Appendix P: Diagnosis

Dementia diagnosis

Review questions

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

P.1 Evidence tables

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

P.1.1 A

Abdel-Aziz K, Larne 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	on-dementia (including MCI)
Index Test: MMSE (<23)

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Results	True positives:	13	False negatives:	9	False positives:	19	True negatives:	109
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Serious (Subgroup comparison to 6CI		sted patients were te	ested with MMSE	e as well; MMSE cut o	ff was not p	re-specified as chose	en for
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: 6-item Co 6-item Cognitive Impa		•	Т) (>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							
Alexander SK, Rittm				alidation of the	new consensus crite	eria for the	diagnosis of cortic	obasal
degeneration. J Neu			4; 85: 923–927.					
Study type	Retrospective coho	ort						
Country	UK							

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Setting	Regional specialist	clinics for D	isorders of Moveme	ent and Cogniti	on and Early-Onset Der	mentia at A	Addenbrooke's Hospita	al.			
Inclusion criteria	Patients attending	the clinics b	etween 1990 and 20	013 for whom o	letailed clinical and path	nological in	formation was availab	le.			
Exclusion criteria	logopenic variant p progranulin levels;	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 yea	ars (SD 8.4)									
Presentation	Suspected CBD										
Reference standard	Neuropathology, details not specified.										
CBD (probable or p	ossible) versus CBI) mimic (co	rticobasal syndroi	me, but not CE	BD pathology)						
Index Test: CBD co Armstrong et al (201	onsensus criteria 3) corticobasal degen	eration (CB	D) consensus criter	ia							
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. Roda	I I. Espana	A. Ros R. Loez Sei	ndon JL. Garc	ia Galloway E et al. Or	n the diag	nosis of CADASII	ournal			
	e 2009; 17: 787-794.		1, 1, 100 1, 2002 001	idon oz, oaro	ia Canonay E of all Of	. the diag	TOOLS OF CADAGIE. O	Jarriar			
Study type	Prospective cohort										
Country	Spain										
Country	- P										

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Ampuero I, Alegre-A			A, Ros R, Loez Ser	ndon JL, Garcia	a Galloway E et al. Or	the diagno	osis of CADASIL. J	ournal of
Inclusion criteria	People with suspec	cted CADAS	SIL referred to the Ba	anco de Tejidos	para Invertigaciones N	leurologicas	3	
Exclusion criteria	Not stated							
Sex	Not stated							
Age	Mean age 53.4 yea	ars (SD 13.1)					
Presentation	Suspected CADAS	SIL						
Reference standard		dementia o			urrent strokes or transi compatible with CADA			
CADASIL versus CA	ADASIL-like syndror	mes						
Index Test: Skin bio	psy							
Skin biopsy, immunos	staining pattern typica	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							

	ntnon L,Davidsson P,vanmechelen E,van-derstichele H,winblad B,et al. Evaluation of CSF-tau and CSF-Abeta 42 as diagnostic neimer disease in clinical practice. ArchNeurol 2001; 58: 373–9.
Study type	Prospective cohort
Country	Sweden
Setting	specialist hospital clinic

Inclusion criteria People referred from primary care or community health service with cognitive impairment

Exclusion criteria not stated

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Sex	45.6% male							
Age	73.4 years (SD 7.1))						
Presentation	Suspected dementia							
Reference standard	DSM-IV for dementia diagnoses, probable and possible AD based on NINCDS-ADRDA criteria, VaD according to the National Institute of Neurological Disorders and Stroke-Association Internationale pour la Recherche et l'Enseignementen Neuroscience criteria, MCI according to the Petersen (1997) criteria, LBD according to consensus criteria (McKeith 1999). Other diagnoses usin the DSM-IV and ICD-10.							
AD disease with var	ying certainty (prob	able and p	ossible AD pooled) verus non- Al	O (VaD, LBD, MCI and	l non-deme	ntia groups pooled).
Index Test: Amyloid	Beta 1-42							
The Amyloid/P- Tau r				•	- ′			
Results	True positives:	106	False negatives:	57	False positives:	32	True negatives:	43
Additional comme nts	Data on people dia	gnosed with	other neurological	conditions exclu	ded from analysis as r	not in access	sible 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							
AD disease with var	ying certainty (prob	able and p	ossible AD pooled) versus VaD				
Index Test: Amyloid The Amyloid/P- Tau r		sing 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	Data on people dia	gnosed with	other neurological	conditions exclu	ded from analysis as r	not in access	sible format. N=3 peo	pple.
Risk of bias	Patient	Low	Index test:	Low	Reference	Low	Flow and	Low

