.10 6 item screener (≥6)

	<u> </u>											
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	RE											
1 study	Droopostivo	651	0.20 (0.26, 0.25)	0.00 (0.07, 1.00)	LR+	46.57 (11.59, 187.06)	Serious	n/a	Not serious	Not serious		MODERATE
(Callahan 2002)	Prospective	100	0.30 (0.20, 0.35)	0.99 (0.97, 1.00)	LR-	0.70 (0.65, 0.75)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of b	ias											

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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
	Descention	0.45	0.00 (0.75, 0.04)	0.70 (0.70, 0.00)	LR+	4.01 (3.01, 5.33)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Abdel-Aziz 2015)	Prospective	245	0.88 (0.75, 0.94)	0.78 (0.72, 0.83)	LR-	0.16 (0.08, 0.34)	Not serious	n/a	Not serious	Not serious	-	HIGH

# 1 P.2.1.12 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality		
MULTIPLE CAMERA														
1 study (Debart 2005)	Droopostivo	24	0.90 (0.65, 0.07)	0.22 (0.09 0.72)	LR+	1.33 (0.74, 2.40)	Serious	n/a	Not serious	Serious		LOW		
T Sludy (Dobert 2005)	Prospective	24	0.89 (0.85, 0.97)	0.33 (0.08, 0.73)	LR-	0.33 (0.06, 1.88)	Serious	n/a	Not serious	Serious	-	LOW		
Notes on risk of bias	Notes on risk of bias													
Dobert 2005: It is unclear wheth	her a consecutiv	e or rand	lom sample of patie	nts was enrolled and	d whether ina	appropriate exclusio	ons were av	/oided.						

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Larner 2007)	Draanaativa	205	0.95 (0.78, 0.00)	0.02 (0.76, 0.00)	LR+	4.93 (3.43, 7.09)	Not serious	n/a	Not serious	Not serious		HIGH
	Prospective	200	0.65 (0.76, 0.90)	0.63 (0.76, 0.66)	LR-	0.18 (0.12, 0.27)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

			, (	,								
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Larner 2007;	2 ×	404	0.04 (0.07, 0.00)	0.04 (0.00, 0.00)	LR+	5.62 (0.81, 39.07)	Serious	Serious	Not serious	Serious		VERY LOW
Mathuranath 2000)	prospective	424	0.91 (0.67, 0.96)	0.64 (0.29, 0.96)	LR-	0.12 (0.04, 0.33)	Serious	Serious	Not serious	Not serious	-	LOW
Notes on risk of bias	ed test-threshold	tused ar	nd it was unclear wh	ether the index test	results were	interpreted without k	nowledge	of the resu	Its of the refer	ance standard		

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



## 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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality		
SECONDARY CARE														
1 study (lubb 2015)	Draanaativa	50	0.81 (0.61 0.02)	0.07 (0.91 1.00)	LR+	26.65 (3.83, 185.32)	Serious	n/a	Serious	Not serious		LOW		
T Sludy (Jubb 2015)	Prospective	59	0.81 (0.81, 0.92)	0.97 (0.61, 1.00)	LR-	0.20 (0.09, 0.44)	Serious	n/a	Serious	Not serious	-	LOW		
Notes on risk of bias Jubb 2015: Optimised t Notes on indirectness Jubb 2015: Study popul	Notes on risk of bias   LR-   0.20 (0.09, 0.44)   Serious   Not serious   LOW     Notes on indirectness   Lubb 2015: Study population was confined to ≥75 years   >75 years													

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	nconsistency	ndirectness	mprecision	Other considerations	Quality
SECONDARY CARE							_					
1 abudu ( Jubb 2015)	Dreamative	50	0.04 (0.04 0.02)	0.70 (0.50, 0.00)	LR+	2.67 (1.54, 4.62)	Not serious	n/a	Serious	Serious		LOW
T Study (Jubb 2015)	Prospective	59	0.81 (0.61, 0.92)	0.70 (0.52, 0.83)	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

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

	<u> </u>		,	<u> </u>									
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE						·							
1  study (1  when  2015)	Draanaatiya	50	0.02 (0.74, 0.08)	0.61 (0.42, 0.76)	LR+	2.34 (1.51, 3.63)	Serious	n/a	Serious	Serious		VERY LOW	
T Study (Jubb 2015)	Prospective	59	0.92 (0.74, 0.98)	0.01 (0.43, 0.76)	LR-	0.13 (0.03, 0.49)	Serious	n/a	Serious	Not serious	-	LOW	
Notes on risk of bias Jubb 2015: Optimised t Notes on indirectness	Notes on risk of bias lubb 2015: Optimised threshold used for analysis. Notes on indirectness												

Jubb 2015: Study population was confined to >75 years

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy ( lubb 2015)	Broopportivo	60	0.06 (0.77, 0.00)	0 50 (0 24 0 66)	LR+	1.92 (1.36, 2.71)	Not serious	n/a	Serious	Serious		LOW
T Sludy (Jubb 2015)	Fiospective	00	0.90 (0.77, 0.99)	0.50 (0.54, 0.66)	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

#### Addenbrooke's Cognitive Examination-Revised, ACE-R (<74) 1 **P.2.1.20**

	<u> </u>	-		<u>, (                                   </u>									
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE	·		·										
1 study (Llansack 2011)	Dreenestive	140	0.00 (0.76, 0.06)	0.02 (0.96, 0.07)	LR+	12.95 (6.29, 26.67)	Serious	n/a	Not serious	Not serious		MODERATE	
	Prospective	140	0.90 (0.76, 0.96)	0.93 (0.86, 0.97)	LR-	0.11 (0.04, 0.28)	Serious	n/a	Not serious	Not serious	-	MODERATE	
Notes on risk of bias	Notes on risk of bias												
Tiancock 2011. Optimised	i test thieshold.												

#### Addenbrooke's Cognitive Examination-Revised, ACE-R (<83) 2 P.2.1.21



## Notes on risk of bias

Terpening 2011: Patients lacking a clinical diagnosis were excluded from the analysis

Bastide 2012: Optimised test cut-offs used.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Terresing 2011)	Dreamative	100	0.05 (0.70, 0.04)		LR+	4.27 (2.28, 7.98)	Serious	n/a	Not serious	Not serious		MODERATE
r study (Terpening 2011)	Prospective	122	0.85 (0.76, 0.91)	0.80 (0.65, 0.90)	LR-	0.18 (0.11, 0.32)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of bias Terpening 2011: Patients la	icking a clinical	diagnosis	s were excluded from	n the analysis								

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ternening 2011)	Dreanactive	100	0.01 (0.83, 0.06)	0.69 (0.52, 0.90)	LR+	2.81 (1.79, 4.42)	Serious	n/a	Not serious	Serious		LOW
r study (Terpening 2011)	Prospective	122	0.91 (0.83, 0.96)	0.08 (0.52, 0.80)	LR-	0.13 (0.06, 0.27)	Serious	n/a	Not serious	Not serious	-	MODERATE
Nation on wheth of these												

### Notes on risk of bias

Terpening 2011: Patients lacking a clinical diagnosis were excluded from the analysis

# 1 P.2.1.24 AD8 (≥2)

//20 (==)												
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Larpor 2015)	Dreenestive	212	0.07 (0.80, 0.00)	0 11 (0 07 0 17)	LR+	1.09 (1.02, 1.17)	Not serious	n/a	Not serious	Not serious		HIGH
r study (Lamer 2015)	Prospective 212 0.97 (0.89, 0.99)	0.11(0.07, 0.17)	LR-	0.26 (0.06, 1.10)	Not serious	n/a	Not serious	Serious	-	MODERATE		

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

Studies PRIMARY CARE	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
					L D L	1 24 (1 17 1 54)		n/a	Not oprigue	Not earieue		
1 study (Flicker 1997) Prosp	Prospective	200	0 97 (0 94 0 99)	0.28 (0.19, 0.38)	LKT	1.54 (1.17, 1.54)	v. senous	n/a	Not serious	Not serious		LOW
	riospective	200	0.07 (0.04, 0.99)	0.20 (0.19, 0.00)	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.

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

Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
				LR+	4.40 (2.51, 7.72)	V. serious	n/a	Not serious	Not serious		LOW
Prospective	299	0.58 (0.52, 0.65)	0.87 (0.78, 0.93)	LR-	0.48 (0.40, 0.57)	V. serious	n/a	Not serious	Serious	-	VERY LOW
	Design	Design Total N Prospective 299	DesignTotal NSens (95%CI)rospective2990.58 (0.52, 0.65)	Design     Total N     Sens (95%Cl)     Spec (95%Cl)       vrospective     299     0.58 (0.52, 0.65)     0.87 (0.78, 0.93)	Design     Total N     Sens (95%CI)     Spec (95%CI)     Measure       vrospective     299     0.58 (0.52, 0.65)     0.87 (0.78, 0.93)     LR+ LR-	Design     Total N     Sens (95%CI)     Spec (95%CI)     Measure     Summary of findings (95%CI)       vrospective     299     0.58 (0.52, 0.65)     0.87 (0.78, 0.93)     LR+     4.40 (2.51, 7.72)       LR-     0.48 (0.40, 0.57)	Design     Total N     Sens (95%Cl)     Spec (95%Cl)     Measure     Summary of findings (95%Cl)     Summary of findings (95%Cl)       rospective     299     0.58 (0.52, 0.65)     0.87 (0.78, 0.93)     LR+     4.40 (2.51, 7.72)     V. serious       LR-     0.48 (0.40, 0.57)     V. serious	$\frac{1}{10} \sum_{\text{Prop}} \frac{1}{10} \sum_{\substack{\text{N} \\ \text{Prop}}} \frac{1}{10} \sum_{\substack{\text{Prop} \\ \text{Prop}}} $	Total DesignSens (95%CI)Spec (95%CI)MeasureSummary of findings (95%CI)set sigset sigset sigTotal NoSens (95%CI)Spec (95%CI)MeasureSummary of findings (95%CI)set sigset sigset sigTotal NoSens (95%CI)Sens (95%CI)MeasureSummary of findings (95%CI)set sigset sigset sigTotal NoSens (95%CI)0.87 (0.78, 0.93)LR+4.40 (2.51, 7.72)V. seriousn/aNot seriousTotal Not serious0.87 (0.78, 0.93)LR+0.48 (0.40, 0.57)V. seriousn/aNot serious	DesignTotal NSens (95%CI)Spec (95%CI)Image: Spec (95%CI)Summary of findings (95%CI)Summary of findings (95%CI)Summary setS	Total DesignSens (95%CI)Spec (95%CI)Spec (95%CI)Summary of findings (95%CI)set sigset <br< td=""></br<>

#### 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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Flicker 1997) Prosp	Droopostivo	200	0.72 (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
	Prospective	299	0.73 (0.66, 0.78)	0.71 (0.80, 0.80)	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.

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

		,					' bias	istency	tness	ision	erations	
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	of findings (95%Cl)	Risk of	Incons	Indirec	Imprec	Other consid	Quality
PRIMARY CARE												
1 study (Flicker	Prospective	200	0 99 (0 92 0 01)	0.52 (0.42, 0.62)	LR+	1.86 (1.47, 2.35)	V. serious	n/a	Not serious	Serious		VERY LOW
1997)	FIOSPECTIVE	299	0.88 (0.82, 0.91)	0.55 (0.42, 0.65)	LR-	0.24 (0.16, 0.35)	V. serious	n/a	Not serious	Not serious	-	LOW
Network and shall a f	In the second se											

#### 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.

## 2 P.2.1.29 Amyloid Beta 1-42 and total tau

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY C	ARE											
1 study (Frisoni 2009) Pro	Droopostivo	04	0.42 (0.21, 0.55)	0.70 (0.60, 0.00)	LR+	1.98 (0.92, 4.25)	Serious	n/a	Not serious	Serious		LOW
	Prospective	94	0.42 (0.31, 0.55)	0.79 (0.80, 0.90)	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.

# 1 P.2.1.30 Applause sign (<3)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Depalls 2016)	Droopootivo	075	0.54 (0.40, 0.67)	0.95 (0.90, 0.90)	LR+	3.64 (2.43, 5.45)	Not serious	n/a	Not serious	Not serious		HIGH
T Study (Bonelio 2016)	Prospective	275	0.54 (0.40, 0.67)	0.85 (0.80, 0.89)	LR-	0.54 (0.40, 0.73)	Not serious	n/a	Not serious	Serious	-	MODERATE

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Beinhoff	Broopostivo	222	0.20 (0.28, 0.52)	0.02 (0.88, 0.06)	LR+	5.94 (3.12, 11.33)	Serious	n/a	Not serious	Not serious		MODERATE
2005)	Prospective	232	0.39 (0.26, 0.52)	0.93 (0.88, 0.96)	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.

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



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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	E											
1 study (Beinhoff	Draanastiva	222	0.71 (0.50, 0.91)	0.62 (0.55, 0.70)	LR+	1.91 (1.49, 2.45)	Serious	n/a	Not serious	Serious		LOW
2005)	Prospective	232	0.71 (0.59, 0.81)	0.03 (0.55, 0.70)	LR-	0.46 (0.31, 0.68)	Serious	n/a	Not serious	Serious	-	LOW
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#### 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.

# 1 P.2.1.34 Brief Neuropsychological Test Battery

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Coutinho 2013)	Dreamanting	404	0.04 (0.70, 0.00)	0.00 (0.70, 0.00)	LR+	5.43 (3.28, 8.99)	Not serious	n/a	Not serious	Not serious		HIGH
	Prospective	131	0.91 (0.79, 0.96)	0.83 (0.73, 0.90)	LR-	0.11 (0.05, 0.26)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

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

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

							bias	stency	less	sion	rations	
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of I	Inconsis	Indirecti	Imprecis	Other conside	Quality
SECONDARY CAP	RE											
1 study (Beinhoff	Droopootivo	222	0 71 (0 50 0 91)	0 88 (0 82 0 02)	LR+	5.91 (3.81, 9.17)	Serious	n/a	Not serious	Not serious		MODERATE
2005)	FIOSpective	232	0.71 (0.59, 0.81)	0.00 (0.02, 0.92)	LR-	0.33 (0.22, 0.48)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of b	ias											

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.

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



#### 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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Berger	Droopostivo	460	0.00 (0.86, 0.03)	0 56 (0 49 0 65)	LR+	2.06 (1.69, 2.51)	Serious	n/a	Not serious	Serious		LOW	
2008)	Prospective	402	0.90 (0.86, 0.93)	0.56 (0.46, 0.65)	LR-	0.18 (0.12, 0.25)	Serious	n/a	Not serious	Not serious	-	MODERATE	
Notes on risk of bias Berger 2008: People wi	Inter a construction of the study of the stu												

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Derger 2009)	Droopostivo	460	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
i sludy (Berger 2008)	udy (Berger 2008) Prospective 462 0.72 (0.67, 0.76) 0.64 (		0.04 (0.55, 0.72)	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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Derger 2008)	Droopostivo	460	0 58 (0 53 0 63)	0.01 (0.74 0.07)	LR+	3.10 (2.14, 4.49)	Serious	n/a	Not serious	Not serious		MODERATE
i sludy (Berger 2006)	Prospective	402	0.56 (0.53, 0.63)	0.01 (0.74, 0.07)	LR-	0.52 (0.44, 0.60)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of bias Berger 2008: People who	o received a fina	al diagnos	sis of FTD. DLB or M	CI were excluded fro	m the study.							

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



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

J					1		oias	stency	less	sion	rations	
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of I	Inconsis	Indirect	Imprecis	Other conside	Quality
SECONDARY CARE												
1 study (Derger 2008)	Draanaativa	460	0.91 (0.77, 0.95)	0.60 (0.61, 0.69))	LR+	2.04 (1.64, 2.54)	Serious	n/a	Not serious	Serious		LOW
i sludy (Berger 2006)	Prospective	402	0.01 (0.77, 0.05)	0.60 (0.51, 0.66))	LR-	0.31 (0.24, 0.41)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of bias Berger 2008: People who	o received a fina	al diagno	sis of FTD. DLB or M	ICI were excluded fro	om the study							

2

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Porgor 2008)	Broopootivo	460	0.02 (0.00, 0.05)	0.27 (0.20, 0.45)	LR+	1.47 (1.29, 1.68)	V. serious	n/a	Not serious	Not serious		LOW
i sludy (Berger 2008)	FIOSPECtive	402	0.93 (0.90, 0.93)	0.37 (0.29, 0.43)	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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Derman 2000)	Dreamative	400	0.00 (0.04, 0.04)	0.40.(0.44.0.50)	LR+	1.73 (1.45, 2.07)	Serious	n/a	Not serious	Serious		LOW
r sludy (berger 2008)	Prospective	402	0.00 (0.04, 0.91)	0.49 (0.41, 0.58)	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.

# 2

# 3 P.2.1.45 CERAD battery

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality		
SECONDARY CAR	SECONDARY CARE													
1 study	study Instantial 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		
(Hentschel 2005)			(, , , , , , , , , , , , , , , , , , ,	, , , , ,	LR-	0.27 (0.17, 0.42)	V. serious	n/a	Not serious	Serious		LOW		
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#### 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

# 1 P.2.1.46 Computed Tomography, CT

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (OlDrian 2000)	Dreeneetius	110	0 54 (0 45 0 64)	0.77 (0.40, 0.00)	LR+	2.36 (0.86, 6.46)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (O Brien 2000)	Prospective	116	0.54 (0.45, 0.64)	0.77 (0.48, 0.92)	LR-	0.59 (0.41, 0.85)	Not serious	n/a	Not serious	Serious	-	MODERATE

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Cruz Orduna 2012)	Draanaatiiya	160	0.87 (0.50, 0.07)	0.02 (0.75, 0.07)	LR+	4.83 (3.24, 7.22)	Serious	n/a	Not serious	Not serious		MODERATE
r study (Gruz-Orduna 2012)	Prospective	100	0.07 (0.59, 0.97)	0.02 (0.75, 0.87)	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.

# 1 P.2.1.48 FDG-PET

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measur e	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
3 studies (Dobert 2005;	3 ×	200	0.87 (0.46,	0.77 (0.69,	LR+	3.70 (2.62, 5.22)	Not serious	Not serious	Not serious	Not serious		HIGH
2001)	prospective	380	0.98)	0.84)	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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Marmont 2012)	Dreenestive	145	0.79 (0.60, 0.95)	0.00 (0.78, 0.06)	LR+	7.66 (3.31, 17.69)	V. serious	n/a	Not serious	Not serious		LOW
i study (ivioimont 2012)	FIUSPECTIVE	140	0.76 (0.09, 0.65)	0.90 (0.76, 0.96)	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.

#### Informant Questionnaire on Cognitive Decline, IQCODE (16 item, >3.5) 1 P.2.1.50

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Garcia	2 ×	426		0.65 (0.27, 0.01)	LR+	2.80 (0.97, 8.10)	Serious	Serious	Not serious	Serious		VERY LOW
2002; Knaefelc 2003)	prospective	430	0.93 (0.90, 0.90)	0.05 (0.27, 0.91)	LR-	0.12 (0.07, 0.18)	Serious	Not serious	Not serious	Not serious	-	MODERATE
Natao an viel, of hiss												

#### 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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Canadhaa 2011)	Dreenestive	204	0.72 (0.64, 0.79)	0.67 (0.54, 0.70)	LR+	2.19 (1.47, 3.28)	Serious	n/a	Not serious	Serious		LOW
r study (Goncalves 2011)	Prospective	204	0.72 (0.04, 0.78)	0.07 (0.54, 0.79)	LR-	0.42 (0.31, 0.58)	Serious	n/a	Not serious	Serious	-	LOW
Nation of states of the second												

#### Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARTCARE	-											
2 studies (Flicker	2 ×	442	0.87 (0.82,	0.49 (0.31,	LR+	1.69 (1.16, 2.47)	V. serious	Serious	Not serious	Serious		VERY LOW
2009)	prospective	440	0.90)	0.67)	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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Cruz-Orduna	Prospective	160	0.80 (0.53,	0.77 (0.69,	LR+	3.14 (2.31, 5.03)	Serious	n/a	Not serious	Not serious		MODERAT E
2012)	Prospective	100	0.93)	0.83)	LR-	0.26 (0.09, 0.72)	Serious	n/a	Not serious	Serious		LOW
SECONDARY CARE												
1 study (Elickor 1007)	Prospective	200	0.81 (0.76,	0.61 (0.51,	LR+	2.11 (1.60, 2.79)	V. serious	n/a	Not serious	Serious		VERY LOW
	Fiospective	299	0.86)	0.71)	LR-	0.30 (0.22, 0.42)	V. serious	n/a	Not serious	Not serious		LOW
ALL EVIDENCE POOLED	/. serious											
2 studies (Cruz-Orduna	2x	450	0.81 (0.76,	0.70 (0.53,	LR+	2.63 (1.65, 4.20)	V. serious	Serious	Not serious	Serious		VERY LOW
2012; Flicker 1997)	prospective	409	0.86)	0.82	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

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

		Total	Sens	Spec		Summary of findings	sk of bias	consistency	directness	precision	ther Insiderations	
SECONDARY C	ADE		(00/001)	(307001)	WedSule	(337601)	Ľ.		<u> </u>	<u> </u>	0 õ	Quanty
SECONDART	ARE											
1 study (Flicker	Dreenestive	200	0.70 (0.70, 0.02)	0.65 (0.54, 0.75)	LR+	2.23 (1.65, 3.01)	V. serious	n/a	Not serious	Serious		VERY LOW
1997)	FIOSPECTIVE	299	0.76 (0.72, 0.83)	0.03 (0.34, 0.75)	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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY C	ARE											
1 study (Flicker	Droopostivo	200	0.75 (0.69, 0.90)	0.71 (0.60, 0.80)	LR+	2.58 (1.82, 3.64)	V. serious	n/a	Not serious	Serious		VERY LOW
1997)	Prospective	299	0.75 (0.88, 0.80)	0.71 (0.80, 0.80)	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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
1 study (Flicker	Prospective	e 200	0.70 (0.64, 0.76)	0.75 (0.64, 0.92)	LR+	2.78 (1.90, 4.07)	V. serious	n/a	Not serious	Serious		VERY LOW
1997)	FIOSPECTIVE	299	0.70 (0.04, 0.70)	0.75 (0.04, 0.03)	LR-	0.40 (0.31, 0.50)	V. serious	n/a	Not serious	Serious	-	VERY LOW
										0011040		

#### 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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY C	ARE											
1 study (Flicker Prospecti	Droopoetive	200	0.65 (0.59, 0.71)	0.90 (0.60, 0.97)	LR+	3.16 (2.05, 4.89)	V. serious	n/a	Not serious	Not serious		LOW
1997)	Prospective 2	299	0.00 (0.38, 0.71)	0.00 (0.09, 0.87)	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.

# 1 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 Measure Summary of findings (95%CI) Summary Summary (95%CI) Summary Summary (95%CI) Summary Summary (95%CI) Summary Summary (95%CI) Summary Summary (95%CI) Summary Summary (95%CI) Summary Summary (95%CI) Summary Summary Summary (95%CI) Summary Summary Summary (95%CI) Summary Summary (95%CI) Summary Sum	Quality
1 study (Flicker Device Contraction of the contract	w
1997)     Prospective     299     0.58 (0.52, 0.65)     0.83 (0.74, 0.90)       LR-     0.50 (0.42, 0.60)     V. serious     n/a     Not serious     Serious	RY 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.

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



### 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.

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

	g ,	· -/										
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Beinhoff	Broonootivo	222	0 44 (0 22 0 56)	0.02 (0.88, 0.06)	LR+	6.08 (3.30, 11.18)	Serious	n/a	Not serious	Not serious		MODERATE
2005)	FIOSPECTIVE	232	0.44 (0.33, 0.50)	0.93 (0.88, 0.90)	LR-	0.60 (0.49, 0.75)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of b	ias											

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.

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



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.

# 1 P.2.1.62 Mini-ACE (<26)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Larpor 2017)	Prospective     260     0.98 (0.85, 1.00)     0.35 (0.29)	appartiva 260	0.09 (0.95, 1.00)	0.25 (0.20, 0.42)	LR+	1.50 (1.35, 1.67)	Not serious	n/a	Not serious	Not serious		HIGH
r sludy (Lamer 2017)		0.35 (0.29, 0.42)	LR-	0.07 (0.01, 0.46)	Not serious	n/a	Not serious	Not serious	-	HIGH		

# 2 P.2.1.63 Mini-Cog (≤2)

							bias	stency	ness	sion	rations	
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of I	Inconsis	Indirecti	Imprecis	Other conside	Quality
PRIMARY CARE												
1 study (Carpora Darda 2012)	Droopootivo	140	0.00 (0.96, 1.00)	0.40 (0.21.0.50)	LR+	1.65 (1.39, 1.95)	Serious	n/a	Not serious	Not serious		MODERATE
i sludy (Gamero-Pardo 2013)	Fiospective	142	0.99 (0.66, 1.00)	0.40 (0.31, 0.50)	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.

#### Mini-Cog (Scanlan and Borson algorithm) 1 P.2.1.64

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY C	ARE											
1 study (Milian	Potroppotivo	502	0 97 (0 92 0 00)	0.00.(0.80, 1.00)	LR+	112.68 (7.12, 1782.71)	Serious	n/a	Not serious	Not serious		MODERATE
2012)	Reirospective	502	0.87 (0.83, 0.90)	0.99 (0.89, 1.00)	LR-	0.13 (0.11, 0.17)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of	f 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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
A study (Osmann Danis 0014)	Descention	447	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
1 study (Carnero-Pardo 2011)	Prospective 11	117			LR-	0.08 (0.02, 0.32)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies	Design	Tota I N	Sens (95%Cl)	Spec (95%Cl)	Measur e	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnero-	Prospective	117	0.97 (0.80,	0.71 (0.61,	LR+	3.36 (2.40, 4.71)	Not serious	n/a	Not serious	Not serious		HIGH
Pardo 2011)	FIOSpective	ective 117 1.00)		0.80)	LR-	0.05 (0.01, 0.32)	Not serious	n/a	Not serious	Not serious	-	HIGH
SECONDARY CAR	RE											
1 study (Beinhoff	Prospective	<b>121</b>	0.82 (0.71,	0.81 (0.75,	LR+	4.38 (3.13, 6.14)	Serious	n/a	Not serious	Not serious		MODERATE
2005)	Flospective	232	0.89)	0.87)	LR-	0.22 (0.13, 0.37)	Serious	n/a	Not serious	Not serious	-	MODERATE
ALL EVIDENCE PO	OOLED											
2 studies (Beinhoff 2005;	2 ×	340	0.90 (0.61,	0.77 (0.66,	LR+	3.84 (2.96, 4.97)	Serious	Not serious	Not serious	Not serious		MODERATE
Carnero-Pardo 2011)	prospective	549	0.98)	0.85)	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.

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

		,										
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE						·					
1 study (Beinhoff	Dreenestive	000	0.00 (0.70, 0.04)	0.70 (0.00, 0.70)	LR+	2.92 (2.28, 3.74)	Serious	n/a	Not serious	Not serious		MODERATE
2005)	Prospective	232	0.00 (0.70, 0.94)	0.70 (0.62, 0.76)	LR-	0.17 (0.09, 0.33)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of h	iae											

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.

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



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.

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

· · / ·		,	- 1 - 1									
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	RE											
1 study (Beinhoff	Dreeneetive	000	0.00 (0.00 4.00)	0.00 (0.05, 0.00)	LR+	1.45 (1.30, 1.61)	Serious	n/a	Not serious	Not serious		MODERATE
2005)	Prospective	232	0.96 (0.90, 1.00)	0.32 (0.25, 0.39)	LR-	0.05 (0.01, 0.34)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of h	liac											

#### 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.

# 2 P.2.1.70 MMSE (<17)



#### MMSE (<18) 1 P.2.1.71

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Cruz Orduna 2012)	Droopostivo	260	0.81 (0.70,	0.92 (0.88,	LR+	9.91 (6.60, 14.88)	Serious	n/a	Not serious	Not serious		MODERAT E
1 study (Cruz-Orduna 2012)	FIOSpective	300	0.88)	0.95)	LR-	0.21 (0.13, 0.33)	Serious	n/a	Not serious	Not serious	-	MODERAT E
SECONDARY CARE												
1 study (Eliskor 1007)	Droopostivo	200	0.50, 0.43,	0.90 (0.82,	LR+	5.19 (2.65, 10.16)	V. serious	n/a	Not serious	Not serious		LOW
i study (Flicker 1997)	Prospective	299	0.57)	0.95)	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	2x	ospective 659	9 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
2012; Flicker 1997)	prospective				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

# 1 P.2.1.72 MMSE (<19)

Studies	Design	Total N	Sens (95%CI)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
2 studies (Carnero-Pardo	2x	520	0.87 (0.78,	0.87 (0.83,	LR+	6.46 (4.97, 8.38)	Serious	Not serious	Not serious	Not serious		MODERAT E
2013, Cruz-Orduna 2012)	3, Cruz-Orduna 2012) prospective	ective <sup>320</sup>	0.92)	0.90)	LR-	0.16 (0.09, 0.26)	Serious	Not serious	Not serious	Not serious	-	MODERAT E
SECONDARY CARE												
1 study (Eliskor 1007)	Brooppotivo	200	0.56 (0.49,	0.97 (0.78,	LR+	4.19 (2.39, 7.36)	V. serious	n/a	Not serious	Not serious		LOW
	Prospective	299	0.62)	0.93)	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	3x	x 819 rospective	0.76 (0.46,	, 0.87 (0.83, 0.89)	LR+	5.95 (4.64, 7.62)	Serious	Not serious	Not serious	Not serious		MODERAT E
Flicker 1997)	prospective		0.93)		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

# 1 P.2.1.73 MMSE (<20)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnero-Pardo	Prospective	260	0.94 (0.85,	0.82 (0.77,	LR+	5.19 (4.02, 6.70)	Serious	n/a	Not serious	Not serious		MODERAT E
2013)	FIOSPECTIVE		0.97)	0.86)	LR-	0.08 (0.03, 0.19)	Serious	n/a	Not serious	Not serious	-	MODERAT E
SECONDARY CARE												
1 study (Elickor 1997)	Prospective	200	0.62 (0.55,	0.84 (0.75,	LR+	3.96 (2.38, 6.60)	V. serious	n/a	Not serious	Not serious		LOW
	Flospective	299	0.68)	0.91)	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	2x	spective 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		MODERAT E
2013; Flicker 1997)	prospective				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

# 1 P.2.1.74 MMSE (<21)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnero-Pardo	Prospective	260	0.95 (0.87,	0.73 (0.68,	LR+	3.53 (2.89, 4.31)	Serious	n/a	Not serious	Not serious		MODER ATE
2013)	Prospective	300	0.98)	0.78)	LR-	0.07 (0.03, 0.18)	Serious	n/a	Not serious	Not serious	-	MODER ATE
SECONDARY CARE												
1 study (Eliskor 1007)	Prospective	200	0.69 (0.63,	0.76 (0.66,	LR+	2.86 (1.93, 4.24)	V. serious	n/a	Not serious	Serious		VERY LOW
T Study (Flicker 1997)	Prospective	299	0.75)	0.84)	LR-	0.41 (0.32, 0.52)	V. serious	n/a	Not serious	Serious	-	VERY LOW
ALL EVIDENCE POOLED	V. serious											
2 studies (Carnero-	2x	650	0.86 (0.43,	0.74 (0.69,	LR+	3.38 (2.83, 4.04)	Serious	Not serious	Not serious	Not serious		MODER ATE
1997)	prospective	ospective 659	0.98)	0.78)	LR-	0.18 (0.03, 1.00)	V. serious	Serious	Not serious	Serious	-	VERYLO W

#### 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
## 1 P.2.1.75 MMSE (<22)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measur e	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE				-								
1 study (Compare Danda 2012)	Prospectiv	200	0.96 (0.89,	0.67 (0.61,	LR+	2.92 (2.46, 3.48)	Serious	n/a	Not serious	Not serious		MODERA TE
T study (Carriero-Pardo 2013)	е	300	0.99)	0.72)	LR-	0.06 (0.02, 0.18)	Serious	n/a	Not serious	Serious	-	MODERA TE
3 studies (Callahan 2002; Flicker	3x	1,	0.69 (0.60,	0.94 (0.64,	LR+	12.43 (1.75, 88.49)	Very serious	Serious	Not serious	Serious		VERY LOW
1997; Kukull 1994)	prospective	089	0.78)	0.99)	LR-	0.35 (0.26, 0.46)	Serious	Serious	Not serious	Serious	-	LOW
ALL EVIDENCE POOLED												
4 studies (Callahan 2002;	4 ×	1,44	0.76 (0.64,	0.89 (0.67,	LR+	6.54 (2.67, 16.01)	Serious	Serious	Not serious	Not serious		LOW
1997; Kukull 1994)	prospective	1,44 3	0.85)	0.97)	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

## 1 P.2.1.76 MMSE (<23)

Studies	Design	Tot al N	Sens (95%Cl)	Spec (95%CI)	Meas ure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Cornero Dordo 2012)	1 ×	260	0.99 (0.91,	0.57 (0.51,	LR+	2.29 (2.00, 2.62)	Serious	n/a	Not serious	Serious		LOW
i study (Camero-Fardo 2013)	ive	300	1.00)	0.63)	LR-	0.02 (0.00, 0.16)	Serious	n/a	Not serious	Not serious	-	MODE RATE
SECONDARY CARE												
5 studies (Abdel-Aziz 2015; Callahan 2002; Flicker 1997;	5 ×	1,3	0.67 (0.55,	0.89 (0.75,	LR+	6.79 (2.70, 15.00)	Very serious	Serious	Not serious	Not serious		VERY LOW
Kukull 1994; Nielsen 2013)	ive	64	0.77)	0.96)	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	6 ×	1,7	0.75 (0.54,	0.85 (0.69,	LR+	5.47 (2.60, 10.80)	V. serious	Serious	Not serious	Not serious		VERY LOW
2013; Flicker 1997; Kukull 1994; Nielsen 2013)	ive	24	0.88)	0.94)	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.

# 1 P.2.1.77 MMSE (<24)

Studies	Design	Tot al N	Sens (95%Cl)	Spec (95%CI)	Meas ure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Corpore Darde 2012)	Prospecti	260	0.99 (0.91,	0.46 (0.40,	LR+	1.84 (1.65 2.05)	Seriou s	n/a	Not serious	Serious		LOW
i study (Camero-Pardo 2013)	ve	300	1.00)	0.52)	LR-	0.08 (0.01, 1.32)	Seriou s	n/a	Not serious	Not serious	-	MODE RATE
SECONDARY CARE		•										
11 studies (Bastide 2012; Callahan 2002; Goncalves 2011; Flicker 1997: Hancock 2011: Knaefelc 2003; Kukull 1994;	11 ×	29	0 73 (0 63	0 91 (0 83	LR+	8.43 (4.47, 14.80)	Seriou s	Serious	Not serious	Not serious		LOW
Mathuranath 2000; Nielsen 2013; Postel-Vinay 2014; Sager 2006)	prospecti ve	75	0.81)	0.96)	LR-	0.31 (0.23, 0.40)	Seriou s	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 ×	3,3	0.75 (0.65,	0.88 (0.78,	LR+	6.65 (3.70, 11.00)	Seriou s	Serious	Not serious	Not serious		LOW
	ve	5	0.75 (0.65, 0.84)	0.94)	LR-	0.29 (0.20, 0.38)	Seriou s	Serious	Not serious	Not serious	-	LOW

#### Dementia Appendix P: Diagnosis evidence tables & GRADE

		Tot	Sens	Spec	Meas	Summary of findings	sk of bias	consistency	directness	precision	ther insiderations
Studies	Design	Ν	(95%CI)	(95%CI)	ure	(95%CI)	Ris	lno	Inc	<u>=</u>	중 중 Qualif

#### 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

# 1 P.2.1.78 MMSE (<25)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measu re	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Comoro Dardo 2012)	1 ×	260	0.99 (0.91,	0.38 (0.33,	LR+	1.61 (1.46, 1.76)	Serious	n/a	Not serious	Not serious		MODER ATE
i study (Camero-Pardo 2013)	e	360	1.00)	0.44)	LR-	0.02 (0.00, 0.27)	Serious	n/a	Not serious	Serious	-	MODER ATE
SECONDARY CARE												
7 studies (Callaban 2002: Elicker 1997:	6 × prospectiv				LR+	5.18 (2.74, 9.37)	V. serious	Serious	Not serious	Not serious		VERY LOW
Kukull 1994; Larner 2015; Milian 2012; Nielsen 2013; Yeung 2014)	e; 1 × retrospecti ve	2,02 0	0.82 (0.73, 0.87)	0.83 (0.70, 0.91)	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	7 × prospectiv	0.00	0.05 (0.75	0.00 (0.00	LR+	4.41 (2.31, 8.1)	V. serious	Serious	Not serious	Not serious		VERY LOW
2013; Flicker 1997; Kukull 1994; Larner 2015; Milian 2012; Nielsen 2013; Yeung 2014)	e; 1 × retrospecti ve	2,38 0	0.85 (0.75, 0.91)	0.80 (0.62, 0.90)	LR-	0.20 (0.12, 0.31)	V. serious	Serious	Not serious	Not serious	-	VERY LOW

#### Dementia Appendix P: Diagnosis evidence tables & GRADE

		Total	Sens	Spec	Measu	Summary of findings	ik of bias	onsistency	irectness	precision	ner nsiderations	
Studies	Design	Ν	(95%CI)	(95%CI)	re	(95%CI)	Ris	lnc	Ind	<u> </u>	5 of	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.

## 1 P.2.1.79 MMSE (<26)

- 1 -1												
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 studies (Callahan 2002;	3 × prospective;	4 500	0.85 (0.77,	0.78 (0.53,	LR+	3.84 (1.68, 8.76)	V. serious	Serious	Not serious	Serious		VERY LOW
Nielsen 2013)	1 × retrospective	1,583	0.91)	0.92)	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.

#### 1 P.2.1.80 MMSE (<27)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measur e	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 studies (Bastide 2012; Callahan	4 ×	4.044	0.86 (0.73,	0.75 (0.66,	LR+	3.43 (2.43, 4.85)	Serious	Serious	Not serious	Not serious		LOW
2002, Mathuranath 2000; Nielsen 2013)	prospective	1,241	0.94)	0.82)	LR-	0.17 (0.09, 0.33)	Serious	Serious	Not serious	Not L	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.

## 1 P.2.1.81 MMSE (<28)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measur e	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Callahan	2 ×	700	0.96 (0.87,	0.70 (0.57,	LR+	3.13 (2.22, 4.41)	Serious	Not serious	Not serious	Not serious		MODERAT E
2002; Mormont 2012)	prospective	796	0.99)	0.81)	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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	E											
2 studies (Chen	2 ×	405	0.93 (0.90,	0.81 (0.44,	LR+	5.18 (1.32, 20.41)	V. serious	Serious	Not serious	Serious		VERY LOW
2011, reung 2014)	prospective	490	0.96)	0.96)	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.

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

Quality
MODERATE
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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Caldetsia 2014)	Dreamanting	04	0.00 (0.70, 0.00)	0.04 (0.04 0.45)	LR+	1.41 (1.16, 1.71)	Not serious	n/a	Serious	Not serious		MODERATE
r study (Goldstein 2014)	Prospective	δI	0.96 (0.78, 0.99)	0.31 (0.21, 0.45)	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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Caldatain 2014)	Dreenetive	04	0.00 (0.77, 4.00)	0.00 (0.14, 0.00)	LR+	1.27 (1.09, 1.48)	Not serious	n/a	Serious	Not serious		MODERATE	
T Study (Goldstein 2014)	Prospective	01	0.96 (0.77, 1.00)	0.23 (0.14, 0.36)	LR-	0.08 (0.00, 1.28)	Not serious	n/a	Serious	Serious	-	LOW	
Notes on indirectness Goldstein 2014: Study only	LR- 0.08 (0.00, 1.28) Not serious n/a Serious Serious LOW   Idstein 2014: Study only recruited African Americans ≥ 50 years old. 50 years												

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



#### 1 P.2.1.87 MRI

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Frisoni 2009;	2 ×	004	0.83 (0.49,	0.57 (0.47,	LR+	1.87 (1.45, 2.37)	V. serious	Not serious	Not serious	Serious		VERY LOW
Hentschel 2005)	prospective	234	0.96)	0.66)	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.

#### 2 P.2.1.88 Orientation, OR (<7)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	RE											
1 study (Beinhoff	Draanaativa	222	0.00 (0.00, 0.50)	0.00 (0.05, 4.00)	LR+	32.70 (7.99, 133.88)	Serious	n/a	Not serious	Not serious		MODERATE
2005)	Prospective	232	0.39 (0.28, 0.52)	0.99 (0.95, 1.00)	LR-	0.61 (0.50, 0.75)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of h	niae											

#### 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.

#### 1 P.2.1.89 Orientation OR (< 8)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Beinhoff	Prochostivo	222	0.65 (0.52, 0.76)	0.00 (0.85, 0.04)	LR+	6.76 (4.11, 11.12)	Serious	n/a	Not serious	Not serious		MODERATE
2005)	Flospective	232	0.05 (0.55, 0.70)	0.90 (0.85, 0.94)	LR-	0.39 (0.28, 0.54)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of b	ias											

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.

#### 2 P.2.1.90 **Palmo-Mental Reflex**



Streit 2015: Patients had to have cognitive complaints, but normal MMSE and CDT tests at baseline.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Strait 2015)	Potrognostivo	154	0.71 (0.46, 0.97)	0.64 (0.55, 0.71)	LR+	1.93 (1.33, 2.82)	Serious	n/a	Not serious	Serious		LOW
r sludy (Streit 2015)	Reliospective	104	0.71 (0.40, 0.87)	0.04 (0.55, 0.71)	LR-	0.46 (0.22, 0.98)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of bias												
O/ 1/ 00/15 D // / /	1 4 1 1 141											

Streit 2015: Patients had to have cognitive complaints, but normal MMSE and CDT tests at baseline..

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Stroit 2015)	Potrognostivo	154	0.24 (0.00, 0.40)	0.02 (0.99, 0.07)	LR+	3.58 (1.24, 10.38)	Serious	n/a	Not serious	Serious		LOW
T study (Streit 2015)	1 study (Streit 2015) Retrospective	104	0.24 (0.09, 0.49)	0.93 (0.88, 0.97)	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.

# 1 P.2.1.93 Phototest (<27)

		0										
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carpora Darda 2011)	Draanaatiya	140	0.81 (0.68, 0.00)	0.90 (0.91 .0.04)	LR+	7.48 (4.10, 13.63)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Carnero-Pardo 2011)	Prospective	140	0.01 (0.08, 0.90)	0.69 (0.81, 0.94)	LR-	0.21 (0.12, 0.38)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	RE											
1 study		004			LR+	6.84 (2.95, 15.87)	Serious	n/a	Not serious	Not serious		MODERATE
(Goncalves 2011)	Prospective	204	0.66 (0.58, 0.73)	0.90 (0.79, 0.96)	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.

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



#### 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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
1 study (Nielsen	Broonostivo	107	0.64 (0.52, 0.74)	0 82 (0 72 0 00)	LR+	3.78 (2.14, 6.65)	V. serious	n/a	Not serious	Not serious		LOW
1 study (Nielsen 2013) Prospective	137	0.04 (0.32, 0.74)	0.83 (0.72, 0.90)	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.

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



#### 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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	RE											
1 study (Nielsen	Dreenestive	107	0.76 (0.65, 0.95)	0.66 (0.54, 0.77)	LR+	2.26 (1.57, 3.25)	V. serious	n/a	Not serious	Serious		VERY LOW
2013)	Prospective	137	0.76 (0.65, 0.65)	0.00 (0.54, 0.77)	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.

#### Rowland Universal Dementia Assessment Scale, RUDAS (<26) 1 P.2.1.99

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	RE											
1 study (Nielsen	Dreenestive	107	0.92 (0.71 0.90)	0.65 (0.52, 0.75)	LR+	2.32 (1.64, 3.27)	V. serious	n/a	Not serious	Serious		VERY LOW
2013)	Prospective	137	0.82 (0.71, 0.89)	0.05 (0.52, 0.75)	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.

## 2P.2.1.100 Seven Minute Screen (P>0.6)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skience 2008)	Draanaatiya	05	0.72 (0.61 0.92)	0.65 (0.46, 0.94)	LR+	2.09 (1.21, 3.62)	Serious	n/a	Not serious	Serious		LOW
r sludy (Skjerve 2008)	Prospective	90	0.72 (0.61, 0.82)	0.05 (0.46, 0.81)	LR-	0.42 (0.26, 0.68)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of hias												

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

# 1P.2.1.101 Seven Minute Screen (P>0.7)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skjerve 2008)	Draanaativa	05	0.72 (0.61, 0.82)	0 60 (0 40 0 84)	LR+	2.36 (1.30, 4.27)	Not serious	n/a	Not serious	Serious		MODERATE
	Prospective	90	0.72 (0.01, 0.82)	0.09 (0.49, 0.84)	LR-	0.40 (0.25, 0.63)	Not serious	n/a	Not serious	Serious	-	MODERATE

# 2P.2.1.102 Seven Minute Screen (P>0.8)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skience 2008)	Dreenestive	05	0.71 (0.50, 0.90)	0 72 (0 52 0 97)	LR+	2.64 (1.38, 5.06)	Serious	n/a	Not serious	Serious		LOW
T Sludy (Skjerve 2006)	dy (Skjerve 2008) Prospective 95 0.		0.71 (0.59, 0.60)	0.73 (0.53, 0.67)	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.