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	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	pable and p	ossible AD pooled) versus LBD				
Index Test: Amyloid	l 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:	3	True negatives:	6
Additional comme nts	Data on people dia	gnosed with	other neurological	conditions exclu	ded from analysis as r	ot in acces	sible 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							
Probable AD verus	non- AD (VaD, LBD,	MCI and n	on-dementia group	s pooled).				
Index Test: Amyloid The Amyloid/P- Tau r		using 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 r	ot in acces	sible format. N=3 peo	pple.
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	Low

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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 The Amyloid/P- Tau r		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	gnosed with	other neurological	conditions exclu	ded from analysis as r	not in acces	sible 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							
Probable AD versus	LBD							
Index Test: Amyloid The Amyloid/P- Tau r		using the for	mula Amyloid Beta	42/(240 + [1.18×	·T-tau])			
Results	True positives:		False negatives:		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 acces	sible 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		
	selection:				standard:			
Overall indirectness	Not serious							
Possible AD verus r	non- AD (VaD, LBD,	MCI and no	on-dementia group	s pooled).				
Index Test: Amyloid The Amyloid/P- Tau i		ising the for	mula Amyloid Beta	42/(240 + [1.18×	T-taul)			
Results	True positives:		False negatives:	· -	False positives:	32	True negatives:	43
Additional comme nts	Data on people dia	gnosed with	other neurological	conditions exclu	ded from analysis as r	not in acces	sible 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							
Possible versus Val	D							
Index Test: Amyloid The Amyloid/P- Tau i		sing the for	mula Amyloid Beta	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 exclu	ded from analysis as r	not in acces	sible 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	Laur	Index test:	Low	Reference	Low		

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Overall	selection: Not serious				standard:			
indirectness								
Possible AD versus	LBD							
Index Test: Amyloid The Amyloid/P- Tau		ısing the for	mula Amyloid Beta	42/(240 + [1.18×	T-tau])			
Results	True positives:	7	False negatives:	51	False positives:	3	True negatives:	6
Additional comme	Data on people dia	gnosed with	other neurological	conditions exclu	ded from analysis as r	not in acces	sible 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	Not serious							

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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Presentation	Suspected dementia								
Reference standard	Dementia was diagnosed using the DSM-IV criteria								
Dementia versus no	t dementia								
Index Test: 10-point 10-point cognitive scr off ≤ 5.			•	eener (Braziliar	n Portuguese language). Points a	dded for education eff	ects. C	
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	l thresholds	were calculated and	people with me	oderate to severe dem	entia were	excluded from the stu	dy.)	
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low			
Overall indirectness	Serious (Included p	oatients wer	e selected to be ≥ 60) years old and	had on average only 4	.7 years o	f schooling)		
Index Test: 10-point 10-point cognitive scr off ≤ 6.	eener (10-CS), a mo	dified version	on of the six-item scr	,	n Portuguese language	,		ects. C	
Results	True positives:	86	False negatives:	20	False positives:	20	True negatives:	104	
Additional comme nts									
iitə	Patient	High	Index test:	High	Reference standard:	Low	Flow and timing:	Low	
	selection:	ŭ			Stanuaru.		9.		
Risk of bias	selection:	I thresholds	were calculated and	I people with me	oderate to severe dem	entia were		dy.)	
Risk of bias Overall risk of bias Indirectness	selection:		were calculated and Index test:	•		entia were Low		ldy.)	

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indirectness	016; 31: 4-12.							
Index Test: 10-point	Cognitive Screene	r (10-CS) (≤	7)					
•		` ' '	•	reener (Brazilian	Portuguese language	e). Points ad	ded for education eff	ects. Cu
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	thresholds	were calculated and	d people with mo	derate to severe dem	entia were e	xcluded from the stu	dy.)
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low		
Overall indirectness	Serious (Included p	oatients were	e selected to be ≥ 6	0 years old and	nad on average only 4	.7 years of s	schooling)	
Index Test: 10-point	_	• • • • • • • • • • • • • • • • • • • •	•	reener (Brazilian	Portuguese language	e). Points add	ded for education eff	ects. Cu
off ≤ 8.	True positives:	103	False negatives:	3	False positives:	74	True negatives:	50
off ≤ 8. Results Additional comme	True positives:	103		3	False positives:	74	True negatives:	50
off ≤ 8. Results Additional comme nts	True positives: Patient selection:			3 High	False positives: Reference standard:	74 Low	True negatives: Flow and timing:	50 Low
off ≤ 8. Results Additional comme nts Risk of bias	Patient selection:	High	negatives:	High	Reference	Low	Flow and timing:	Low
off ≤ 8. Results Additional comme nts Risk of bias Overall risk of bias Indirectness	Patient selection:	High I thresholds	negatives:	High	Reference standard:	Low	Flow and timing:	Low

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Arslan E, Ekmekcioglu O, Gortan FA, Engin Akcan ZF, Erkan ME, Emlu HM, Hala M, Cermik TF, Sonmezoglu K. The value of FDG-PET/CT by using 3-dimensional stereotactic surface projection software analysis in the differential diagnosis of dementia. Turkish Journal of Medical Sciences, 2016; 45: 1149-1158.

Study type	Retrospective cohort
Country	Turkey
Setting	Not stated
Inclusion criteria	People with dementia who had been subjected to PET imaging as part of their dementia diagnosis.
Exclusion criteria	Not stated
Sex	29.0% male
Age	Mean age 61.4 years (8.6)
Presentation	Dementia subtype diagnosis
Reference standard	Probable diagnosis of dementia based on criteria developed by NINCDS-ADRDA and/or frontotemporal lobar degeneration. Data from neuropsychological tests were also taken into consideration.

AD versus non-AD dementias

Index Test: FDG-PET

18F-FDG PET attenuation-corrected PET/CT (Siemens Biograph LSO HI-RES PET-CT, USA) images were acquired. After iterative reconstruction, 0.3-cm-thick section images from both CT and PET were obtained in the transaxial, coronal, and sagittal planes. Visual assessment of PET images was performed by evaluating the changes in FDG uptake in both the cortical and subcortical areas. The axial sectional images of PET were also evaluated with 3D-SSP software (NEUROSTAT). The images were imported into a template with the Talairach coordinates in a standard format and were compared with a normal database of matched ages.

Results	True positives:	12	False negatives:	5	False positives:	14	True negatives:	17
Risk of bias	Patient selection:	Unclear	Index test:	Unclear	Reference standard:	Unclear	Flow and timing:	Low
Overall risk of bias	avoided; the index	test was into	erpreted without kno	wledge of the re	ble patients was enrol ference standard and e index test results.)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

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Arslan E, Ekmekcioglu O, Gortan FA, Engin Akcan ZF, Erkan ME, Emlu HM, Hala M, Cermik TF, Sonmezoglu K. The value of FDG-PET/CT by using 3-dimensional stereotactic surface projection software analysis in the differential diagnosis of dementia. Turkish Journal of Medical Sciences, 2016; 45: 1149-1158.