#### 1P.2.1.103 Short smell test

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Strait 2015)	Detrespective	154	0.52 (0.20, 0.74)	0.75 (0.67, 0.82)	LR+	2.13 (1.25, 3.64)	Serious	n/a	Serious	Serious		VERY LOW
r sludy (Streft 2015)	Reliospective	154	0.55 (0.50, 0.74)	0.75 (0.67, 0.82)	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.

### 2P.2.1.104 Short Portable Mental Status Questionnaire, SPMSQ (≥4)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CA	RE						·						
1 study (Malhotra	Dreamastica	407	0.70 (0.70, 0.00)	0.75 (0.54, 0.00)	LR+	3.15 (1.56, 6.34)	V. serious	n/a	Not serious	Serious		VERY LOW	
2013)	Prospective	127	0.79 (0.70, 0.86)	0.75 (0.54, 0.88)	LR-	0.28 (0.18, 0.44)	V. serious	n/a	Not serious	Not serious	-	LOW	
Notes on risk of b Malhotra 2013: It w	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  $\geq$  6 years education

# 1P.2.1.105 Short Portable Mental Status Questionnaire, SPMSQ (≥5)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Malbatra 2012)	Droopostivo	107	0.79 (0.60, 0.95)	0.75 (0.54, 0.99)	LR+	3.11 (1.54, 6.26)	Serious	n/a	Serious	Serious		VERY LOW	
r study (Manotra 2013)	Prospective	127	0.76 (0.69, 0.65)	0.75 (0.54, 0.66)	LR-	0.30 (0.19, 0.46)	Serious	n/a	Serious	Not serious	-	LOW	
Notes on risk of bias Malhotra 2013: It was uncle	lotes on risk of bias												

Notes on indirectness

Malhotra 2013: 60% participants had < 6 years education

### 2P.2.1.106 Short Portable Mental Status Questionnaire, SPMSQ (≥6)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	E											
1 study (Malhotra	Broopportivo	107	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
2013)	Prospective	127	0.72 (0.62, 0.60)	0.42 (0.24, 0.62)	LR-	0.68 (0.38, 1.19)	V. serious	n/a	Serious	Serious	-	VERY LOW
Notes on risk of bi	as											

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  $\geq$  6 years education).

Notes on indirectness

Malhotra 2013: Participants had < 6 years education

# 1P.2.1.107 Syndrom Kurztest (≥7)

	- (=- )											
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Okierys 2000)	Dreamantiva	05	0.74 (0.50, 0.00)	0 54 (0 25 0 72)	LR+	1.54 (0.99, 2.39)	Serious	n/a	Not serious	Serious		LOW
i sludy (Skjerve 2008)	Prospective	90	0.71 (0.59, 0.80)	0.54 (0.55, 0.72)	LR-	0.54 (0.32, 0.90)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of bias												
		1.1.1.11	a fear of a contract of the second state of th									

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

## 2P.2.1.108 Syndrom Kurztest (≥8)



#### Notes on risk of bias

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

# 1P.2.1.109 Syndrom Kurztest (≥9)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skjerve 2008)	Dreanactive	05	0.59 (0.46, 0.60)	0.60 (0.40, 0.84)	LR+	1.88 (1.02, 3.47)	Not serious	n/a	Not serious	Serious		MODERATE
	Prospective	90	0.56 (0.46, 0.69)	0.09 (0.49, 0.84)	LR-	0.61 (0.42, 0.89)	Not serious	n/a	Not serious	Serious	-	MODERATE

# **2P.2.1.110** Total recall score of 5-word test, $\leq$ 9

Studies SECONDARY CARE	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
					1.0.	7 00 (2 45 40 27)						
1 study (Mormont 2012)	Prospective	1/15	0.81 (0.72, 0.88)	0 00 (0 78 0 06)	LR+	7.96 (3.45, 18.37)	v. serious	n/a	Not serious	Not serious		LOW
	Trospective	145	0.01 (0.72, 0.00)	0.90 (0.70, 0.90)	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.

# 1P.2.1.111 Total weighted score of 5-word test, ≤ 15

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
CECCIDART CARE											1	
1 study (Marmont 2012)	Broonactivo	145	0.75 (0.65 0.92)	0.06 (0.95, 0.00)	LR+	18.38 (4.71, 71.75)	V. serious	n/a	Not serious	Not serious		LOW
r study (Mormont 2012)	Flospective	145	0.75 (0.05, 0.85)	0.90 (0.85, 0.99)	LR-	0.26 (0.18, 0.37)	V. serious	n/a	Not serious	Not serious	-	LOW
Notes on risk of bias	of >35% populat	tion at an	alveis and use of on	timicad tast thrashold	le							

# 2P.2.1.112 Test Your Memory, TYM (≤30)



Hancock 2011: Optimised test threshold.

# 1P.2.1.113 Test Your Memory, TYM (≤42)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Hancock 2011) P	Dreenestive	224		0 45 (0 07 0 50)	LR+	1.73 (1.48, 2.02)	Not serious	n/a	Not serious	Serious		MODERATE
	Prospective	224	0.95 (0.87, 0.98)	0.45 (0.37, 0.53)	LR-	0.11 (0.04, 0.30)	Not serious	n/a	Not serious	Not serious	-	HIGH

# 2P.2.1.114 Test Your Memory (≤39)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Destal Viney 2014)	Draanaatiya	201		0.70 (0.62, 0.77)	LR+	2.98 (2.27, 3.91)	Serious	n/a	Not serious	Not serious		MODERATE
T Sludy (Postel-Villay 2014)	Prospective	201	0.90 (0.80, 0.95)	0.70 (0.62, 0.77)	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

# 1P.2.1.115 Verbal category fluency (animal naming), VF (<14)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 abudu (Camar 2000)	Dreamative	204		0.00 (0.50, 0.00)	LR+	2.14 (1.68, 2.72)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Sager 2006) P	Prospective	304	0.85 (0.80, 0.89)	0.60 (0.50, 0.69)	LR-	0.25 (0.18, 0.35)	Not serious	n/a	Not serious	Not serious	-	HIGH

# 2P.2.1.116 Verbal category fluency (animal naming), VF (<19)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
1 study (Beinhoff					LR+	2.31 (1.85, 2.89)	Serious	n/a	Not serious	Serious		LOW
2005) P	Prospective	232	0.85 (0.74, 0.92)	0.63 (0.56, 0.70)	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.

#### Verbal category fluency (animal naming), VF (<20) 1P.2.1.117

Ŭ		u .		, ,		Summary	of bias	ısistency	ectness	ecision	r iderations	
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	of findings (95%Cl)	Risk o	Incons	Indired	Impred	Other consid	Quality
SECONDARY CAR	RE											
1 study (Beinhoff	Broopostivo	222	0.04 (0.95, 0.09)	0.59 (0.50, 0.65)	LR+	2.23 (1.85, 2.69)	Serious	n/a	Not serious	Serious		LOW
2005)	Flospective	232	0.94 (0.65, 0.96)	0.56 (0.50, 0.05)	LR-	0.10 (0.04, 0.27)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of h	ias											

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.

#### Verbal category fluency (animal naming), VF (<21) 2P.2.1.118



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.

# 1P.2.1.119 Verbal category fluency (animal naming), VF (<22)

Ŭ		Total	Sone	Shee		Summary	k of bias	unsistency	rectness	recision	er siderations	
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	of findings (95%Cl)	Risk	Incor	Indire	Impre	Othel cons	Quality
SECONDARY CAP	RE		·	·								
1 study (Beinhoff	Broopostivo	222	0.05 (0.97, 0.00)	0.46 (0.28, 0.52)	LR+	1.76 (1.52, 2.04)	Serious	n/a	Not serious	Serious		LOW
2005)	Flospective	232	0.95 (0.87, 0.99)	0.40 (0.38, 0.33)	LR-	0.10 (0.03, 0.30)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of b	ias											

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.

#### Verbal category fluency (animal naming), VF (<23) 2P.2.1.120

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAP	RE											
1 study (Beinhoff	Broonactivo	222	0.07 (0.80, 0.00)	0.20 (0.21, 0.46)	LR+	1.58 (1.39, 1.79)	Serious	n/a	Not serious	Not serious		MODERATE
2005)	Fiospective	232	0.97 (0.69, 0.99)	0.39 (0.31, 0.40)	LR-	0.08 (0.02, 0.31)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of b	ias											

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.

# 1P.2.1.121 Verbal category fluency (animal naming), VF (<24)

0	<u> </u>	<b>`</b>	0,,	<u>\ /</u>								
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAP	RE											
1 study (Beinhoff	Dreenestive	222	0.08 (0.00, 1.00)	0.21 (0.24, 0.28)	LR+	1.42 (1.28, 1.58)	Serious	n/a	Not serious	Not serious		MODERATE
2005) F	Prospective	232	0.96 (0.90, 1.00)	0.31 (0.24, 0.36)	LR-	0.05 (0.01, 0.35)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of h	iac											

#### 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.

# 2 P.2.2 AD versus DLB

### 3 P.2.2.1 Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (As days a sec 0001)	December	470	0.05 (0.57, 0.70)	0.07 (0.00, 0.00)	LR+	1.95 (0.77, 4.95)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Andreasen 2001)	Prospective	172	0.65 (0.57, 0.72)	0.67 (0.33, 0.89)	LR-	0.52 (0.32, 0.87)	Not serious	n/a	Not serious	Serious	-	MODERATE

# 1 P.2.2.2 FDG-PET

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Prochostivo	70	0 58 (0 46 0 70)		LR+	0.73 (0.45, 1.19)	V. serious	n/a	Serious	Serious		VERY LOW
(Ossenkoppele 2013)	FIOSPECLIVE	70	0.56 (0.46, 0.70)	0.20 (0.03, 0.09)	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.

#### 2 P.2.2.3 MRI

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Draanaativa	270	0.20 (0.24, 0.25)	0.72 (0.59, 0.92)	LR+	1.05 (0.64, 1.75)	Serious	n/a	Not serious	Not serious		MODERATE
(Koikkalainen 2016)	Prospective	270	0.29 (0.24, 0.35)	0.72 (0.58, 0.83)	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.

# 1 P.2.3 AD versus FTD

## 2 P.2.3.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA	-											
2 studies (Launes 1991;	2 ×	50	0.70 (0.40, 0.04)	0.74 (0.40, 0.00)	LR+	2.78 (1.20, 6.42)	V. serious	Not serious	Not serious	Serious		VERY LOW
Velakoulis 1997)	prospective	59	0.73 (0.42, 0.91)	0.71 (0.43, 0.89)	LR-	0.41 (0.23, 0.74)	Serious	Not serious	Not serious	Serious	-	LOW
MULTIPLE CAMERA												
1 study (Boutoleau-	Descention	00	0.70 (0.54, 0.04)	0 70 (0 44 0 04)	LR+	2.85 (1.05, 7.72)	V. serious	n/a	Not serious	Serious		VERY LOW
Bretonniere 2012)	Prospective	29	0.78 (0.54, 0.91)	0.73 (0.41, 0.91)	LR-	0.31 (0.12, 0.78)	V. serious	n/a	Not serious	Serious	-	VERY LOW
ALL EVIDENCE POOLED												
3 studies (Boutoleau-	3 ×		0.70 (0.50, 0.00)	0 70 (0 54 0 00)	LR+	2.81 (1.48, 5.33)	V. serious	Not serious	Not serious	Serious		VERY LOW
Bretonniere 2012; Launes 1991; Velakoulis 1997)	prospective	88	0.72 (0.56, 0.83)	0.72 (0.51, 0.86)	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 reference.

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

## 1 P.2.3.2 Amyloid Beta 1-42 and Total Tau

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Tolodo 2012)	Detrespective	100	0.00 (0.81, 0.05)	0.92 (0.65, 0.02)	LR+	5.23 (2.35, 11.65)	Serious	n/a	Not serious	Not serious		MODERATE
r sludy (roledo 2012)	Reirospective	100	0.90 (0.81, 0.95)	0.63 (0.05, 0.93)	LR-	0.12 (0.06, 0.25)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of bias												
T     0040 . 400/						1.11.1 1. 1.6.01						

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

# 2 P.2.3.3 FDG-PET

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Droopootivo	02	0.59 (0.46, 0.70)	0.79 (0.54 .0.01)	LR+	2.63 (1.08, 6.39)	V. serious	n/a	Serious	Serious		VERY LOW
(Ossenkoppele 2013)	nkoppele 2013) Prospective 83 0.58 (0.46, 0.7	0.56 (0.46, 0.70)	0.78 (0.54, 0.91)	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.

#### 1 P.2.3.4 MRI

IVIIXI												
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Droopootivo	215	0.20 (0.24, 0.25)	0.77 (0.69, 0.95)	LR+	1.28 (0.83, 1.96)	Serious	n/a	Not serious	Not serious		MODERATE
(Koikkalainen 2016)	FIOSPECTIVE	515	0.29 (0.24, 0.33)	0.77 (0.08, 0.85)	LR-	0.92 (0.80, 1.06)	Serious	n/a	Not serious	Not serious	-	MODERATE
Made a survivial of the sec												

#### 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.

# 2 P.2.3.5 p-tau 181

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Tolodo 2012)	Potroopootivo	100	0.00 (0.00, 1.00)	0.95 (0.69, 0.04)	LR+	6.62 (2.82, 15.52)	Serious	n/a	Not serious	Not serious		MODERATE
1 Study (10ledo 2012)	Reirospective	100	0.99 (0.90, 1.00)	0.05 (0.08, 0.94)	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

# 1 P.2.4 AD versus no dementia

# 2 P.2.4.1 Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Brooppotivo	70	0.84 (0.72, 0.02)	0.84 (0.61, 0.05)	LR+	5.34 (1.88, 15.19)	Serious	n/a	Not serious	Serious		LOW
(Maddalena 2003)	Prospective	70	0.84 (0.72, 0.92)	0.84 (0.61, 0.95)	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.

# 3 P.2.4.2 FDG-PET

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Valuation 2010)	Dreamanting	40	0.70 (0.50, 0.04)	0.01 (0.70, 0.00)	LR+	8.71 (2.29, 33.17)	Serious	n/a	Not serious	Not serious		MODERATE
T Study (Yakushev 2010)	Prospective	40	0.79 (0.59, 0.91)	0.91 (0.70, 0.98)	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												

# 1 P.2.5 Free recall score of 5- word test, $\leq$ 5 for AD

Studies SECONDARY CARE	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
4 - turke (Marris and 0040)			0.04 (0.70, 0.00)		LR+	81.45 (5.15, 1287.53)	V. serious	n/a	Not serious	Not serious		LOW
T Study (Mormont 2012)	Prospective	110	0.81 (0.70, 0.89)	0.99 (0.86, 1.00)	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												

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
OLOONDANT OA								_				
1 study (Sikkes	Broopostivo	260		0 42 (0 22 0 52)	LR+	1.64 (1.38, 1.96)	V. serious	n/a	Not serious	Not serious		LOW
2010)	Flospective	209	0.90 (0.92, 0.98)	0.42 (0.32, 0.52)	LR-	0.09 (0.04, 0.20)	V. serious	n/a	Not serious	Not serious	-	LOW
Notes on risk of	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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAP	RE											
1 study (Sikkes	Broopootivo	260	0.06 (0.01.0.08)	0 47 (0 27 0 59)	LR+	1.81 (1.48, 2.21)	V. serious	n/a	Not serious	Serious		VERY LOW
2010)	Prospective 2	tive 269 (	0.96 (0.91, 0.98)	0.47 (0.37, 0.56)	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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
1 study (Sikkes	Draanaatiwa	260	0.02 (0.97, 0.05)	0.62 (0.52, 0.72)	LR+	2.47 (1.88, 3.25)	V. serious	n/a	Not serious	Serious		VERY LOW
2010)	Prospective	269	0.92 (0.87, 0.95)	0.03 (0.52, 0.72)	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.
# 1 P.2.5.4 Informant Questionnaire on Cognitive Decline, IQCODE (16 item, >3.5)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	RE											
1 study (Sikkes	Dreenestive	260	0.80 (0.84, 0.02)	0.60 (0.69, 0.77)	LR+	2.84 (2.08, 3.88)	V. serious	n/a	Not serious	Not serious		LOW
2010) Pi	Fiospective	209	0.09 (0.04, 0.93)	0.09 (0.36, 0.77)	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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	RE											
1 study (Sikkes	Droopostivo	260	0.86 (0.80, 0.00)	0.74 (0.64 .0.92)	LR+	3.31 (2.32, 4.73)	V. serious	n/a	Not serious	Not serious		LOW
2010) Pr	Prospective	209	0.00 (0.00, 0.90)	0.74 (0.04, 0.82)	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.

# 1 P.2.5.6 MMSE (<28)

Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
Dreanactiva	110	0.08 (0.80, 1.00)	0.79 (0.64 .0.97)	LR+	4.38 (2.60, 7.38)	V. serious	n/a	Not serious	Not serious		LOW
Frospective	110	0.96 (0.69, 1.00)	0.76 (0.04, 0.87)	LR-	0.02 (0.00, 0.15)	V. serious	n/a	Not serious	Not serious	-	LOW
f > 250/ populati	on of on	alucia and use of opti	miand toot througholds								
	Design Prospective	Design Total N   Prospective 110	DesignTotal NSens (95%Cl)Prospective1100.98 (0.89, 1.00)I >35% population at analysis and use of optice	Design Total N Sens (95%CI) Spec (95%CI)   Prospective 110 0.98 (0.89, 1.00) 0.78 (0.64, 0.87)	Design Total N Sens (95%Cl) Spec (95%Cl) Measure   Prospective 110 0.98 (0.89, 1.00) 0.78 (0.64, 0.87) LR+   LR- LR-	DesignTotal NSens (95%CI)Spec (95%CI)MeasureSummary of findings (95%CI)Prospective1100.98 (0.89, 1.00)0.78 (0.64, 0.87)LR+4.38 (2.60, 7.38)LR-0.02 (0.00, 0.15)	DesignTotal NSens (95%CI)Spec (95%CI)MeasureSummary of findings (95%CI)Sig Summary of findings (95%CI)Prospective1100.98 (0.89, 1.00)0.78 (0.64, 0.87)LR+4.38 (2.60, 7.38)V. seriousImage: Interpret to the series of optimized test thresholdsImage: Image: Ima	DesignTotal NSens (95%CI)Spec (95%CI)MeasureSummary of findings (95%CI)Summary summary findings (95%CI)Summary summary findings (95%CI)Summary summary findings (95%CI)Summary summary findings (95%CI)Summary summary findings (95%CI)Summary summary findings (95%CI)Summary summary findings (95%CI)Summary summary findings (95%CI)Summary summary findings (95%CI)Summary summary findings (95%CI)Summary summary findings findings (95%CI)Summary findings findings fin	Design   Total N   Sens (95%Cl)   Spec (95%Cl)   Measure   Summary of findings (95%Cl)   Sige Sige Sige Sige Sige Sige Sige Sige	Design   Total N   Sens (95%CI)   Spec (95%CI)   Measure   Summary of findings (95%CI)   Summary of findings (95%CI) <th< td=""><td>Design   Total N   Sens (95%CI)   Spec (95%CI)   Measure   Summary of findings (95%CI)   state   Summary state   state   state</td></th<>	Design   Total N   Sens (95%CI)   Spec (95%CI)   Measure   Summary of findings (95%CI)   state   Summary state   state   state

# 2 P.2.5.7 p-tau 181



### 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.

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

p												
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE	Ξ											
1 study	Dreenestive			0.00 (0.00 0.07)	LR+	7.64 (2.04, 28.53)	Serious	n/a	Not serious	Not serious		MODERATE
(Maddalena 2003)	Prospective	70	0.80 (0.67, 0.89)	0.89 (0.66, 0.97)	LR-	0.22 (0.12, 0.39)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on rick of his	-											

#### 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.

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



Mormont 2012: Exclusion of >35% population at analysis and use of optimised test thresholds.

# 1 P.2.5.10 Total Tau

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Vakushay 2010)	Dreenestive	46	0.46 (0.27, 0.65)	0.05 (0.74, 0.00)	LR+	10.08 (1.42, 71.85)	V. serious	n/a	Not serious	Serious		VERY LOW	
T Study (Fakushev 2010)	Prospective	40	0.46 (0.27, 0.65)	0.95 (0.74, 0.99)	LR-	0.57 (0.39, 0.83)	V. serious	n/a	Not serious	Serious	-	VERY LOW	
Notes on risk of bias	lotes on risk of bias												
Takushev 2010. Subgroup	analysis with >	10 /0 pop	alation choluded, use	s of optimised thesh									

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



### Notes on risk of bias

Mormont 2012: Exclusion of >35% population at analysis and use of optimised test thresholds.

# 1 P.2.6 AD versus non-AD dementia plus unclassifiable

# 2 P.2.6.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA												
1 study (Boutoleau- Bretonniere 2012)	Dreenestive	50	0.79 (0.54, 0.04)	0.66 (0.50, 0.70)	LR+	2.27 (1.37, 3.77)	Serious	n/a	Not serious	Serious		LOW
	Prospective	00	0.78 (0.54, 0.91)	0.00 (0.50, 0.79)	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

### 3 P.2.6.2 MRI

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Boutoleau-	Droopootivo	56	0.22 (0.16, 0.57)	0.66 (0.50, 0.70)	LR+	0.97 (0.44, 2.14)	Serious	n/a	Not serious	V. serious		VERY LOW
Bretonniere 2012)	Fiospective	50	0.33 (0.16, 0.57)	0.00 (0.50, 0.79)	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

# 1 P.2.7 AD versus non-AD

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Duits 2014) P	Broopootivo	1 1 4 0		0.72 (0.69, 0.76)	LR+	3.10 (2.68, 3.57)	Not serious	n/a	Not serious	Not serious		HIGH
	Frospective	1,149	0.00 (0.03, 0.09)	0.72 (0.00, 0.70)	LR-	0.19 (0.16, 0.24)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Prandt 2008)	Detreenentive	147	0.42 (0.20, 0.56)	0.00 (0.82, 0.04)	LR+	4.13 (2.10, 8.11)	Not serious	n/a	Not serious	Not serious		HIGH
T Sludy (Branul 2006)	Reirospective	147	0.42 (0.29, 0.50)	0.90 (0.62, 0.94)	LR-	0.65 (0.51, 0.83)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Brandt	1x prospective,	205	0.00.00.00.007)	0.02/0.02.4.00	LR+	6.85 (0.73, 64.28)	Serious	Seri ous	Not serious	Serious		VERY LOW
2008; Jahn 2011)	1x retrospective	225	0.62 (0.08, 0.97)	0.93 (0.22, 1.00)	LR-	0.39 (0.10, 1.50)	Serious	Seri ous	Not serious	Serious	-	VERY LOW
Notoo on rick of high												

#### 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

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMER	A											
2 studies (Kaneta	2x		0.70 (0.00, 0.00)	0.07 (0.40.0.00)	LR+	4.56 (0.31, 66.33)	Serious	Serious	Not serious	V serious		VERY LOW
2016; Tripathi 2010)	prospective	206	0.72 (0.09, 0.99)	0.87 (0.49, 0.98)	LR-	0.26 (0.02, 3.24)	Serious	Serious	Not serious	V. serious		VERY LOW
Natao an viele of his												

#### 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.

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

Studies MULTIPLE CAMERA	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
1 study (Kaneta 2016)	Prospective	89	0.71 (0.57,	0.68 (0.53,	LR+	2.31 (1.38, 3.63)	Serious	n/a	Not serious	Serious	_	LOW
	·		0.82)	0.81)	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 results of the index test.

# 2 P.2.7.6 99mTc-ECD SPECT, automated method

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA	4											
1 study (Kaneta	Dreamanting	00	0 40 (0 07 0 54)	0.00.00.00.000	LR+	2.32 (1.08, 4.96)	Not serious	n/a	Not serious	Serious		MODERATE
2016)	Prospective	89	0.40 (0.27, 0.54)	0.83 (0.88, 0.92)	LR-	0.73 (0.56, 0.95)	Not serious	n/a	Not serious	Not serious	-	HIGH

# 1 P.2.7.7 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
5 studies (Bergman 1997; Holman 1992; Launes 1991;	5 ×	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
Masterman 1997; McMurdo 1994)	prospective	505	0.70 (0.00, 0.01)	0.02 (0.00, 0.00)	LR-	0.52 (0.37, 0.84)	Not serious	Serious	Not serious	Serious		LOW
MULTIPLE CAMERA												
2 studies (Dobert	1x				LR+	6.80 (1.98, 23.36)	Not serious	Not serious	Not serious	Serious		MODERATE
2005; Rollin-Sillaire 2012)	prospective 1x retrospective	72	0.45 (0.24, 0.69)	0.93 (0.77, 0.98)	LR-	0.60 (0.40, 0.90)	Serious	Not serious	Not serious	Serious	-	LOW
ALL EVIDENCE POO	LED											
7 studies (Bergman 1997; Dobert 2005; Holman 1992;	6 ×				LR+	2.10 (1.29, 3.43)	Not serious	Serious	Not serious	Serious		LOW
Launes 1991; Masterman 1997; McMurdo 1994; Rollin-Sillaire 2012)	1 × retrospective	577	0.63 (0.49, 0.75)	0.74 (0.45, 0.90)	LR-	0.56 (0.43, 0.73)	Not serious	Not serious	Not serious	Serious	-	MODERATE
Notes on risk of bias	i											

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.

# 1 P.2.7.8 Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
ALL EVIDENCE POULED												
10 studies (Andreasen 2001; Brandt 2008; Duits 2014: Dumurgier 2015					LR+	2.88 (2.23, 3.67)	Serious	Serious	Not serious	Not serious		LOW
2001; Brandt 2006; 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-	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.

# 1 P.2.7.9 Amyloid Beta 1-42 and total tau

<b>,</b>												
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY C	ARE											
1 study (Frisoni	Droopostivo	04	0.71 (0.55, 0.92)	0.99 (0.76, 0.04)	LR+	5.68 (2.76, 11.70)	Serious	n/a	Not serious	Not serious		MODERATE
2009)	Prospective	94	0.71 (0.55, 0.65)	0.88 (0.76, 0.94)	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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Duits 2014)	Draanaativa	1 1 1 0	0.74 (0.70, 0.77)	0.96 (0.93, 0.90)	LR+	5.40 (4.33, 6.73)	Not serious	n/a	Not serious	Not serious		HIGH
i study (Duits 2014)	Prospective	1,149	0.74 (0.70, 0.77)	0.00 (0.83, 0.89)	LR-	0.30 (0.26, 0.35)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studios	Decign	Total	Sens (95% CI)	Spec	Magguro	Summary of findings	isk of bias	Iconsistency	Idirectness	nprecision	ther onsiderations	Quality
Studies	Design	IN	(95/60)	(95/001)	Weasure	(33 /001)	₩	<u> </u>	<u> </u>	<u> </u>	Οŭ	Quanty
PRIMARY CARE												
2 studies (Gabelle	2 ×	1 200	0.83 (0.78,	0.83 (0.79,	LR+	4.74 (3.67, 6.12)	Serious	Not serious	Not serious	Not serious		MODERAT E
2012 (Lille); Gabelle 2012 (Montpellier))	prospective	1,200	0.87)	0.86)	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.

### 2 P.2.7.12 Amyloid Beta 1-42/Total Tau

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

### 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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measur e	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
3 studies (Dumurgier 2015	3 ×	007	0.83 (0.60,	0.77 (0.66,	LR+	3.33 (2.31, 4.78)	V. serious	Not serious	Not serious	Not serious		LOW
Dumurgier 2015 (Montpellier))	prospective	307	0.94)	0.85)	LR-	0.22 (0.09, 0.54)	V. serious	Serious	Not serious	Serious	-	VERY LOW
Notes on risk of higs												

#### Notes on risk of blas

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.

# 2 P.2.7.14 EEG

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Epgedel 2015)	Droopootivo	270	0.70 (0.61.0.77)	0 40 (0 24 0 46)	LR+	1.16 (1.00, 1.35)	Not serious	n/a	Not serious	Not serious		HIGH
i study (⊏ngedal 2015)	Fiospective	312	0.70 (0.01, 0.77)	0.40 (0.34, 0.46)	LR-	0.76 (0.56, 1.02)	Not serious	n/a	Not serious	Not serious	-	HIGH

### 1 P.2.7.15 FDG-PET

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measur e	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
6 studies (Dobert 2005; Frisoni 2009;	6 ×	<b>F</b> 4 4	0.72 (0.53,	0.77 (0.70,	LR+	3.19 (2.05, 4.60)	Seriou s	Seriou s	Seriou s	Not serious		VERY LOW
Silverman 2001; Yakushev 2010)	prospective	544	0.86)	0.83)	LR-	0.37 (0.18, 0.62)	Seriou s	Seriou s	Seriou s	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.

# 1 P.2.7.16 FDG-PET/CT

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
1 study (Motara	Potrognostivo	09	0.97 (0.74, 0.04)		LR+	22.61 (5.78, 88.40)	Serious	n/a	Serious	Not serious		LOW
2017)	Reirospective	90	0.07 (0.74, 0.94)	0.90 (0.66, 0.99)	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

# 2 P.2.7.17 [18F] flutemetamol PET

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 shulls (7	Descentions	011	0.70 (0.00, 0.00)	0.66 (0.54, 0.76)	LR+	2.23 (1.58, 3.14)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Zwan 2017)	Prospective	211	0.76 (0.69, 0.83)	0.66 (0.54, 0.76)	LR-	0.36 (0.26, 0.51)	Not serious	n/a	Not serious	Serious	-	MODERATE

# 1 P.2.7.18 Formula Hulstaert (biomarkers)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Duits 2014) Pro	Droopostivo	1 1 4 0	0.02 (0.01.0.05)	0 74 (0 70 0 77)	LR+	3.54 (3.06, 4.10)	Not serious	n/a	Not serious	Not serious		HIGH
	Prospective	1,149	0.95 (0.91,0.95)	0.74 (0.70, 0.77)	LR-	0.09 (0.07, 0.13)	Not serious	n/a	Not serious	Not serious	-	HIGH

# 2 P.2.7.19 Formula Mattson (biomarkers)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Duits 2014) P	Draanaatiwa	1 1 4 0	0.90 (0.77, 0.92)	0.95 (0.91.0.99)	LR+	5.26 (4.28,6.47)	Not serious	n/a	Not serious	Not serious		HIGH
	Prospective	1,149	0.00 (0.77, 0.83)	005 (0.81, 0.88)	LR-	0.24 (0.20, 0.28)	Not serious	n/a	Not serious	Not serious	-	HIGH

# 1 P.2.7.20 Formula Mulder (biomarkers)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Duits 2014) Pro	Dreamantiva	1 1 1 0		0.72 (0.00, 0.70)	LR+	3.38 (2.93, 3.91)	Not serious	n/a	Not serious	Not serious		HIGH
	Prospective	1,149	0.93 (0.91, 0.95)	0.73 (0.68, 0.76)	LR-	0.10 (0.07, 0.13)	Not serious	n/a	Not serious	Not serious	-	HIGH

# 2 P.2.7.21 Formula Schoonenboom (biomarkers)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
1 study (Duits 2014) P	Dreenestive	1 1 10	0.01 (0.00, 0.02)	0.70 (0.74, 0.04)	LR+	4.10 (3.48, 4.82)	Not serious	n/a	Not serious	Not serious		HIGH
	Prospective	1,149	0.91 (0.88, 0.93)	0.78 (0.74, 0.81)	LR-	0.12 (0.09, 0.15)	Not serious	n/a	Not serious	Not serious	-	HIGH

Dementia Appendix P: Diagnosis evidence tables & GRADE

# 1 P.2.7.22 Mass Spectrometry

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Jahn 2011) Pro	Brooportivo	96	0.97 (0.77 0.04)	0.92 (0.62, 0.02)	LR+	5.02 (2.05, 12.29)	Serious	n/a	Not serious	Serious		MODERATE
	Frospective	00	0.07 (0.77, 0.94)	0.03 (0.02, 0.93)	LR-	0.15 (0.08, 0.30)	Serious	n/a	Not serious	Serious	-	MODERATE

2

3

# 4 P.2.7.23 MRI

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Frisoni	2 ×	007		0.70 (0.00, 0.04)	LR+	1.91 (1.56, 2.35)	Not serious	Not serious	Not serious	Serious		MODERATE
2009; Koikkalainen p 2016)	prospective	637	0.62 (0.09, 0.96)	0.72 (0.39, 0.91)	LR-	0.47 (0.13, 1.66)	Not serious	Serious	Not serious	Serious	-	LOW

# 1 P.2.7.24 MRI Total Hippocampal grey matter volume, Hv. Cut off 4.95ml.

	<u> </u>												
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Suppo 201E)	Detrespective	100	0.61 (0.46, 0.74)	0.96 (0.74, 0.02)	LR+	4.30 (2.17, 8.50)	Serious	n/a	Not serious	Not serious		MODERATE	
T study (Suppa 2015)	Reliospective	100	0.01 (0.46, 0.74)	0.00 (0.74, 0.93)	LR-	0.45 (0.31, 0.66)	Serious	n/a	Not serious	Serious	-	LOW	
Notes on risk of bias	Notes on risk of bias												
Suppa 2015: It was unc	lear whether the ir	ndex test	results were interpre	eted without knowled	ge of the resu	ults of the reference	standard; a	ssay cu	it-offs were det	ermined using I	ROC anal	ysis.	

# 2 P.2.7.25 MRI Hippocampal grey matter volume left, HVL. Cut- off 2.69 ml

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Suppo 2015)	Botroopootivo	100	0.70 (0.56, 0.92)	0.71 (0.59, 0.92)	LR+	2.47 (1.56, 3.89)	Serious	n/a	Not serious	Serious		LOW
r study (Suppa 2015)	Reirospeciive	100	0.70 (0.50, 0.62)	0.71 (0.36, 0.62)	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.

# 1 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%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Suppo 2015)	Potrospostivo	100	0.80 (0.65, 0.80)	0.66 (0.52, 0.77)	LR+	2.34 (1.58, 3.48)	Serious	n/a	Not serious	Serious		LOW
r siduy (Suppa 2015)	Reirospective	100	0.00 (0.05, 0.09)	0.00 (0.55, 0.77)	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.

# 2 P.2.7.27 MRI Hippocampal grey matter volume right, HVR. Cut off 2.70ml.

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Suppo 2015)	Detrespective	100	0.75 (0.60, 0.96)	0.77 (0.64, 0.96)	LR+	3.23 (1.95, 5.36)	Serious	n/a	Not serious	Serious		LOW
i sludy (Suppa 2015)	Reirospective	100	0.75 (0.00, 0.00)	0.77 (0.04, 0.00)	LR-	0.33 (0.19, 0.55)	Serious	n/a	Not serious	Serious	-	LOW
Notos on risk of higs												

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.

# 1 P.2.7.28 MRI Hippocampal grey matter volume right/ total grey matter volume (HVR/GMV). Cut-off 4.54 per mille.

		Total	Sens	Spec	Ì	Summary of findings	sk of bias	onsistency	lirectness	precision	าer nsiderations	
Studies	Design	Ν	(95%CI)	(95%CI)	Measure	(95%CI)	Ris	lnc	Ind	Ē	5 S	Quality
SECONDARY CARE		·					·					
1 study (Suppo 201E)	Detrespective	100	0.90 (0.65, 0.90)	0.90 (0.69, 0.90)	LR+	4.05 (2.34, 7.02)	Serious	n/a	Not serious	Not serious		MODERATE
i siduy (Suppa 2015)	Renospective	100	0.00 (0.05, 0.89)	0.00 (0.08, 0.89)	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.

# 2 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%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDART CARE												
1 study (Suppo 2015)	Botroopootivo	100	0.66 (0.51, 0.79)	0.99 (0.76, 0.04)	LR+	5.27 (2.55, 10.88)	Serious	n/a	Not serious	Not serious		MODERATE
r study (Suppa 2015)	Renospective	100	0.00 (0.31, 0.78)	0.00 (0.70, 0.94)	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.

# 1 P.2.7.30 Olfactory Test ≥ 3 errors

· · · · · · · · · · · · · · · · · · ·		-											
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study					LR+	1.47 (0.97, 2.22)	Not serious	n/a	Not serious	Serious		MODERATE	
(Christensen 2017)	Prospective	50	0.79 (0.59, 0.91)	0.46 (0.28, 0.65)	LR-	0.45 (0.19, 1.09)	Not serious	n/a	Not serious	Serious	-	MODERATE	
Notes on risk of k Christensen 2017:	<b>bias</b> Although the th	reshold v	was not pre-specified	l, data was presented	l for all possil	ble cut offs.							

# 2 P.2.7.31 Olfactory Test ≥ 4 errors



### 1 P.2.7.32 Olfactory Test ≥ 5 errors

•		-											
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study					LR+	1.35 (0.41, 4.46)	Not serious	n/a	Not serious	Serious		MODERATE	
(Christensen 2017)	Prospective	50	0.21 (0.09, 0.41)	0.85 (0.65, 0.94)	LR-	0.94 (0.72, 1.22)	Not serious	n/a	Not serious	Serious	-	MODERATE	
Notes on risk of I Christensen 2017:	<b>bias</b> Although the th	reshold v	was not pre-specified	l, data was presented	l for all possil	ble cut offs							

# 2 P.2.7.33 p-tau 181

Studies	Design	Tot al N	Sens (95%Cl)	Spec (95%Cl)	Meas ure	Summar y of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
ALL EVIDENCE POOLED												
9 studies (Brandt 2008; Duits 2014; Dumurgier 2015 (Lille); Dumurgier 2015 (Data 2015 (Data 2015))	7 × prospecti ve;	3,44	0.75	0.84	LR+	4.87 (3.37, 6.92)	V. seriou s	Serio us	Not serious	Not serious		VERY LOW
Paris); Gabelle 2012 (Montpellier); Knapskgog 2016; Mulder 2010)	2 × retrospe ctive	8	(0.82, 0.84)	0.90)	LR-	0.30 (0.20, 0.43)	V. seriou s	Serio us	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.

### 1 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 2 was used in place of Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	E											
1 study	Droopostivo	220	0.99 (0.92, 0.02)	0.01 (0.86, 0.05)	LR+	10.29 (6.41, 16.50)	V. serious	n/a	Not serious	Not serious		LOW
(Dumurgier 2015)	Dumurgier 2015) Prospective 329	0.00 (0.82, 0.92)	0.91 (0.86, 0.95)	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).

### 3 P.2.7.35 p-tau and Amyloid Beta 42/40

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	E											
1 study	Dreanactive	202	0.07 (0.01 0.02)		LR+	9.79 (6.01, 15.93)	V. serious	n/a	Not serious	Not serious		LOW
(Dumurgier 2015)	Prospective	303	0.07 (0.81, 0.92)	0.91 (0.86, 0.95)	LR-	0.14 (0.09, 0.22)	V. serious	n/a	Not serious	Not serious	-	LOW
Notes on risk of his	as											

# 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).

# 1 P.2.7.36 p-tau/Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Duits 2014;	2 ×	4 404	0.87 (0.81,	0.90 (0.74,	LR+	8.77 (2.95, 26.08)	V. serious	Serious	Not serious	Not serious		VERY LOW
Dumurgier 2015)	prospective	1,434	0.92)	0.97)	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).

### 1 P.2.7.37 Total Tau

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measur e	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
ALL EVIDENCE POOLED												
9 studies (Brandt 2008; Duits 2014; Dumurgier (Lille) 2015; Dumurgier 2015	7 ×				LR+	3.62 (3.14, 4.17)	Serious	Serious	Not serious	Not serious		LOW
(Paris); Dumurgier 2015 (Montpellier); Gabelle 2012 (Lille and Paris); Gabelle 2012 (Montpellier); Knapskgog 2016; Mulder 2010)	prospective; 2 × retrospective	3,447	0.78 (0.71, 0.84)	0.78 (0.74, 0.82)	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.

### 2 P.2.7.38 Total Tau/Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Duits 2014) Pr	Draanaatiya	1 1 4 0	0.95 (0.92, 0.99)	0.92 (0.70, 0.95)	LR+	4.78 (3.96, 5.77)	Not serious	Not serious	Not serious	Not serious		HIGH
	Prospective	1,149	0.85 (0.82, 0.88)	0.82 (0.79, 0.85)	LR-	0.18 (0.15, 0.22)	Not serious	Not serious	Not serious	Not serious	-	HIGH

## 1 P.2.7.39 Urinary AD7c-NTP (22ug/ml)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Coodmon 2007)	Detreenestive	169	0.50 (0.40, 0.60)	0.72 (0.62, 0.91)	LR+	2.15 (1.45, 3.19)	Not serious	n/a	Not serious	Serious		MODERATE
r sludy (Goodman 2007)	Reliospective	108	0.59 (0.49, 0.69)	0.73 (0.62, 0.81)	LR-	0.56 (0.42, 0.75)	Not serious	n/a	Not serious	Serious	-	MODERATE

# 2 **P.2.8** AD versus other dementias

# 3 P.2.8.1 99mTc-HMPAO SPECT



### 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.

# 1 **P.2.8.2 AD** scale (≥6)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Custofeen 2010)	Draanaativa	100	0.00 (0.71 0.07)	0.97 (0.79, 0.02)	LR+	6.18 (3.53, 10.82)	Not serious	n/a	Not serious	Not serious		HIGH	
r study (Gustalson 2010)	Prospective	190	0.80 (0.71, 0.87)	0.87 (0.78, 0.93)	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 downg	raded for	subgroup analysis a	as <10% population v	vas excluded	I.							

### 2 P.2.8.3 Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE		-			-							
3 studies (Boutoleau-Bretonniere	3 ×	240	0.74 (0.67,	0.62 (0.53,	LR+	1.96 (1.46, 2.62)	V. serious	Not serious	Not serious	Serious		VERY LOW
2012; Ibach 2006; Maddalena 2003)	prospective	249	0.81)	0.71)	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.

# 1 P.2.8.4 Amyloid Beta 1-42 and total tau

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
					I P+	10 80 (2 87 137 80)	V sorious	n/a	Not sorious	Not sorious		
1 study (Frisoni	Prospective	66	0 71 (0 55 0 83)	0.96 (0.79, 0.99)	LNT	19.09 (2.07, 137.00)	v. senous	n/a	NOL SEITOUS	NOL SEITOUS	_	LOW
2009)					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.

# 2 P.2.8.5 Apo E (≥1 allele)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Mayour 1000)	Detre en estive	0.400		0.00 (0.04, 0.70)	LR+	2.03 (1.75, 2.34)	Not serious	n/a	Not serious	Serious		MODERATE
i study (mayeux 1998)	Retrospective	2,188	0.65 (0.62, 0.67)	0.68 (0.64, 0.72)	LR-	0.52 (0.48, 0.57)	Not serious	n/a	Not serious	Serious	-	MODERATE

# 1 P.2.8.6 CSF 14-3-3, total Tau and p-tau

Quality
VERY LOW
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.

### 2 P.2.8.7 Computed Tomography, CT

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (O'Brian 2000)	Droopootivo	102	0.51 (0.20, 0.62)	0.29 (0.24, 0.55)	LR+	0.82 (0.58, 1.17)	Serious	n/a	Not serious	Not serious		MODERATE
r study (O Brien 2000)	Fiospective	103	0.51 (0.39, 0.62)	0.36 (0.24, 0.55)	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

# 1 P.2.8.8 FDG-PET

Studies SECONDARY CARE	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
6 studies (Arslan 2015; Frisoni 2009: Hoffman 2000: Jacust 2007:	4 × prospective;		0.71 (0.60	0.66 (0.57	LR+	2.07 (1.52, 2.78)	Serious	Not serious	Not serious	Serious		LOW
Ossenkoppele 2013; Yakushev 2010)	2 × retrospectiv e	300	0.80)	0.74)	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.

### 1 P.2.8.9 MRI

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE							·			·		
2 studies (Frisoni 2009;	2 ×	474	0.62 (0.09,	0.67 (0.40,	LR+	1.54 (1.08, 2.19)	Serious	Serious	Not serious	Serious		VERY LOW
Koikkalainen 2016)	prospective	471	0.96)	0.86)	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.

### 1 P.2.8.10 p-tau 181

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
3 studies (Boutoleau-Bretonniere	3 ×	2240	0.75 (0.64,	0.74 (0.61,	LR+	2.97 (1.73, 5.09)	V. serious	Serious	Not serious	Serious		VERY LOW
2003)	prospective	2249	0.84)	0.83)	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.

# 1 P.2.8.11 p-tau/Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Ibach 2006;	2 ×	205	0.79 (0.71,	0.74 (0.64,	LR+	3.07 (2.08, 4.52)	V. serious	Not serious	Not serious	Not serious		LOW
Maddalena 2003)	prospective	205	0.85)	0.83)	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.

### 1 P.2.8.12 Total tau

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measur e	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
3 studies (Boutoleau-Bretonniere	3 ×	005	0.71 (0.52,	0.82 (0.63,	LR+	4.28 (1.75, 9.99)	V. serious	Not serious	Not serious	Not serious		LOW
2012; Ibach 2006; Yakushev 2010)	e	205	0.85)	0.93)	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.

### 2 P.2.8.13 Total Tau/Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY C	ARE											
1 study (Ibach			0.75 (0.04, 0.00)	0.75 (0.04, 0.05)	LR+	3.00 (1.81, 4.98)	V. serious	n/a	Not serious	Serious		VERY LOW
2006)	Prospective	124	0.75 (0.04, 0.03)	0.75 (0.01, 0.65)	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.

# 1 P.2.9 AD versus VaD

# 2 P.2.9.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measur e	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
2 studies (Launes 1991;	2 ×	07	0.61 (0.49,	0.85 (0.69,	LR+	4.13 (1.85, 9.21)	Serious	Not serious	Not serious	Serious		LOW
McMurdo 1994)	prospective	97	0.72)	0.93)	LR-	0.45 (0.31, 0.66)	Serious	Not serious	Not serious	Serious	-	LOW
MULTIPLE CAMERA												
1 study (Boutoleau-Bretonniere	Dreenestive	26	0.78 (0.54,	0.50 (0.20,	LR+	1.56 (0.75, 3.25)	V. serious	n/a	Not serious	Serious		VERY LOW
2012)	Prospective	Prospective 26	0.91)	0.80)	LR-	0.44 (0.15, 1.35)	V. serious	n/a	Not serious	Serious	-	VERY LOW
ALL EVIDENCE POOLED												
3 studies (Boutoleau-Bretonniere	ere 3 ×		0.64 (0.53,	0.74 (0.45.	LR+	2.54 (1.19, 5.41)	V. serious	Not serious	Not serious	Serious		VERY LOW
1994)	prospective	123	0.74)	0.91)	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
### 1 P.2.9.2 Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Andreasen 2001)	Dreenestive	100	0.05 (0.57, 0.70)	0.40.00.00.000	LR+	1.25 (0.83, 1.87)	Not serious	n/a	Not serious	Not serious		HIGH
	Prospective	190	0.05 (0.57, 0.72)	0.48 (0.29, 0.68)	LR-	0.73 (0.45, 1.18)	Not serious	n/a	Not serious	Serious	-	MODERATE

# 2 P.2.9.3 Computed Tomography, CT

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (O'Brian 2000)	Draanaativa	04	0.51 (0.20, 0.62)	0.22 (0.17, 0.52)	LR+	0.75 (0.52, 1.06)	Serious	n/a	Not serious	Not serious		MODERATE
i study (O Briefi 2000)	FIOSPECTIVE	94	0.51 (0.39, 0.62)	0.32 (0.17, 0.52)	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

#### 1 P.2.9.4 MRI



#### 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.

## 2 P.2.10 bv-FTD versus non-bv-FTD

### 3 P.2.10.1 FDG-PET

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	E											
1 study (Vijverberg	Draanaativa	111	0.80 (0.71 0.06)	0 69 (0 57 0 77)	LR+	2.77 (1.97, 3.88)	Serious	n/a	Not serious	Serious		LOW
2016b)	Prospective	111	0.09 (0.71, 0.96)	0.00 (0.37, 0.77)	LR-	0.16 (0.06, 0.48)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notoo on rick of his												

#### 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.

### 1 P.2.10.2 FDG-PET and MRI

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE	Ξ											
1 study (Vijverberg	Broopootivo	111	0.06 (0.78, 0.00)	0 72 (0 62 0 91)	LR+	3.52 (2.46, 5.02)	Serious	n/a	Not serious	Not serious		MODERATE
2016b)	Flospective		0.90 (0.78, 0.99)	0.73 (0.02, 0.81)	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.

### 2 P.2.10.3 FTDC criteria for bv FTD

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Lorris 2012)	Detrespective	147	0.70 (0.60, 0.97)	0.06 (0.88, 0.00)	LR+	18.48 (6.07, 56.26)	Serious	n/a	Not serious	Not serious		MODERATE
T Study (Hams 2013)	Reliospective	147	0.79 (0.69, 0.67)	0.96 (0.66, 0.99)	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

#### 1 P.2.10.4 FTDC criteria for possible bvFTD

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Vijverberg	Broopootivo	116	0.95 (0.67, 0.04)	0.27 (0.10, 0.27)	LR+	1.17 (0.95, 1.43)	Serious	n/a	Not serious	Not serious		MODERATE
2016a)	Prospective 116 0.85 (0.67		0.85 (0.87, 0.94)	0.27 (0.19, 0.37)	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.

#### 2 P.2.10.5 FTDC criteria for probable bvFTD



#### 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.

#### 1 P.2.10.6 MRI



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.

# 2 P.2.11 bvFTD/fd+ versus non-bvFTD/fd+

### 3 P.2.11.1 FDG-PET

	Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
	SECONDARY CARE		·					·		·	·		
	1 study (Kerklaan 2014)	Detresenting	50	0.47 (0.04, 0.74)	0.00 (0.70, 0.07)	LR+	5.76 (1.71, 19.34)	Not serious	n/a	Not serious	Serious		MODERATE
		Retrospective	52	0.47 (0.24, 0.71)	0.92 (0.78, 0.97)	LR-	0.58 (0.36, 0.94)	Not serious	n/a	Not serious	Serious	-	MODERATE

## 1 P.2.12 CADASIL versus CADASIL-like syndromes

### 2 P.2.12.1 Skin biopsy

okiii biopsy												
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ampuero 2009) P	Brooncetive	00	0.06 (0.78, 0.00)	0.69 (0.56, 0.70)	LR+	3.03 (2.10, 4.39)	Not serious	n/a	Not serious	Not serious		HIGH
	Prospective	90	0.96 (0.76, 0.99)	0.00 (0.50, 0.79)	LR-	0.05 (0.01, 0.37)	Not serious	n/a	Not serious	Not serious	-	HIGH

# 3 P.2.13 CBD versus non-CBD

### 4 P.2.13.1 CBD consensus criteria

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 -t	Determention	00	0.00 (0.70, 0.00)	0.00 (0.00 0.07)	LR+	0.96 (0.82, 1.12)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Alexander 2014)	Retrospective	33	0.93 (0.70, 0.98)	0.03 (0.00, 0.37)	LR-	2.25 (0.10, 51.46)	Not serious	n/a	Not serious	V. serious	-	LOW

# 1 P.2.14 CJD versus non-CJD

### 2 P.2.14.1 Amyloid Beta 1-42 and total tau

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
SECONDARY CARE 1 study (Van Everbroeck 2003)	Detressestive	250	0.07 (0.74, 0.02)	0.00.(0.05.0.00)	LR+	42.84 (16.14, 113.67)	Not serious	n/a	Not serious	Not serious		HIGH
	Retrospective	250	0.87 (0.74, 0.93)	0.98 (0.95, 0.99)	LR-	0.14 (0.07, 0.27)	Not serious	n/a	Not serious	Not serious	-	HIGH

### 3 P.2.14.2 CSF 14-3-3 Automated Capillary Western Assay

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 study (Esurier 2017)	Detressestive	000	0.04 (0.05, 0.07)	0.05 (0.04.0.00)	LR+	19.84 (10.46, 37.65)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Fourier 2017)	Retrospective	268	0.94 (0.85, 0.97)	095 (0.91, 0.98)	LR-	0.07 (0.03, 0.16)	Not serious	n/a	Not serious	Not serious	-	HIGH

4

#### 1 P.2.14.3 CSF 14-3-3 (multiple methods)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Tschampa	Potrospostivo	174	0.01 (0.96, 0.05)	0.44 (0.20, 0.61)	LR+	1.64 (1.21, 2.21)	Not serious	n/a	Not serious	Serious		MODERATE
2005) F	Reirospective	174	0.91 (0.86, 0.95)	0.44 (0.29, 0.61)	LR-	0.19 (0.10, 0.38)	Not serious	n/a	Not serious	Not serious	-	HIGH

### 2 P.2.14.4 CSF 14-3-3 ELISA



#### 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.

#### 1 P.2.14.5 CSF 14-3-3 immunoblotting

Studies	Design	Tot al N	Sens (95%Cl)	Spec (95%CI)	Mea sure	Summa ry of finding s (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Qualit y
17 studies (Bahl 2008; Beudry 1998; Burkhard 2001; Chohan 2010; Coulthart 2011; Cuadrado-Corrales 2006; Fourier 2017, Foutz 2017; Hamlin 2012; Kenney 2000;	8 × prospe ctive;	6,0	0.87	0.83	LR+	5.44 (3.28, 8.78)	Seri ous	Serio us	Not seriou s	Not seriou s		LOW
Lattanzio 2017; Lemstra 2000; Rohan 2015; Tagliapietra 2013; Van Everbroeck 2003; Zerr 1998; Zerr 2000)	9 × retrosp ective	86	(0.84, 0.90)	(0.73, 0.90)	LR-	0.16 (0.13, 0.19)	Seri ous	Not seriou s	Not seriou s	Not seriou s	-	MODE RATE

#### 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

### 1 P.2.14.6 CSF 14-3-3 (presence) and S100B (>1.0ng/ml)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	RE											
1 study (Chohan 2010) Re	Potroopoetivo	111	0.62 (0.56, 0.68)	0.05 (0.00, 0.07)	LR+	11.72 (6.16, 22.29)	Serious	n/a	Not serious	Not serious		MODERATE
	Reliospective	411	0.02 (0.50, 0.08)	0.95 (0.90, 0.97)	LR-	0.40 (0.34, 0.47)	Serious	n/a	Not serious	Not serious	-	MODERATE
,						0.40 (0.04, 0.47)	Ochous	Π/a	Not Schous	Not Schous		WODERATE

#### 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.

### 2 P.2.14.7 CSF 14-3-3 and Amyloid Beta 1-42



#### 1 P.2.14.8 CSF 14-3-3 and total Tau

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	RE											
1 study (Chohan	Detresses	054	0.75 (0.00, 0.00)	0.00 (0.02, 0.02)	LR+	6.33 (3.97, 10.09)	Serious	n/a	Not serious	Not serious		MODERATE
2010) Retrospective 351		351	0.75 (0.69, 0.80)	0.88 (0.82, 0.93)	LR-	0.28 (0.22, 0.36)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of	hiaa											

#### 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.

#### 2 P.2.14.9 CSF 14-3-3, total Tau and S100B



#### 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.

### 1P.2.14.10 EEG

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	E											
2 studies					LR+	1.95 (0.42, 9.15)	Not serious	Serious	Not serious	V. serious		VERY LOW
(Tagliapietra 2013; Tschampa 2005)	2 × retrospective	202	0.71 (0.05, 0.99)	0.49 (0.00, 1.00)	LR-	0.73 (0.63, 0.84)	Not serious	Not serious	Not serious	Not serious	-	HIGH

### 2P.2.14.11 European criteria for CJD

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Brandel 2000)	Detreenestive	226		0.29 (0.16, 0.42)	LR+	1.26 (1.04, 1.53)	Not serious	n/a	Not serious	Not serious		HIGH
	Reliospective	230	0.91 (0.86, 0.95)	0.20 (0.16, 0.43)	LR-	0.32 (0.16, 0.62)	Not serious	n/a	Not serious	Serious	-	MODERATE

### 1P.2.14.12 French criteria for CJD

	-											
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Brandal 2000)	Detrespective	226	0.99 (0.93, 0.03)	0.50 (0.25, 0.65)	LR+	1.77 (1.29, 2.42)	Not serious	n/a	Not serious	Serious		MODERATE
i sludy (Brandel 2000)	Renospective	230	0.00 (0.83, 0.92)	0.50 (0.35, 0.65)	LR-	0.23 (0.14, 0.38)	Not serious	n/a	Not serious	Not serious	-	HIGH

### 2P.2.14.13 Master's criteria for CJD

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Brandel 2000) R	Detrespective	226	0.09 (0.05 1.00)	0 10 (0 04 0 24)	LR+	1.09 (0.99, 1.21)	Not serious	n/a	Not serious	Not serious		HIGH
	Reliospective	230	0.96 (0.95, 1.00)	0.10 (0.04, 0.24)	LR-	0.15 (0.04, 0.66)	Not serious	n/a	Not serious	Serious	-	MODERATE

### 1P.2.14.14 MRI

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
4 studies (Schroter	1 ×				LR+	5.40 (2.46, 11.88)	Not serious	Serious	Not serious	Not serious		MODERATE	
2000; Tagliapietra 2013; Tschampa 2005; Van Everbroeck 2004)	prospective; 3 × retrospective	564	0.54 (0.40, 0.67)	0.90 (0.79, 0.96)	LR-	0.52 (0.37, 0.72)	Not serious	Serious	Not serious	Serious	-	LOW	
Notes on risk of bias	es on risk of bias												
Van Everbroeck 2004:	> 10% population	on exclud	led from analysis										

### 2P.2.14.15 MRI, DWI

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Tagliapietra	Potroopootivo	21	0.72 (0.41.0.01)	0.05 (0.72, 0.00)	LR+	14.55 (2.08, 101.66)	Not serious	n/a	Not serious	Not serious		HIGH
2013)	Reirospective	31	0.73 (0.41, 0.91)	0.95 (0.72, 0.99)	LR-	0.29 (0.11, 0.76)	Not serious	n/a	Not serious	Serious	-	MODERATE

### 1P.2.14.16 Neuron-specific enolase

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Bahl	2 ×	205	0.74 (0.65,	0.90 (0.85,	LR+	8.00 (5.05, 12.69)	Serious	Not serious	Not serious	Not serious		MODERAT E
2008; Beudry 1998)	prospective	290	0.82)	0.94)	LR-	0.28 (0.20, 0.40)	Serious	Not serious	Not serious	Not serious	-	MODERAT E

#### 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

#### 2P.2.14.17 New criteria for sporadic CJD

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY	CARE											
1 study (Zerr	Detressestive	74	0.00 (0.07 4.00)	0.74 (0.50, 0.05)	LR+	3.36 (1.80, 6.28)	V. serious	n/a	Not serious	Serious		VERY LOW
2009)	Reliospective	74	0.96 (0.87, 1.00)	0.71 (0.50, 0.85)	LR-	0.03 (0.00, 0.20)	V. serious	n/a	Not serious	Not serious	-	LOW
Notoo on rick	fhice											

#### 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-tau 181/total tau 1**P.2.14.18**

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	E											
2 studies (Bahl	1 ×				LR+	8.10 (5.35, 12.26)	V. serious	Not serious	Not serious	Not serious		LOW
2008; Leitao 2016)	prospective; 1 × retrospective	282	0.93 (0.71, 0.99)	0.89 (0.84, 0.93)	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.

#### 1P.2.14.19 RT-QuIC



### 2P.2.14.20 S100B, 1.0ng/ml



#### 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.

### 1P.2.14.21 S100B, 2.5ng/ml

<u> </u>												
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Beudry 2 1998; Coulthart 2011)	2 ×	4 052	0.87 (0.82,	0.87 (0.84,	LR+	6.65 (5.52, 8.00)	Serious	Not serious	Not serious	Not serious		MODERAT E
	prospective	1,053	0.91)	0.89)	LR-	0.15 (0.10, 0.21)	Serious	Not serious	Not serious	Not serious	-	MODERAT E

#### 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.

#### 2P.2.14.22 S100B, 4.2ng/ml

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	RE											
1 study	Brooncotivo	024	0.52 (0.42, 0.60)	L 97 (0.96, 0.98)	LR+	17.26 (11.23, 26.52)	Not serious	n/a	Not serious	Not serious		HIGH
(Coulthart 2011)	FIOSPECTIVE	924	0.52 (0.43, 0.00)	0.97 (0.90, 0.96)	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.

#### 1P.2.14.23 Total Tau

Studies	Design	Tot al N	Sens (95%Cl)	Spec (95%Cl)	Mea sure	Summar y of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Qua lity
SECONDARY CARE												
11 studies (Bahl 2008; Chohan 2010; Coulthart 2011; Foutz 2017; Hamlin 2012;	4 × prospec tive;	3,	0.87	0.88	LR+	7.22 (4.34, 11.60)	Seri ous	Seri ous	Not seriou s	Not seriou s		LO W
2003; Van Everbroeck 2004)	7 × retrospe ctive	614	(0.84, 0.90)	(0.80, 0.93)	LR-	0.15 (0.12, 0.19)	Seri ous	Seri ous	Not seriou s	Not seriou s	-	LO W

#### 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.

#### Total Tau and S100B 1P.2.14.24

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	RE											
1 study (Chohan	Detrespective	251	0.50 (0.52, 0.65)	0.05 (0.00, 0.08)	LR+	11.34 (5.46, 23.53)	Serious	n/a	Not serious	Not serious		MODERATE
2010)	Reliospective	351	0.59 (0.52, 0.65)	0.95 (0.90, 0.96)	LR-	0.43 (0.37, 0.51)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of	hias											

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.

#### WHO CJD criteria 2P.2.14.25



#### 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

### 1 P.2.15 DLB versus AD

### 2 P.2.15.1 Lewy body composite risk score, LBCRS, $\geq$ 3

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Calvin 2015)	Droopostivo	150	0.04 (0.84, 0.08)	0.79 (0.60, 0.95)	LR+	4.29 (2.95, 6.24)	Serious	n/a	Not serious	Not serious		MODERATE
i Sludy (Galvill 2015)	Frospective	100	0.94 (0.04, 0.96)	0.76 (0.09, 0.65)	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.

#### 3 P.2.15.2 MRI

								l.				
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Dreenestive	270	0 42 (0 20 0 57)	0.71 (0.65, 0.77)	LR+	1.48 (1.00, 2.19)	Serious	n/a	Not serious	Serious		LOW
(Koikkalainen 2016)	Prospective	270	0.43 (0.29, 0.57)	0.71 (0.65, 0.77)	LR-	0.81 (0.62, 1.04)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on visit of his												

#### 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.

### 1 P.2.16 DLB versus FTD



#### 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.

## 1 P.2.17 DLB versus non-DLB

### 2 P.2.17.1 123I-FP-CIT SPECT

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAME	RA											
1 study	Detrognactive	22	0.05 (0.55, 1.00)	0.80 (0.61, 0.08)	LR+	8.91 (1.95, 40.64)	Serious	n/a	Not serious	Serious		LOW
(Walker 2009)	Reliospective	23	0.95 (0.55, 1.00)	0.69 (0.61, 0.96)	LR-	0.05 (0.00, 0.77)	Serious	n/a	Not serious	Serious	-	LOW
MULTIPLE CA	MERA											
2 studies	1x				LR+	15.40 (6.24, 38.01)	Serious	Not serious	Not serious	Not serious		MODERATE
(Kemp 2011; O'Brien 2009; Thomas 2017)	prospective, 2x retrospective	161	0.78 (0.59, 0.89)	0.95 (0.87, 0.98)	LR-	0.25 (0.13, 0.48)	Not serious	Serious	Not serious	Not serious	-	MODERATE
ALL EVIDENCE	E POOLED											
3 studies					LR+	13.34 (6.14, 29.01)	Serious	Not serious	Not serious	Not serious		MODERATE
(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-	0.22 (0.11, 0.44)	Not serious	Not serious	Not serious	Not serious	-	HIGH
Notes on risk o	of bias											
Walker 2009: S	ome of the includ	ed indivi	duals had a presume	ed dementia diagnos	sis at baselir	ie						

Kemp 2011: Index test used as part of the reference standard

#### 1 P.2.17.2 123I-IMP SPECT



### 2 P.2.17.3 123I-IMP SPECT and 123I-MIBG cardiac scintigraphy combined

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measur e	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA		·					·		·	·		
1 study (Sakamoto	Retrospectiv	100	0.88 (0.70,	0.86 (0.77,	LR+	6.55 (3.62, 11.84)	Serious	n/a	Not serious	Not serious		MODERAT E
2014)	e	100	0.96)	0.93)	LR-	0.13 (0.05, 0.39)	Serious	n/a	Not serious	Not serious	-	MODERAT E

#### 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.

#### 1 P.2.17.4 123I-MIBG cardiac scintigraphy

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
5 studies (Estorch 2008; Manabe 2017;	4 ×		0 89 (0 81	0 91 (0 82	LR+	10.80 (4.89, 21.50)	Serious	Serious	Not serious	Not serious		LOW
Sakamoto 2014; Sakamoto 2017, Slaets 2015)	1 × retrospective	607	0.93)	0.96)	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.

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Epsedal 2015)	Droopostivo	207	0.97 (0.50, 0.07)	0.99 (0.94 .0.01)	LR+	7.01 (5.01, 9.80)	Not serious	n/a	Not serious	Not serious		HIGH
r study (Engedal 2015)	Prospective	307	0.07 (0.59, 0.97)	0.00 (0.84, 0.91)	LR-	0.15 (0.04, 0.55)	Not serious	n/a	Not serious	Serious	-	MODERATE

### 2 P.2.17.5 EEG

### 1 P.2.17.6 FDG-PET

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Ossenkoppele	2 ×	255	0.53 (0.06,	0.97 (0.91,	LR+	19.64 (1.28, 301.23)	Serious	Serious	Serious	Serious		VERY LOW
2013; Panegyres 2009)	prospective	200	0.96)	0.99)	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.

#### 2 P.2.17.7 MRI

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen	Brooportivo	504	0 42 (0 20 0 57)	0.76 (0.72, 0.90)	LR+	1.80 (1.24, 2.61)	Not serious	n/a	Not serious	Serious		MODERATE
2016)	Prospective	rospective 504 0.	0.43 (0.29, 0.57)	0.76 (0.72, 0.80)	LR-	0.75 (0.59, 0.97)	Not serious	n/a	Not serious	Not serious	-	HIGH

### 1 P.2.17.8 RBD or two or more of visual hallucinations, Parkinsonism, and fluctuating attention and concentration

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
1 study (Ferman 2011)	Prospective	234	0.00 (0.82, 0.04)	0 73 (0 65 0 80)	LR+	3.30 (2.49, 4.38)	Not serious	n/a	Not serious	Not serious		HIGH
	Fiospective	204	0.90 (0.02, 0.94)	0.75 (0.05, 0.80)	LR-	0.14 (0.08, 0.25)	Not serious	n/a	Not serious	Not serious	-	HIGH

### 2 P.2.17.9 Two or more of fluctuating attention and concentration, visual hallucinations and Parkinsonism

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ferman 2011)	Dreenactive	004	0.85 (0.76, 0.01)	0.72 (0.65, 0.80)	LR+	3.11 (2.34, 4.15)	Not serious	n/a	Not serious	Not serious		HIGH
	Prospective	234	0.05 (0.76, 0.91)	0.75 (0.65, 0.80)	LR-	0.21 (0.13, 0.34)	Not serious	n/a	Not serious	Not serious	-	HIGH

#### Other considerations Inconsistency Indirectness **Risk of bias** Imprecision Summary Total Sens Spec of findings (95%CI) (95%CI) Quality **Studies** Design Ν (95%CI) Measure SECONDARY CARE LR+ 5.35 (3.58, 8.01) Not serious Not serious HIGH n/a Not serious 1 study (Ferman 2011) 0.83 (0.74, 0.89) 0.85 (0.77, 0.90) Prospective 234 0.21 (0.13, 0.32) HIGH LR-Not serious n/a Not serious Not serious

### 1P.2.17.10 Two or more of visual hallucinations, Parkinsonism or RBD

### 2P.2.17.11 Two or more of visual hallucinations, Parkinsonism, fluctuating attention and concentration or RBD

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ferman 2011)	Draanaativa	024	0.99 (0.90, 0.02)	0.72 (0.65, 0.80)	LR+	3.23 (2.43, 4.29)	Not serious	n/a	Not serious	Not serious		HIGH
	Prospective	234	0.00 (0.80, 0.93)	0.73 (0.85, 0.80)	LR-	0.17 (0.10, 0.29)	Not serious	n/a	Not serious	Not serious	-	HIGH

### 1 P.2.18 DLB versus other dementias

### 2 P.2.18.1 123I-FP-CIT SPECT

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAME	RA											
1 study	Dreenestive	24	0.00 (0.69, 0.07)	0.01 (0.56, 0.00)	LR+	9.90 (1.52, 64.52)	Not serious	n/a	Not serious	Serious		MODERATE
(Treglia 2012)	Prospective	31	0.90 (0.66, 0.97)	0.91 (0.56, 0.99)	LR-	0.11 (0.03, 0.42)	Not serious	n/a	Not serious	Not serious	-	HIGH
MULTIPLE CAN	<b>MERA</b>											
1 study	Detresses	20	0.00 (0.40, 0.07)	0.00 (0.00, 4.00)	LR+	21.67 (1.43, 333.42)	Not serious	n/a	Not serious	Serious		MODERATE
(Walker 2007)	Retrospective	20	0.83 (0.46, 0.97)	0.96 (0.60, 1.00)	LR-	0.17 (0.04, 0.75)	Not serious	n/a	Not serious	Serious	-	MODERATE
ALL EVIDENCE	POOLED											
2 studies	1 ×				LR+	12.72 (2.71, 59.68)	Not serious	Not serious	Not serious	Not serious		HIGH
(Treglia 2012; Walker 2007)	prospective; 1 × retrospective	51	0.88 (0.70, 0.96)	0.93 (0.72 0.99)	LR-	0.14 (0.05, 0.36)	Not serious	Not serious	Not serious	Not serious	-	HIGH
Notes on risk o	of bias											

Treglia 2012: Specific criteria used as the reference standard not reported

### 1 P.2.18.2 123I-MIBG cardiac scintigraphy

	<u> </u>												
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Tracilia 2012)	Dreamantiva	24	0.00 (0.00, 0.07)	0.04 (0.50, 0.00)	LR+	9.90 (1.52, 64.52)	Not serious	n/a	Not serious	Serious		MODERATE	
T study (Treglia 2012)	Prospective	31	0.90 (0.68, 0.97)	0.91 (0.56, 0.99)	LR-	0.11 (0.03, 0.42)	Not serious	n/a	Not serious	Not serious	-	HIGH	
Notes on risk of bias Treglia 2012: Specific ci	otes on risk of bias												

### 2 P.2.18.3 DLB consensus criteria



### 1 P.2.18.4 FDG-PET

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
SECONDARY CARE 1 study (Ossenkoppele P	Prospective	98	0.20 (0.03,	0.95 (0.88,	LR+	3.72 (0.53, 26.13)	V. serious	n/a	Serious	Serious	_	VERY LOW
2013)	•		0.69)	0.98)	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.

### 2 P.2.18.5 Lewy body composite risk score, LBCRS, ≥ 3

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
A study (Ostic 0045)	Descentions	477	0.00 (0.00, 4.00)	0.00 (0.70, 0.04)	LR+	7.16 (4.59, 11.15)	Serious	n/a	Not serious	Not serious		MODERATE	
1 study (Galvin 2015)	Prospective	177	0.98 (0.88, 1.00)	0.86 (0.79, 0.91)	LR-	0.02 (0.00, 0.15)	Serious	n/a	Not serious	Not serious	-	MODERATE	
Notes on risk of bias Galvin 2015: Subgroup	lotes on risk of bias Balvin 2015: Subgroup analysis was carried out excluding >30% study population.												

#### 1 P.2.18.6 MRI

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE	l .											
1 study (Koikkalainen P 2016)	Dreenestive	200	0.43 (0.29,	0.76 (0.72,	LR+	1.80 (1.23, 2.65)	Serious	n/a	Not serious	Serious		LOW
	Prospective	300	0.57)	0.81)	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.

### 2 P.2.19 DLB versus VaD

#### 3 P.2.19.1 MRI

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Draanaatiwa	71	0.42 (0.20, 0.57)	0.99 (0.69, 0.06)	LR+	3.40 (1.12, 10.32)	Serious	n/a	Not serious	Serious		LOW
(Koikkalainen 2016)	Prospective	/ 1	0.43 (0.29, 0.57)	0.00 (0.08, 0.90)	LR-	0.66 (0.49, 0.88)	Serious	n/a	Not serious	Serious	-	LOW
Network and shale of laters												

#### 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.

# 1 P.2.20 FTD versus AD

### 2 P.2.20.1 99mTc-HMPAO SPECT

Studies	Design	Tota I N	Sens (95%Cl)	Spec (95%Cl)	Measu re	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
	3 × prospective		/ /		LR+	13.11 (6.13, 28.05)	V. serious	Not serious	Not serious	Not serious		LOW
4 studies (Launes 1991; Read 1995; Talbot 1998; Velakoulis 1997)	; 1 × retrospecti ve	291	0.51 (0.35, 0.67)	0.96 (0.92, 0.98)	LR-	0.55 (0.45, 0.66)	V. serious	Not serious	Not serious	Serious	-	VERY LOW
MULTIPLE CAMERA												
	1 × prospective		/		LR+	18.12 (3.71, 88.60)	V. serious	Not serious	Not serious	Not serious		LOW
2 studies (Boutoleau-Bretonniere 2012; Rollin-Sillaire 2012)	; 1 × retrospecti ve	64	0.73 (0.52, 0.87)	0.96 (0.82, 0.99)	LR-	0.28 (0.15, 0.54)	V. serious	Not serious	Not serious	Serious	-	VERY LOW
ALL EVIDENCE POOLED												
6 studies (Boutoleau-Bretonniere 2012	4 × prospective				LR+	13.50 (6.77, 24.20)	V. serious	Not serious	Not serious	Not serious		LOW
Launes 1991; Read 1995; Rollin-Sillaire 2012; Talbot 1998; Velakoulis 1997)	; 2 × retrospecti ve	355	0.58 (0.44, 0.72)	0.96 (0.92, 0.98)	LR-	0.44 (0.30, 0.59)	V. serious	Not serious	Not serious	Serious	-	VERY LOW

#### Dementia Appendix P: Diagnosis evidence tables & GRADE

		Tota I	Sens	Spec	Measu	Summary of findings	sk of bias	consistency	directness	precision	her nsiderations
Studies	Design	N	(95%CI)	(95%CI)	re	(95%CI)	ä	lne	<u>l</u>	<u>=</u>	ÖS 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 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

#### 1 P.2.20.2 MRI



#### 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.

#### 1 P.2.20.3 FTD versus DLB

### 2 P.2.20.4 FDG-PET

100121												
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Droopostivo	22	0.24 (0.17, 0.57)	0.02 (0.28, 0.00)	LR+	4.11 (0.27, 62.70)	V. serious	n/a	Serious	V. serious		VERY LOW
(Ossenkoppele 2013)	Prospective 23 0.34 (0.17, 0.57) 0.92		0.92 (0.38, 0.99)	LR-	0.72 (0.48, 1.08)	V. serious	n/a	Serious	Serious	-	VERY LOW	
Notos on risk of higs												

#### 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.

#### 3 P.2.20.5 MRI

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECUNDARY 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
Made an atol at blan												

#### 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.

### 1 P.2.21 FTD versus non-FTD dementia plus unclassifiable

### 2 P.2.21.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	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

### 3 P.2.22 MRI

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Boutoleau- Bretonniere 2012)	Dreeneetive	rospective 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
	Prospective				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.
## 1 P.2.23 FTD versus non-FTD

#### 2 P.2.23.1 99mTc-ECD SPECT, visual assessment

Studies MULTIPLE CAMERA	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
A shada (Tsin shai					LR+	86.67 (12.32, 609.43)	Serious	n/a	Not serious	Not serious		MODERATE	
1 study (Tripathi 2010)       Prospective       117       0.96 (0.78, 0.99)       0.99 (0.93, 1.00)       LR+       86.07 (12.32, 609.43)       Serious       In/a       Not serious       Not serious       Not serious       MODERATE         2010)       117       0.96 (0.78, 0.99)       0.99 (0.93, 1.00)       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 wei	re lost to	follow up and did no	t receive a reference	standard; it	is unclear whether the ind	ex test was	interp	reted without ki	nowledge of the	reference	e standard.	

#### 1 P.2.23.2 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measur e	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA						-						
	2 × prospective				LR+	6.05 (2.77, 13.22)	V. serious	Not serious	Not serious	Not serious		LOW
3 studies (Launes 1991; Read 1995; Talbot 1998)	; 1 × retrospectiv e	501	0.51 (0.20, 0.81)	0.93 (0.90, 0.95)	LR-	0.63 (0.40, 1.01)	V. serious	Not serious	Not serious	Serious	-	VERY LOW
MULTIPLE CAMERA												
	1 × prospective				LR+	7.88 (1.14, 54.71)	Serious	Serious	Not serious	Serious		VERY LOW
2 studies (Boutoleau-Bretonniere 2012; Rollin-Sillaire 2012)	; 1 × retrospectiv e	108	0.74 (0.53, 0.88)	0.90 (0.53, 0.99)	LR-	0.30 (0.15, 0.59)	Serious	Not serious	Not serious	Serious	-	LOW
ALL EVIDENCE POOLED												
5 studies (Boutoleau-Bretonniere 2012)	3 × prospective				LR+	7.03 (3.36, 13.10)	V. serious	Not serious	Not serious	Not serious		LOW
Launes 1991; Read 1995; Rollin-Sillaire 2012; Talbot 1998)	; 2 × retrospectiv e	609	0.59 (0.37, 0.78)	0.91 (0.84, 0.95)	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

## 1 **P.2.23.3** SPECT/PET

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
1 study (Mandar 2007)	Dreenestive	104	0.00 (0.80, 0.06)	0.75 (0.62, 0.92)	LR+	3.57 (2.38, 5.36)	Not serious	n/a	Serious	Not serious		HIGH
1 study (Mendez 2007)	Prospective	154	0.90 (0.80, 0.96)	0.75 (0.83, 0.83)	LR-	0.13 (0.06, 0.28)	Not serious	n/a	Serious	Not serious	-	HIGH

2

#### 3 P.2.23.4 FDG-PET

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measur e	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Ossenkoppele	2 ×	255	0.43 (0.25,	0.93 (0.87,	LR+	6.20 (2.12, 18.11)	Seriou s	Serious	Seriou s	Not serious		VERY LOW
2013; Panegyres 2009)	prospective	205	0.63)	0.96)	LR-	0.63 (0.43, 0.92)	Seriou s	Not serious	Seriou s	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.

## 1 P.2.23.5 FTD consensus criteria

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Mandar 2007)	Detrognactive	104	0.27 (0.26, 0.40)	0.00 (0.00, 1.00)	LR+	52.88 (3.28, 853.00)	Not serious	n/a	Not serious	Not serious		HIGH
r study (mendez 2007)	Renospective	134	0.37 (0.26, 0.49)	0.99 (0.90, 1.00)	LR-	0.64 (0.53, 0.77)	Not serious	n/a	Not serious	Not serious	-	HIGH

#### 2 P.2.23.6 MRI

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies	1 ×				LR+	2.66 (1.85, 3.82)	Not serious	Serious	Not serious	Serious		LOW
(Koikkalainen 2016; Mendez 2007)	prospective; 1 × retrospective	638	0.56 (0.43, 0.69)	0.78 (0.63, 0.89)	LR-	0.57 (0.48, 0.69)	Not serious	Not serious	Not serious	Serious	-	MODERATE

## 1 P.2.24 FTD versus other dementias

#### 2 P.2.24.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
1 study	Droopootivo	tive 33 0.56 (0.25.0.82)	0.56 (0.25, 0.92)	0.06 (0.76, 0.00)	LR+	13.33 (1.79, 99.08)	V. serious	n/a	Not serious	Serious		VERY LOW
(Velakoulis 1997)	Prospective 33 0.56 (0.25, 0.82		0.50 (0.25, 0.62)	0.90 (0.76, 0.99)	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.

#### 1 P.2.24.2 FDG-PET

-												
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE		·					·					
2 studies (Arslan 2015;	1 × prospective;	140	0.40 (0.25,	0.78 (0.49,	LR+	1.78 (0.91, 3.51)	V. serious	Not serious	Serious	Serious		VERY LOW
Ossenkoppele 2013)	1 × retrospective	140	0.57)	0.93)	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.

#### 2 P.2.24.3 FTD scale (≥6)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Quetoface 2010)	Dreenestive	100	0.00 (0.04 0.07)		LR+	11.58 (6.53, 20.52)	Not serious	n/a	Not serious	Not serious		HIGH
T study (Gustalson 2010)	Prospective	190	0.92 (0.81, 0.97)	0.92 (0.86, 0.96)	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.

#### 1 P.2.24.4 MRI

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Draanaatiwa	296	0.50 (0.40, 0.60)	0 70 (0 72 0 82)	LR+	2.23 (1.66, 2.99)	Serious	n/a	Not serious	Serious		LOW
(Koikkalainen 2016)	FIOSPECTIVE	386 0.50 (0.40, 0.60)		0.76 (0.72, 0.82)	LR-	0.64 (0.52, 0.80)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of bias	5											

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.

#### 1 P.2.25 FTD versus VaD

#### 2 P.2.25.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measur e	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
2 studies (Launes 1991; Talbot	2 ×	106	0.46 (0.36,	0.85 (0.51,	LR+	2.58 (0.77, 8.64)	V. serious	Serious	Not serious	Serious		VERY LOW
1998)	prospective	190	0.57)	0.97)	LR-	0.72 (0.58, 0.91)	V. serious	Not serious	Not serious	Not serious	-	LOW
MULTIPLE CAMERA												
1 study (Boutoleau-Bretonniere	Dreenestive	10	0.73 (0.41,	0.75 (0.38,	LR+	2.91 (0.83, 10.19)	V. serious	n/a	Not serious	Serious		VERY LOW
2012)	Prospective	19	0.91)	0.94)	LR-	0.36 (0.13, 1.03)	V. serious	n/a	Not serious	Serious	-	VERY LOW
ALL EVIDENCE POOLED												
3 studies (Boutoleau-	3 ×	215	0.51 (0.35,	0.82 (0.61,	LR+	2.23 (1.20, 4.16)	V. serious	Not serious	Not serious	Serious		VERY LOW
1991; Talbot 1998)	prospective	215	0.67)	0.93)	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.

#### 1 P.2.25.2 MRI

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study	Dreenestive	116	0.50 (0.40, 0.60)	0.06 (0.76, 0.00)	LR+	12.00 (1.74, 82.64)	Serious	n/a	Not serious	Serious		LOW	
(Koikkalainen 2016)	Prospective	110	0.50 (0.40, 0.60)	0.96 (0.76, 0.99)	LR-	0.52 (0.42, 0.65)	Serious	n/a	Not serious	Serious	-	LOW	
Notes on risk of bias Koikkalainen 2016: Su avoided; the index test	otes on risk of bias oikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were voided: the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.												

# 2 P.2.26 HAND versus other neurological disorders in HIV+ people

## 3 P.2.26.1 HIV dementia scale (<10)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skinner 2009)	Dreenestive	22	0.40 (0.00, 0.70)	0.00 (0.57, 0.02)	LR+	2.31 (0.80, 6.63)	Not serious	n/a	Not serious	Serious		MODERATE
	Prospective	33	0.46 (0.22, 0.72)	0.80 (0.57, 0.92)	LR-	0.67 (0.39, 1.17)	Not serious	n/a	Not serious	Serious	-	MODERATE

## 1 P.2.26.2 HIV dementia scale (<11)

	<u>= \ /</u>											
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE											· · · · ·	
1 study (Chingson 2000)	Dreamanting	22	0.00 (0.04, 0.00)	0.00 (0.57, 0.00)	LR+	3.08 (1.16, 8.17)	Serious	n/a	Not serious	Serious		LOW
i study (Skinner 2009)	Prospective	33	0.02 (0.34, 0.03)	0.80 (0.57, 0.92)	LR-	0.48 (0.23, 0.99)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of bias												
Skinner 2009: Use of an op	otimised thresho	ld.										

## 2 P.2.26.3 International HIV Dementia scale (IHDS) (<10)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skinner 2009) F	Dreenestive	22	0.77 (0.49, 0.02)	0.65 (0.42, 0.82)	LR+	2.20 (1.13, 4.28)	Not serious	n/a	Not serious	Serious		MODERATE
	Prospective	33	0.77 (0.48, 0.92)	0.00 (0.43, 0.82)	LR-	0.36 (0.13, 1.01)	Not serious	n/a	Not serious	Serious	-	MODERATE

## 1 P.2.26.4 Grooved pegboard test

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDART CARE						-						
1 study (Davis 2002)		455	0.71 (0.62, 0.78)	0.46 (0.41, 0.52)	LR+	1.31 (1.13, 1.52)	Serious	n/a	Serious	Not serious		LOW
1 study (Davis 2002) P	FIOSPECTIVE	400	0.71 (0.03, 0.78)	0.40 (0.41, 0.52)	LR-	0.63 (0.48, 0.84)	Serious	n/a	Serious	Serious	-	VERY LOW

## 2 P.2.26.5 Modified HIV dementia scale (m-HDS) (<7.5)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Davis 2002)	tudy (Davia 2002) Broopertive		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
1 study (Davis 2002) F	Prospective	400	0.70 (0.62, 0.77)	0.71 (0.66, 0.76)	LR-	0.42 (0.32, 0.55)	Serious	n/a	Serious	Serious	-	VERY LOW

# 1 P.2.26.6 Modified HIV dementia scale (m-HDS) and grooved pegboard combined.

Studies SECONDARY CARE	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
1 study (Davis 2002)	Draanaativa	455	0.77 (0.70, 0.82)	0.40 (0.25, 0.45)	LR+	1.28 (1.13, 1.46)	Serious	n/a	Serious	Not serious		LOW
1 study (Davis 2002) P	Prospective	400	0.77 (0.70, 0.83)	0.40 (0.35, 0.45)	LR-	0.57 (0.41, 0.80)	Serious	n/a	Serious	Serious	-	VERY LOW

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## 3 P.2.27 Neurosyphilis versus not neurosyphilis

## 4 P.2.27.1 CSF EIA

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
OLOONDANT OANL								1		1		
1 study (Chan 2014) P	Dreenestive	45	0.07 (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
	Prospective	40	0.97 (0.66, 1.00)	0.47 (0.30, 0.64)	LR-	0.06 (0.00, 0.94)	Not serious	n/a	Not serious	Serious	-	MODERATE

#### 1 P.2.27.2 FTA-ABS



#### 2 P.2.27.3 INNO-LIA

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE											·	
4 -tt- (D	Detres estive	00	0.00 (0.00 4.00)	0.40 (0.00, 0.04)	LR+	1.09 (0.95, 1.25)	Not serious	n/a	Serious	Not serious		MODERATE
1 study (Dumaresq 2013)	Retrospective	83	0.96 (0.60, 1.00)	0.12 (0.06, 0.21)	LR-	0.33 (0.02, 5.31)	Not serious	n/a	Serious	V. serious	-	VERY LOW
Notes on indirectness	n who have sex w	/ith men										

## 1 P.2.27.4 PCR for T. pallidum genes: polA, Tpp47, and bmp.

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Dumenson 2012)	Detressetive	100		0.01 (0.51.0.71)	LR+	1.03 (0.53, 2.02)	Not serious	n/a	Serious	Serious		LOW	
T study (Dumaresq 2013)	Retrospective	108	0.40 (0.19, 0.65)	0.61 (0.51, 0.71)	LR-	0.98 (0.63, 1.53)	Not serious	n/a	Serious	Not serious	-	MODERATE	
Notes on indirectness	otes on indirectness												

#### 2 P.2.27.5 TPPA



## 1 P.2.28 PDD and DLB versus other dementias

#### 2 P.2.28.1 123I-MIBG cardiac scintigraphy

		<b>U</b> 1										
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY C	ARE											
1 study (Hanyu	Dreanactive	06	0.05 (0.82, 0.00)	0.07 (0.76, 0.04)	LR+	7.47 (3.73, 14.98)	Serious	n/a	Not serious	Not serious		MODERATE
2006)	Prospective	90	0.95 (0.62, 0.99)	0.87 (0.76, 0.94)	LR-	0.06 (0.01, 0.22)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notoo on rick of	hina											

#### 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.

#### 3 P.2.29 PDD versus non-PDD

#### 4 P.2.29.1 FCSRT-IR 3- FR (≤22)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 - to the (16)	Descention	10	0.04 (0.07, 0.00)	0.70 (0.40, 0.04)	LR+	3.77 (1.10, 12.94)	Serious	n/a	Not serious	Serious		LOW	
T study (Klesman 2013)	Prospective	40	0.84 (0.67, 0.93)	0.78 (0.42, 0.94)	LR-	0.21 (0.09, 0.50)	Serious	n/a	Not serious	Not serious	-	MODERATE	
Notes on risk of bias Kiesman 2013: Test thres	hold was not pr	e-specifie	ed.										

#### 1 P.2.29.2 Movement disorders criteria for PDD (≤120)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Kissman 2012)	Dreenestive	40	0.80 (0.62, 0.00)	0.05 (0.52, 1.00)	LR+	15.94 (1.06, 238.88)	Serious	n/a	Not serious	Serious		LOW	
T Sludy (Riesman 2013)	Prospective	40	0.80 (0.82, 0.90)	0.95 (0.53, 1.00)	LR-	0.21 (0.11, 0.43)	Serious	n/a	Not serious	Not serious	-	MODERATE	
Notes on risk of bias Kiesman 2013: Test thres	lotes on risk of bias												

#### 2 P.2.29.3 Movement disorders criteria for PDD (≤123)



Kiesman 2013: Test threshold was not pre-specified.

## 1 P.2.29.4 Movement disorders criteria for PDD (≤132)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Kissman 2012)	Dreenestive	40	0.08 (0.70, 1.00)	0 45 (0 10 0 74)	LR+	1.79 (1.02, 3.14)	Serious	n/a	Not serious	Serious		LOW
T Study (Klesman 2013)	Prospective	40	0.96 (0.79, 1.00)	0.45 (0.19, 0.74)	LR-	0.03 (0.00, 0.59)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of bias Kiesman 2013: Test thresho	old was not pre-s	pecified.										

## 2 P.2.29.5 Rey-Osterrieth complex figure test, ROCF (≤22)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
OLOONDANT OANL												
1 study (Kiesman 2012)	Prospective	40	0.00 (0.74, 0.07)	0.78 (0.42, 0.04)	LR+	4.06 (1.19, 13.87)	Serious	n/a	Not serious	Serious		LOW
r study (Neshian 2013)	riospective	40	0.30 (0.74, 0.37)	0.70 (0.42, 0.94)	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.

#### 1 P.2.30 PPA versus non-PPA

#### 2 P.2.30.1 FDG-PET

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Danagyraa 2000)	Dreenestive	102	0 50 (0 10 0 81)	0.00 (0.02, 1.00)	LR+	97.00 (5.54, 1697.47)	Not serious	n/a	Serious	Not serious		MODERATE
T study (Panegyres 2009)	Prospective	102	0.50 (0.19, 0.81)	0.99 (0.92, 1.00)	LR-	0.50 (0.24, 1.05)	Not serious	n/a	Serious	Serious	-	LOW
lotes on indirectness												
Fallegyles 2009. The study	only recruited	heobie A	any onset dem	entia (<05 years olu	).							

#### 3 P.2.31 VaD and mixed dementias versus AD

#### 4 P.2.31.1 Hachinski ischemic score, HIS (≥5)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY C	ARE											
1 study (Siritho	Dreamantiva	014	0.00 (0.77, 0.02)	0.70 (0.05, 0.00)	LR+	3.17 (2.36, 4.25)	V. serious	n/a	Not serious	Not serious		LOW
2006)	D6)         Prospective         214         0.86 (0.77, 0.92)		0.86 (0.77, 0.92)	0.73 (0.65, 0.80)	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.

## 1 P.2.32 VaD versus AD and mixed dementia (AD plus VaD)

## 2 P.2.32.1 ADDTC (possible)

\I												
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Gold 2002) R	Detrespective	00	0.70 (0.47, 0.96)	0.79 (0.67 0.96)	LR+	3.22 (1.89, 5.48)	Not serious	n/a	Not serious	Serious		MODERATE
	Renospective	09	0.70 (0.47, 0.86)	0.76 (0.07, 0.86)	LR-	0.38 (0.19, 0.76)	Not serious	n/a	Not serious	Serious	-	MODERATE

#### 3 P.2.32.2 ADDTC (probable)



#### ADDTC criteria 1 P.2.32.3

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Dashatta 2007)	Detresses	110	0 50 (0 40 0 70)	0.74 (0.02, 0.02)	LR+	2.27 (1.41, 3.66)	Not serious	n/a	Serious	Serious		LOW
T Sludy (Bachella 2007)	Reliospective	110	0.56 (0.42, 0.73)	0.74 (0.63, 0.63)	LR-	0.56 (0.37, 0.84)	Not serious	n/a	Serious	Serious	-	LOW
Notes on indirectness Bachetta 2007: Participants	s were selected to	be >90 ve	ears old									

#### Hachinski ischemic score, HIS (≥7) 2 P.2.32.4



Bachetta 2007: Participants were selected to be >90 years old

## 1 P.2.32.5 NINDS-AIREN (possible)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Cold 2002)	2002) Botrospostivo 80 0.55 (0.24.0.7	0 55 (0 24 0 75)	0.94 (0.72, 0.01)	LR+	3.45 (1.76, 6.75)	Not serious	n/a	Not serious	Serious		MODERATE	
i study (Gold 2002)	Reliospective	rospective 89 0.55 (0.34, 0.75)		0.04 (0.73, 0.91)	LR-	0.54 (0.33, 0.88)	Not serious	n/a	Not serious	Serious	-	MODERATE

## 2 P.2.32.6 NINDS-AIREN (probable)

-												
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Cold 2002)	ald 2002) Potrospective 80 0.20 (0.08 0.43) 0.0	0.02 (0.94, 0.07)	LR+	2.76 (0.82, 9.32)	Not serious	n/a	Not serious	Serious		MODERATE		
1 Sludy (GOId 2002)	Reirospective	09	0.20 (0.08, 0.43)	0.95 (0.84, 0.97)	LR-	0.86 (0.69, 1.08)	Not serious	n/a	Not serious	Not serious	-	HIGH

#### 1 P.2.32.7 NINDS-AIREN criteria

Studies SECONDARY CARE	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
					LR+	2.06 (1.28, 3.31)	Not serious	n/a	Serious	Serious		LOW	
1 study (Bachetta 2007)	Retrospective	110	0.56 (0.39, 0.71)	0.73 (0.62, 0.82)	LR-	0.61 (0.41, 0.90)	Not serious	n/a	Serious	Serious	-	LOW	
Notes on indirectness Bachetta 2007: Participants	LR-       0.61 (0.41, 0.90)       Not serious       n/a       Serious       Serious       LOW         otes on indirectness         achetta 2007: Participants were selected to be >90 years old												

## 2 P.2.33 VaD versus AD

#### 3 P.2.33.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
2 studies (Launes 1991;	2 ×	07	0.70 (0.00 0.07)	0.77 (0.04, 0.00)	LR+	3.21 (1.90, 5.43)	Serious	Not serious	Not serious	Serious		LOW
McMurdo 1994)	prospective	97	0.76 (0.60, 0.87)	0.77 (0.04, 0.00)	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.												

#### 1 P.2.33.2 MRI



#### 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.

# 2 P.2.34 VaD versus DLB

#### 3 P.2.34.1 MRI

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Prospective	71	0.71 (0.50,	0.96 (0.85,	LR+	16.65 (4.19, 66.18)	Serious	n/a	Not serious	Not serious	_	MODERATE
(Koikkalainen 2016)			0.85)	0.99)	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.

## 1 P.2.35 VaD versus FTD

## 2 P.2.35.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality		
SINGLE CAMERA														
1 study (Lourses 1001)	Dreenestive	20	0.76 (0.59, 0.97)	0 60 (0 20 0 00)	LR+	1.89 (0.64, 5.64)	Serious	n/a	Not serious	Serious		LOW		
T Sludy (Lauries 1991)	Prospective	30	0.76 (0.56, 0.67)	0.60 (0.20, 0.90)	LR-	0.40 (0.16, 1.03)	Serious	n/a	Not serious	Serious	-	LOW		
Notes on risk of bias Launes 1991: Subgroup a	LR-     0.40 (0.16, 1.03)     Serious     Not serious     Serious     LOW       otes on risk of bias       aunes 1991: Subgroup analysis used with >10% study population excluded													

#### 3 P.2.35.2 MRI

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	e 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.

# 1 P.2.36 VaD versus non-VaD dementia plus unclassifiable

#### 2 P.2.36.1 MRI

IVIINI												
Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Boutoleau- Bretonniere 2012)	Prospective	e 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.

#### 3 P.2.37 VaD versus non-VaD

#### 4 P.2.37.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	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

#### 1 P.2.38 MRI



## 2 P.2.39 VaD versus other dementias

#### 3 P.2.39.1 HIS (≥7)



#### 1 P.2.39.2 MRI

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	e 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.

Dementia Appendix P: Diagnosis evidence tables & GRADE

# 1 P.3 Meta-analyses

#### 2 P.3.1 Dementia versus no dementia

3 P.3.1.1 ACE (<83)



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#### 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

#### 1 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

#### 1 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

1 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

#### 1 P.3.1.5 FDG-PET



Figure 9 Dementia versus no dementia: FDG-PET – forest plot: likelihood ratios


Figure 10Dementia versus no dementia: FDG-PET – forest plot: sensitivity and specificity

#### 1 P.3.1.6 IQCODE (16 item, >3.5)



Figure 11Dementia 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

#### 1 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

#### 1 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

#### 1 P.3.1.9 MIS (<5)



Figure 17Dementia versus no dementia: MIS (<5) – forest plot: likelihood ratios



1 2 2

3 Figure 18Dementia versus no dementia: MIS (<5) – forest plot: sensitivity and specificity

# 4 P.3.1.10 MMSE (<18)

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Figure 19Dementia versus no dementia: MMSE (<18) – forest plot: likelihood ratios



Figure 20Dementia versus no dementia: MMSE (<18) – forest plot: sensitivity and specificity

# 1 P.3.1.11 MMSE (<19)



Figure 21Dementia versus no dementia: MMSE (<19) – forest plot: likelihood ratios



Figure 22Dementia versus no dementia: MMSE (<19) – forest plot: sensitivity and specificity

# 1 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

# 1 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

# 1 P.3.1.14 MMSE (<22)



Figure 27Dementia versus no dementia: MMSE (<22) – forest plot: likelihood ratios

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Figure 28Dementia versus no dementia: MMSE (<22) – forest plot: sensitivity and specificity

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## 1 P.3.1.15 MMSE (<23)



Figure 29Dementia versus no dementia: MMSE (<23) – forest plot: likelihood ratios



Figure 30Dementia versus no dementia: MMSE (<23) – forest plot: sensitivity and specificity

# 1 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

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## 1 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

## 1 P.3.1.18 MMSE (<26)





Figure 35Dementia versus no dementia: MMSE (<26) – forest plot: likelihood ratios

Study	TP	FN	FP	τN	Sens. (95%CI)	Spec. (95%CI)							
PRIMARY													
Reference standard: clinical	crite ria												
no data													
Reference standard: clinician	diagno	sis											
Flicker 1997	199	17	45	38	0.92 (0.88, 0.95)	0.48 (0.35, 0.57)	→                       • • • • • • • •						
Reference standard: neuropa	thology	1											
no data													
RE subtotal					0.92 (0.88, 0.95)	0.46 (0.35, 0.57)							
SECONDARY													
Reference standard: clinical	crite ria												
no data													
Reference standard: clinician	diagno	DSIS											
Callahan 2002	308	37	49	257	0.89 (0.86, 0.92)	0.84 (0.79, 0.88)	+ +						
Nielsen 2013	54	17	16	44	0.76 (0.65, 0.85)	0.73 (0.61, 0.83)							
RE subtotal					0.84 (0.67, 0.93)	0.80 (0.68, 0.88)							
Within-substratum heterogene	eity, sen	s: Tau	°=0.41;	Chi <sup>2</sup> =8	3.62, df=1 (p=0.003); I	2=88.4%							
Within-substratum heterogene	eity, spe	c: Tau	<b>≈=0.15</b> ;	Chi <sup>2</sup> =3	3.81, df=1 (p=0.051); I	2=73.7%							
Reference standard: neuropa	thology	/											
Milian 2012	347	91	0	64	0.79 (0.75, 0.83)	0.99 (0.89, 1.00)	+ <b>-</b>						
RE subtotal					0.83 (0.73, 0.89)	0.84 (0.68, 0.93)							
Within-stratum heterogeneity, se	ans: Tai	u²=0.22	2; Chi²=	16.05,	df=2 (p<0.001); I <sup>2</sup> =87	.596							
Within-stratum heterogeneity, sp	ec: Tai	u²=0.38	B; Chi₽=	9.31, a	#=2 (p=0.010); I*=78.5	596							
RE meta-analysis					0.85 (0.77, 0.91)	0.78 (0.53, 0.92)							
Overall heterogeneity, sens: Tau <sup>2</sup> =	0.10; C	hi*=13.	.33, df=	=3 (p=0	0.004); 1*=77.5%								
Overall heterogeneity, spec: Tau <sup>2</sup> =	0.55; C	hi*=57.	.08, df=	=3 (p<0	0.001); / =94.7%		0.00 0.20 0.40 0.60 0.80 1.00 1.00 0.80 0.60 0.40 0.	20 0.00					
Between-stratum heterogeneity, se	ens: Chi	P=0.24	, df=1 (	p=0.62	21); /=0.0%								
Between-stratum heterogeneity, spec: Chi²=45.68, df=1 (p<0.001); l²=97.8%						Sensitivity Specificity	Specificity						

Figure 36Dementia versus no dementia: MMSE (<26) – forest plot: sensitivity and specificity

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# 1 P.3.1.19 MMSE (<27)



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Figure 37Dementia versus no dementia: MMSE (<27) – forest plot: likelihood ratios

Study	TP	FN	FP	TN	Sens. (95%CI)	Spec. (95%Cl)													
PRIMARY							-												
Reference standard: clinical	crite ria																		
no data																			
Reference standard: clinicia	n diagno	osis																	
no data																			
Reference standard: neurop	athology	1																	
no data																			
SECONDARY																			
Reference standard: clinical	crite ria																		
no data																			
Reference standard: clinicia	n diagno	osis																	
Bastide 2012	103	25	49	143	0.80 (0.73, 0.86)	0.74 (0.68, 0.80)									-				
Callahan 2002	326	19	67	239	0.94 (0.92, 0.96)	0.78 (0.73, 0.82)						-							
Mathuranath 2000	85	30	1	23	0.74 (0.65, 0.81)	0.98 (0.76, 0.99)				-	•		-						
Nielsen 2013	63	8	22	38	0.89 (0.79, 0.94)	0.63 (0.51, 0.74)					_	-		-	-				
RE subtotal					0.86 (0.73, 0.94)	0.75 (0.66, 0.82)					-			- •	•				
Within-substratum heteroger	ne <i>ity</i> , sen	s: Tau	°=0.67;	ChiP=3	35.50, df=3 (p<0.001);	/==91.596					_			-					
Within-substratum heteroger	neity, spe	c: Tau	P=0.11;	Chi <sup>2</sup> =9	9.77, df=3 (p=0.021); I	=69.3%													
Reference standard: neurop	athology	<i>,</i>																	
no data																			
RE subtotal					0.86 (0.73, 0.94)	0.75 (0.66, 0.82)					-			-					
Within-stratum heterogeneity, a	ens: Tau	u²=0.6)	7; Chi <sup>2</sup> =	35.50,	df=3 (p<0.001); I2=91.	596					-			- T					
Within-stratum heterogeneity, a	epec: Tau	u²=0.1	1; Chi <sup>p</sup> =	9.77, 0	#=3 (p=0.021); /==69.3	96													
RE meta-analysis					0.86 (0.73, 0.94)	0.75 (0.66, 0.82)					-			•	•				
Overall heterogeneity, sens: Tau	=0.37; C	hi*=27	.29, df=	=3 (p<0	0.001); 1=89.0%							_						_	
Overall heterogeneity, spec: Tau	=0.08; C	ihi²=11	.53, df=	=3 (p=0	0.009); / =74.0%		0.00	0.20	0.40	0.60	0.80	1.00	1.00	0.80	0.60	0.40	0.20	0.0	
								Sensitivity						Specificity					

Figure 38Dementia versus no dementia: MMSE (<27) – forest plot: sensitivity and specificity

# 1 P.3.1.20 MMSE (<28)



Figure 39Dementia versus no dementia: MMSE (<28) – forest plot: likelihood ratios



Figure 40Dementia versus no dementia: MMSE (<28) – forest plot: sensitivity and specificity

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### 1 P.3.1.21 MoCA (<19)



Figure 41Dementia versus no dementia: MoCA (<19) – forest plot: likelihood ratios



Figure 42Dementia versus no dementia: MoCA (<19) – forest plot: sensitivity and specificity

#### 1 P.3.1.22 MRI



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Figure 44 Dementia versus no dementia: MRI – forest plot: sensitivity and specificity

Dementia Appendix P: Diagnosis evidence tables & GRADE

# 1 P.3.2 AD versus FTD

#### 2 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

# 1 P.3.3 AD versus non-AD

# 2 P.3.3.1 99mTc-ECD SPECT, visual assessment method



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Figure 48AD versus non-AD: 99mTc-ECD SPECT, visual assessment method – forest plot: sensitivity and specificity

### 1 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

# 1 P.3.3.3 Amyloid Beta 1-42



Figure 51AD versus non-AD: Amyloid Beta 1-42 – forest plot: likelihood ratios



Figure 52 AD versus non-AD: Amyloid Beta 1-42 – forest plot: sensitivity and specificity

# 1 P.3.3.4 Amyloid Beta 1-42/p-tau



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Figure 54AD versus non-AD: Amyloid Beta 1-42/p-tau – forest plot: sensitivity and specificity

# 1 P.3.3.5 Amyloid Beta 1-42/Total Tau



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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

# 1 P.3.3.6 Amyloid Beta 42/40





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Figure 58AD versus non-AD: Amyloid Beta 42/40 – forest plot: sensitivity and specificity

# 1 P.3.3.7 Amyloid Beta 1-42, Total tau and p-tau 181 abnormal



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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

# 1 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

### 1 P.3.3.9 MRI

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Figure 63AD versus non-AD: MRI – forest plot: likelihood ratios



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# Figure 64AD versus non-AD: MRI – forest plot: sensitivity and specificity

#### p-tau 181 4 P.3.3.10

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# 3 Figure 65AD versus non-AD: p-tau 181 – forest plot: likelihood ratios

# 4 P.3.3.11 p-tau/Amyloid Beta 1-42

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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

# 1 P.3.3.12 Total Tau

Study	TP	FN	FP	ΤN	Sens. (95%CI)	Spec. (95%CI)												
PRIMARY							-											
Reference standard: clinical of	criteria																	
no data																		
Reference standard: clinician	diagn	osis																
no data																		
Reference standard: neuropa	thology	y																
no data																		
SECONDARY																		
Reference standard: clinical of	criteria																	
no data																		
Reference standard: clinician	diagn	osis																
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)					<b>•</b>			•				
Within-substratum heterogene	eity, sen	is: Tau	<sup>2</sup> =0.21;	Chi2=5	6.60, df=8 (p<0.001);	l²=85.9%												
Within-substratum heterogene	eity, spe	c: Tau	<sup>2</sup> =0.08;	Chi2=2	25.91, df=8 (p=0.001);	l²=69.1%												
Reference standard: neuropa	thology	y																
no data																		
RE subtotal					0.78 (0.71, 0.84)	0.78 (0.75, 0.82)					<b>•</b>			•				
Within-stratum heterogeneity, se	ens: Tau	u²=0.21	1; Chi²=	56.60,	df=8 (p<0.001); I <sup>2</sup> =85.	9%												
Within-stratum heterogeneity, sp	bec: Tai	u²=0.08	3; Chi²=	25.91,	df=8 (p=0.001); I <sup>2</sup> =69.	1%												
RE meta-analysis					0.78 (0.71, 0.84)	0.78 (0.75, 0.82)					•			•				
Overall heterogeneity, sens: Tau2=	0.12; C	hi²=49	.23, df=	=8 (p<0	.001); I <sup>2</sup> =83.8%							_		<b>.</b>				
Overall heterogeneity, spec: Tau2=	0.02; C	chi²=16	.14, df=	=8 (p=0	.040); 1²=50.4%		0.00	0.20	0.40	0.60	0.80	1.00	1.00	0.80	0.60	0.40	0.20	0.00
									Sens	itivity					Snec	ificity		
									5011						Shee			

Study	TP	FN	FP	ΤN	Sens. (95%CI)	Spec. (95%CI)	_											
PRIMARY																		
Reference standard: clinical o	riteria																	
no data																		
Reference standard: clinician	diagn	osis																
no data																		
Reference standard: neuropa	tholog	У																
no data																		
SECONDARY																		
Reference standard: clinical of	riteria																	
no data																		
Reference standard: clinician	diagn	osis																
Brandt 2008	25	23	11	88	0.52 (0.38, 0.66)	0.89 (0.81, 0.94)							-	<u> </u>				
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)						-	- I -		-			
Dumurgier 2015 (Montpellier)	37	13	26	85	0.74 (0.60, 0.84)	0.77 (0.68, 0.84)					<u> </u>				-			
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)					<b>•</b>			- 🔶				
Within-substratum heterogene	ity, ser	ns: Tau	²=0.21;	Chi <sup>2</sup> ={	56.60, df=8 (p<0.001);	12=85.9%												
Within-substratum heterogene	ity, spe	ec: Tau	²=0.08;	Chi <sup>2</sup> =2	25.91, df=8 (p=0.001);	l²=69.1%												
Reference standard: neuropa	tholog	У																
no data																		
RE subtotal					0.78 (0.71, 0.84)	0.78 (0.75, 0.82)					-			- 🔶				
Within-stratum heterogeneity, se	ns: Ta	u <sup>2</sup> =0.21	; Chi <sup>2</sup> =	56.60,	df=8 (p<0.001); I <sup>2</sup> =85.	9%												
Within-stratum heterogeneity, sp	ec: Ta	u²=0.08	3; Chi <sup>2</sup> =	25.91,	df=8 (p=0.001); 1 <sup>2</sup> =69.	1%												
RE meta-analysis					0.78 (0.71, 0.84)	0.78 (0.75, 0.82)					•			•				
Overall heterogeneity, sens: Tau <sup>2</sup> =	0.12; C	Chi²=49	23, df=	=8 (p<0	.001); 12=83.8%		- I											
Overall heterogeneity, spec: Tau <sup>2</sup> =	0.02; C	chi²=16	14, df=	=8 (p=0	.040); I²=50.4%		0.00	0.20	0.40	0.60	0.80	1.00	1.00	0.80	0.60	0.40	0.20	0.00
									Sens	sitivity					Spec	ificity		
									Jene						Shee			

Figure 68AD versus non-AD: Total Tau – forest plot: sensitivity and specificity

Dementia Appendix P: Diagnosis evidence tables & GRADE

# 1 P.3.4 AD versus other dementias

### 2 P.3.4.1 Amyloid Beta 1-42



Figure 69AD versus other dementias: Amyloid Beta 1-42 – forest plot: likelihood ratios

1 2 3



Figure 70AD versus other dementias: Amyloid Beta 1-42 – forest plot: sensitivity and specificity

# 1 P.3.4.2 FDG-PET



Figure 71AD versus other dementias: FDG-PET – forest plot: likelihood ratios

2



Figure 72AD versus other dementias: FDG-PET – forest plot: sensitivity and specificity

### 1 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

### 1 **P.3.4.4 p-tau 181**



Figure 75AD versus other dementias: p-tau 181 – forest plot: likelihood ratios

1 2 3



Figure 76AD versus other dementias: p-tau 181 – forest plot: sensitivity and specificity

# 1 P.3.4.5 p-tau/Amyloid Beta 1-42



2

Study	TP	FN	FP	TN	LR- (95%CI)	LR+ (95%CI)													
PRIMARY																			
Reference standard: clinical cr	iteria																		
no data																			
Reference standard: clinician c	liagno	sis																	
no data																			
Reference standard: neuropath	ology																		
no data																			
SECONDARY																			
Reference standard: clinical cr	iteria																		
no data																			
Reference standard: clinician c	liagno	sis																	
lbach 2006	59	17	12	36	0.30 (0.19, 0.47)	3.11 (1.87, 5.14)									<u> </u>				
Maddalena 2003	41	10	8	22	0.27 (0.15, 0.49)	3.01 (1.64, 5.54)									<u> </u>				
RE subtotal					0.29 (0.20, 0.41)	3.07 (2.08, 4.52)													
Within-substratum heterogeneit	y, LR-:	Tau <sup>2</sup> =(	0.00; 0	Chi <sup>2</sup> =0.0	08, df=1 (p=0.774); l <sup>2</sup> =0.	.0%													
Potoronoo standard, neuropath		. Tau –	0.00,	C/// =0.	01, 01-1 (p=0.942), 1=0	.0%													
no data	lology																		
RE subtotal					0.29 (0.20, 0.41)	3.07 (2.08, 4.52)													
Within-stratum heterogeneity, LR-	: Tau <sup>2</sup> =	=0.00; (	Chi <sup>2</sup> =0	.08, df=	=1 (p=0.774); I <sup>2</sup> =0.0%														
Within-Stratum neterogeneity, Err	. Tau	-0.00,		J.01, UN	-1 (p=0.342), 1 =0.078														
RE meta-analysis					0.29 (0.20, 0.41)	3.07 (2.08, 4.52)					-								
Overall heterogeneity, LR-: Tau <sup>2</sup> =0.0	00; Chi <sup>2</sup>	²=0.08,	df=1	(p=0.77	(4); 1²=0.0%			-	1	1	1	1	1	1		1	1		
Overall heterogeneity, LR+: Tau <sup>2</sup> =0.	00; Chi	i²=0.01	, df=1	(p=0.94	42); I²=0.0%		.01	.02	.05	.1	.2	.5	1	2	5	10	20	50	100
												Like	lihood	ratio					
							~	decrea of dise (positiv	sing prol ase, give /e or neg	bability en ative) re	esult				(pos	increa c itive or	ising pro f diseas negative	bability e, given e) result	$\rightarrow$

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Figure 77AD versus other dementias: p-tau/Amyloid Beta 1-42 – forest plot: sensitivity and specificity
#### 1 P.3.4.6 Total tau



Figure 78AD versus other dementias: Total tau – forest plot: likelihood ratios

2



- 3
- Figure 79AD versus other dementias: Total tau forest plot: sensitivity and specificity
- 4 P.3.5 AD versus VaD
- 5 P.3.5.1 99mTc-HMPAO SPECT



Figure 80AD versus VaD: 99mTc-HMPAO SPECT – forest plot: likelihood ratios



3

- Figure 81AD versus VaD: 99mTc-HMPAO SPECT forest plot: sensitivity and specificity
- 4 P.3.6 CJD versus non-CJD
- 5 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

Study	TP	FN	FP	TN	LR- (95%CI)	LR+ (95%CI)	_												
PRIMARY																			
Reference standard: clinica	l criteria																		
no data																			
no data	in diagn	OSIS																	
Reference standard: neurop	atholog	у																	
no data	-	-																	
SECONDARY																			
Reference standard: clinica	I criteria																		
no data																			
Reference standard: clinicia	ın diagn	osis																	
Bahl 2008	18	1	33	117	0.07 (0.01, 0.46)	4.31 (3.13, 5.93)									<u> </u>				
Beudry 1998	66	15	0	48	0.19 (0.12, 0.30)	79.48 (5.03, 1255.	21			-									
Burkhard 2001	2	0	12	86	0.19 (0.02, 2.40)	6.60 (3.20, 13.62	)												
Coulthart 2011	112	15	244	629	0.16 (0.10, 0.26)	3.16 (2.79, 3.57)	<i>,</i>				·			-	-				
Cuadrado-Corrales 2006	155	22	15	480	0.13 (0.09, 0.19)	28.90 (17.50, 47.7	1)				_								
Fourier 2017	71	6	29	162	0.09 (0.04, 0.20)	6.07 (4.32, 8.54)	<i>,</i>				_					_			
Kennev 2000	59	4	2	82	0.07 (0.03, 0.17)	39.33 (9.99, 154.9	2)	_			_							_	
Lemstra 2000	32	1	10	67	0.03 (0.01, 0.24)	7.47 (4.18, 13.35	) ´—												
Tagliapietra 2013	11	0	13	10	0.10 (0.01, 1.49)	1.70 (1.17, 2.47)	´ —												
Van Everbroeck 2003	52	0	15	183	0.01 (0.00, 0.16)	12.72 (7.88, 20.53	) —				-								
Zerr 1998	161	24	7	97	0.14 (0.10, 0.20)	12.93 (6.31, 26,50	ý								-				
Zerr 2000	497	114	34	358	0.20 (0.17, 0.24)	9.38 (6.79, 12.96	ý												
RE subtotal					0.14 (0.11, 0.18)	8.03 (4.65, 13.50	ś								-				
Within-substratum heteroge	neitv. LR-	-: Tau <sup>2</sup>	=0.07:	Chi²=21.	97. df=11 (p=0.025); I	<sup>2</sup> =49.9%	, 												
Within-substratum heteroge	neitv. LR	+: Tau	<sup>2</sup> =0.57:	Chi <sup>2</sup> =17	7.13. df=11 (p<0.001)	/ <sup>2</sup> =93.8%													
Reference standard: neuron	atholog	v			· · · · · · · · · · · · ·														
Chohan 2010	210	35	44	127	0.19 (0.14, 0.26)	3.33 (2.57, 4.32)								_	<u> </u>				
Foutz 2017	53	12	8	6	0.43 (0.20, 0.95)	1.43 (0.89, 2.28)							_						
Hamlin 2012	183	10	76	30	0.18 (0.09, 0.36)	1.32 (1.17, 1.50)					•	_	_	-					
Lattanzio 2017	298	61	118	585	0.20 (0.16, 0.26)	4.95 (4.17, 5.87)													
Rohan 2015	32	4	5	18	0.14 (0.05, 0.37)	4.09 (1.87, 8.96)			_			_							
RE subtotal					0.19 (0.16, 0.23)	2.71 (1.60, 4.80)					•			-					
Within-substratum heteroge	neitv. LR-	-: Tau <sup>2</sup>	=0.00:	Chi2=4.2	1. df=4 (p=0.378); l2=	5.1%													
Within-substratum heteroge	neitv. LR	+: Tau	<sup>2</sup> =0.58;	Chi <sup>2</sup> =16	6.20. df=4 (p<0.001);	l <sup>2</sup> =97.6%													
RE subtotal	,,		,		0.16 (0.13, 0.19)	5.44 (3.28, 8.78)				•						-			
Within-stratum heterogeneity.	LR-: Tau <sup>:</sup>	<sup>2</sup> =0.04:	Chi <sup>2</sup> =2	28.75. df	=16 (p=0.026); 1 <sup>2</sup> =44.3	3%					Ť								
Within-stratum heterogeneity,	LR+: Tau	1²=0.59	; Chi²=	451.23,	df=16 (p<0.001); l²=96	5.5%													
															_				
RE meta-analysis	-0.04.04		75 46	10 / 0	0.16 (0.13, 0.19)	5.44 (3.28, 8.78)													
Overall heterogeneity, LR-: Tall*	-0.04, Ch -0.50.0	11 = 20. 1 hi2=15	1 22 A	10 (p=0. = 16 (c-	0201, 1=44.3%				1		1			1			1		
overan neterogeneity, LR+: Tau	-0.09, 0	n-+9	1.23, UI	-10 (p<	0.001), 1-90.076		.01	.02	.05	.1	.2	.5	1	2	5	10	20	50	1
												Like	lihood	ratio					
								decrea	sing prol	bability						increa	sing prol	bability	
	← of disease, given											0	fdisease	, given	$\rightarrow$				
	(positive or negative) result											(pos	itive or	negative	) result				

## Figure 84CJD versus non-CJD: CSF 14-3-3 ELISA – forest plot: sensitivity and specificity







Figure 85CJD versus non-CJD: CSF 14-3-3 immunoblotting – forest plot: likelihood ratios

1

Study	TP	FN	FP	TN	Sens. (95%CI)	Spec. (95%/CI)						_						
PRIMARY																		
Reference standard: clinical (	criteria																	
no data																		
Reference standard: clinician	diagn	osis																
no data																		
Reference standard: neuropa	thology	1																
no data																		
SECONDA RY																		
Reference standard: clinical (	criteria																	
no data																		
Reference standard: clinician	diagn	osis																
Bahl 2008	18	1	33	117	0.95 (0.71, 0.99)	0.78 (0.71, 0.84)						_		_				
Beudry 1998	66	15	0	48	0.81 (0.71, 0.88)	0.99 (0.86, 1.00)								_				
Burkhard 2001	2	0	12	86	0.83 (0.19, 0.99)	0.87 (0.79, 0.93)						-	-   -					
Coul thart 2011	112	15	244	629	0.88 (0.81, 0.93)	0.72 (0.69, 0.75)					-			-				
Cuadrado-Corrales 2006	155	22	15	480	0.88 (0.82, 0.92)	0.97 (0.95, 0.98)					-		-					
Fourier 2017	71	6	29	162	0.92 (0.84, 0.96)	0.85 (0.79, 0.89)					_	-		_				
Kenney 2000	59	4	2	82	0.94 (0.84, 0.98)	0.98 (0.91, 0.99)					_	-	-					
Lemstra 2000	32	1	10	67	0.97 (0.81, 1.00)	0.87 (0.78, 0.93)					_	-						
Tagliapietra 2013	11	0	13	10	0.96 (0.58, 1.00)	0.44 (0.26, 0.64)				_		-				•	_	
Van Everbroeck 2003	52	0	15	183	0.99 (0.87, 1.00)	0.92 (0.88, 0.95)					_	-	-	-				
Zerr 1998	161	24	7	97	0.87 (0.81, 0.91)	0.93 (0.87, 0.97)								-				
Zerr 2000	497	114	34	358	0.81 (0.78, 0.84)	0.91 (0.88, 0.94)					-		-	-				
RE subtotal					0.88 (0.84, 0.91)	0.87 (0.81, 0.94)					•		·   ◄	•				
Within-substratum heterogene	eity, sen	s: Tau	<sup>2</sup> =0.16	; Chi²=2	29.37, df=11 (p=0.002)	); /*=62.5%												
Within-substratum heterogene	eity, spe	c: Tau	r²=1.10	; Chi?=2	247.09, df=11 (p<0.00	1); 1=95.5%												
Reference standard: neuropa	thology	1																
Chohan 2010	210	35	44	127	0.86 (0.81, 0.90)	0.74 (0.67, 0.80)					_			-	-			
Foutz 2017	53	12	8	6	0.82 (0.70, 0.89)	0.43 (0.21, 0.68)					-					•	_	
Hamlin 2012	183	10	76	30	0.95 (0.91, 0.97)	0.28 (0.21, 0.38)					-	-				_	-	
Lattanzio 2017	298	61	118	585	0.83 (0.79, 0.87)	0.83 (0.80, 0.86)								-				
Rohan 2015	32	4	5	18	0.89 (0.74, 0.96)	0.78 (0.57, 0.91)						-	· · ·					
RE subtotal					0.88 (0.82, 0.92)	0.66 (0.43, 0.83)								-				
Within-substratum heterogene	eity, sen	s: Tau	r <sup>2</sup> =0.19	; Chi²= 1	16.77, df=4 (p=0.002);	l²=76.1%												
Within-substratum heterogene	eity, spe	c: Tau	r <sup>2</sup> =1.72	; Chi²= 1	157.78, df=4 (p<0.001)	); 1²=97.5%								-				
RE subtota l					0.87 (0.84, 0.90)	0.83 (0.73, 0.90)					•							
Within-stratum heterogeneity, se	ens: Tau	r <sup>2</sup> =0.13	3; Chi≈	=45.93,	df=16 (p<0.001); I=6	5.2%												
Within-stratum heterogeneity, sp	ec: Tal	12=1.16	6; Chi³	=463.81	, df=16 (p<0.001); l²=	96.6%												
														-				
RE meta-a nalysis					0.87 (0.84, 0.90)	0.83 (0.73, 0.90)					•							
Overall heterogeneity, sens: Tau*=	0.04; C	hr=28	.75, df	= 16 (p=	0.026); 1=44.3%			0.00		0.00			+	0.00	0.00	0.40	0.00	
Overall heterogeneity, spec: Tau*=	0.59; C	nr=45	1.23, 0	n=16 (p	<0.001); 1=96.5%		0.00	0.20	0.40	0.00	0.80	1.00	1.00	0.80	0.00	0.40	0.20	0.00
									C						C			
									sens	uvity					spec	пску		

Figure 86CJD versus non-CJD: CSF 14-3-3 immunoblotting – forest plot: sensitivity and specificity

#### 1 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

#### 1 P.3.6.4 MRI



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5 Figure 89CJD versus non-CJD: EEG – forest plot: sensitivity and specificity

#### 6 P.3.6.5 MRI

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#### Figure 90CJD versus non-CJD: MRI – forest plot: likelihood ratios



Figure 91CJD versus non-CJD: MRI – forest plot: sensitivity and specificity

#### 1 P.3.6.6 Neuron-specific enolase



2 3 4

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

#### 3 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

#### 1 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

#### 1 P.3.6.9 S100B, 2.5ng/ml



Figure 98CJD versus non-CJD: S100B, 2.5ng/ml – forest plot: likelihood ratios



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### Figure 99CJD versus non-CJD: S100B, 2.5ng/ml – forest plot: sensitivity and specificity

4 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

#### 1 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

Dementia Appendix P: Diagnosis evidence tables & GRADE

#### 1 P.3.7 DLB versus non-DLB

#### 2 P.3.7.1 123I-FP-CIT SPECT







Figure 105 DLB versus non-DLB: 123I-FP-CIT SPECT – forest plot: sensitivity and specificity

#### 1 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

#### 1 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

#### 1 P.3.8 DLB versus other dementias

#### 2 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
- 4 P.3.9 FTD versus AD
- 5 P.3.9.1 99mTc-HMPAO SPECT

6

Study	TP	FN	FP	TN	LR- (95%CI)	LR+ (95%CI)	_												
SINGLE CAMERA																			
Reference standard: clinical of	riteria																		
no data																			
Reference standard: clinician	diagno	sis																	
Launes 1991	2	3	1	35	0.62 (0.30, 1.27)	14.40 (1.58, 131.3	6)				-						-		
Talbot 1998	37	43	5	127	0.56 (0.45, 0.69)	12.21 (5.01, 29.78	5)									-			
Velakoulis 1997	5	4	0	9	0.47 (0.24, 0.95)	11.00 (0.70, 173.6	6)												
RE subtotal					0.56 (0.46, 0.67)	12.36 (5.60, 27.30	)					- 🔶			-				
Within-substratum heterogene	ity, LR-:	Tau <sup>2</sup>	=0.00; (	Chi²=0.2	8, df=2 (p=0.867); I <sup>2</sup> =0	0.0%													
Within-substratum heterogene	ity, LR+	: Tau	²=0.00;	Chi2=0.0	03, df=2 (p=0.987); I <sup>2</sup> =	0.0%													
Reference standard: neuropa	thology																		
Read 1995	7	0	0	13	0.06 (0.00, 0.95)	26.25 (1.72, 401.5	68)												
RE subtotal					0.55 (0.45, 0.66)	13.11 (6.13, 28.05	5)					- 🔶			-				
Within-stratum heterogeneity, LF	R-: Tau²	=0.00;	Chi <sup>2</sup> =2	2.73, df=	3 (p=0.435); I <sup>2</sup> =0.0%														
Within-stratum heterogeneity, LF	R+: Tau	<sup>2</sup> =0.00	; Chi <sup>2</sup> =	0.30, df=	=3 (p=0.961); I²=0.0%														
Boforonco standard: clinical	ritoria																		
no data	interna																		
Poforonco standard: clinician	diagno	eie																	
Routoleau Bretonniere 2012	alagine	313	1	17	0.20 (0.11 0.76)	13 00 /1 88 00 00	n						_						
Bolucoleau-Bieloniniere 2012 Reference standard: nourona	o			17	0.29 (0.11, 0.70)	13.09 (1.00, 90.98	"												
Rollin-Sillaire 2012	a	3	0	23	0.27 (0.11, 0.67)	35 08 (2 21 555 6	(3)			_									
RE subtotal	0	0	Ū	20	0.28 (0.15, 0.54)	18 12 (3 71 88 60	N)				-								_
Within stratum beterogeneity 1	- Tau2	-0.00-	Chi2-C	01 df-	1 (n=0.042): 12=0.0%	10.12 (0.71, 00.00	"										_		
Within-stratum heterogeneity, Li	< rau · ⊃⊥· Toui	-0.00, 2-0.00	· Chi2-	033 df-	-1 (p=0.342), 1 =0.078														
within-stratum neterogeneity, Li	( <i>i. iau</i>	-0.00	, 011 -	0.33, ui-	-1 (p=0.301), 1 =0.078														
RE meta-analysis					0.44 (0.30, 0.59)	13.50 (6.77, 24.20	)				-								
Overall heterogeneity, LR-: Tau <sup>2</sup> =0	.03; Chi	<sup>2</sup> =6.40	0, df=5	(p=0.26	9); I²=21.9%					_				-					
Overall heterogeneity, LR+: Tau2=	0.00; Ch	i²=0.7	'5, df=5	5 (p=0.98	30); 1²=0.0%		01	02	05	1	2	5	1	2	5	10	20	50	100
Between-stratum heterogeneity, LH	R-: Chi²=	3.67,	df=1 (p	=0.055),	; 12=72.7%		.01	.02	.05	. 1	.2	.5		2	5	10	20	50	100
Between-stratum heterogeneity, LH	R+: Chi <sup>2</sup>	=0.13,	df=1 (	p=0.718,	); 1²=0.0%							Like	lihood	ratio					
							decreasing probability										sing prot	ability	
							← of disease, given of disea										f disease	, given	$\rightarrow$
							(positive or negative) result (positive or negative) result												






# 1 P.3.10 FTD versus non-FTD

#### 2 P.3.10.1 99mTc-HMPAO SPECT

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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

#### 1 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

#### 1 P.3.10.3 MRI



Figure 118 FTD versus non-FTD: MRI – forest plot: likelihood ratios

Study	TP	FN	FP	TN	Sens	(95%CI)		Spec. (95%CI)												
PRIMARY									— F											
Reference standard: clin	ical criteria																			
no data																				
Reference standard: clin	ician diagn	osis																		
no data																				
Reference standard: neu	ro path olog	у																		
no data																				
SECONDARY																				
Reference standard: clin	ical criteria																			
no data																				
Reference standard: clin	ician diagn	osis																		
Koikkalainen 2016	46	48	66	346	0.50	(0.40, 0.	60)	0.84 (0.80, 0.8	87)		_	<u> </u>				-				
Mendez 2007	40	23	21	50	0.63	(0.51, 0.	74)	0.70 (0.59, 0.8	80)			-	_			_				
RE subtotal					0.56	(0.43, 0.	69)	0.78 (0.63, 0.8	89)		-									
Within-substratum hetero	ogeneity, ser	ns: Tau	1 <sup>2</sup> =0.10;	ChiP=2	2.74, df=	1 (p=0.0)	98); / º=(	63.4%				-								
Within-substratum hetero	geneity, spe	ec: Tau	1 <sup>2</sup> =0.27;	Chi <sup>2</sup> =7	7.27, df=	1 (p=0.00	07); / ==	86.2%												
Reference standard: neu	ropatholog	у																		
no data		-																		
RE subtotal					0.56	(0.43, 0.	69)	0.78 (0.63, 0.8	89)		-									
Within-stratum heterogenei	ty, sens: Ta	u <sup>2</sup> =0.1	0; Chi <sup>2</sup> =	2.74, 0	#=1 (p=	0.098); /*	=63.4%		·											
Within-stratum heterogenei	ty, spec: Ta	u²=0.2	7; ChiP=	7.27, a	#=1 (p=	0.007); /*	=86.2%													
RE meta-analysis					0.56	(0.43. 0.	69)	0.78 (0.63. 0.8	89)		-									
Overall heterogeneity, sens:	Tau <sup>2</sup> =0.00; 0	Chi <sup>2</sup> =0.	43. df=	1 (p=0.8	513); I <sup>2</sup> =	0.0%	- C		· _			_		_						_
Overall heterogeneity, spec:	Tau²=0.04; (	Chi²=2	11, df=	1 (p=0.	146); 1*=	52.7%			0.00	0.20	0.40	0.60	0.80	1.00	1.00	0.80	0.60	0.40	0.20	0.00
												Specificity								

2 Figure 119 FTD versus non-FTD: MRI – forest plot: sensitivity and specificity

# 3 P.3.11 FTD versus other dementias

# 4 P.3.11.1 FDG-PET

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Figure 120 FTD versus other dementias: FDG-PET – forest plot: likelihood ratios





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- Figure 122 FTD versus other dementias: FDG-PET – forest plot: sensitivity and specificity
- 4 P.3.12 FTD versus VaD
- 5 P.3.12.1 99mTc-HMPAO SPECT







Figure 124 FTD versus VaD: 99mTc-HMPAO SPECT – forest plot: sensitivity and specificity

Dementia Appendix P: Diagnosis evidence tables & GRADE

# 1 P.3.13 VaD versus AD

#### 2 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

1 2

Dementia Appendix P: Diagnosis evidence tables & GRADE

### 1 P.3.14 VaD versus non-VaD

#### 2 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

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