FTD versus non-FTD dementias

Index Test: FDG-PET

18F-FDG PET attenuation-corrected PET/CT (Siemens Biograph LSO HI-RES PET-CT, USA) images were acquired. After iterative reconstruction, 0.3-cm-thick section images from both CT and PET were obtained in the transaxial, coronal, and sagittal planes. Visual assessment of PET images was performed by evaluating the changes in FDG uptake in both the cortical and subcortical areas. The axial sectional images of PET were also evaluated with 3D-SSP software (NEUROSTAT). The images were imported into a template with the Talairach coordinates in a standard format and were compared with a normal database of matched ages.

Results	True positives:	8	False negatives:	9	False positives:	11	True negatives:	20
Risk of bias	Patient selection:	Unclear	Index test:	Unclear	Reference standard:	Unclear	Flow and timing:	Low
Overall risk of bias	avoided; the index	test was inte	erpreted without kno	wledge of the re	ble patients was enrol ference standard and le index test results.)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

P.1.2 B

Bachetta J-P, Kovari E, Merlo M, Canuto A, Herrman FR, Bouras C, Gold G, Hof PR and Giannakopoulos P. Validation of the clinical criteria for possible vascular dementia in the oldest-old.

Study type	Retrospective cohort
Country	Switzerland
Setting	Department of Geriatrics and Psychiatry at the University of Geneva School of Medicine
Inclusion criteria	Diagnosis of dementia and subsequent autopsy examination; > 90 years old; evaluated within 6 months of death (including complete neuropsychological, neurology and mental status assessments).
Exclusion criteria	Patients with major neuropsychiatric illness, alcoholism or Parkinson's disease.
Sex	19.1% male

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Age	Mean age 94.6 yea	rs (SD 2.8)						
Presentation	Dementia	(02 2.0)						
Reference standard	macroscopic and m	nicroscopic v		Cases that s	criteria. VaD was assess atisfied both neuropatholo			
VaD versus AD ar	d mixed dementia (Al	D plus VaD						
Index Test: NINDS NINDS-AIREN crite								
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 bia	s Not serious							
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low		
Overall indirectness	Serious (Participan	ts were sele	ected to be >90 year	rs old)				
Index Test: ADDT ADDTC criteria (Sta	C criteria ate of California Alzheir	mer's Diseas	se Diagnostic and T	reatment Cei	ntres criteria)			
Results	True positives:	21	False negatives:	15	False positives:	19	True negatives:	55
Additional comme	,							
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bia	s Not serious							
Indirectness	Patient	High	Index test:	Low	Reference	Low		
	selection:	o .			standard:			

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indirectness								
Index Test: Hachinsl HIS, Hachinski ischen		• •						
Results	True positives:	20	False negatives:	16	False positives:	25	True negatives:	49
Additional comme								
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	rs old)				

	NH, Falkenhorst G, Laursen H, Hogenhaven H, Molbak K, Jespersgaard C, Hougs L, Waldemar G, Johannsen P, diagnostic efficiency of biomarkers in sporadic Creutzfeldt-Jakob disease compared to Alzheimer's disease. Neurobiol I–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**

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Index Test: Total	Tau							
total tau (500pg/ml	l)							
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 bia	S Very serious (Exclu	usion of pos	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/	total tau							
CSF P-tau/total tau	u of above 0.04 is CJD _I	positive						
Results	True positives:	18	False negatives:	3	False positives:	12	True negatives:	104
Additional commonts	e							
Risk of bias	Patient selection:	High	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bia	Very serious (Exclu	usion of pos	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: Neuro	on-specific enolase							
CSF neuron-specif	fic enolase (NSE) using	35ng/ml cu	t off					
Results	True positives:	16	False negatives:	4	False positives:	15	True negatives:	132

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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)			
ndirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall Indirectness	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							
Rastide I De Breuc	ker S. Van den Berg	ne M. Fervi	P Penersack T Rig	or IC The Adde	nbrooke's Cognitive	Fyaminat	ion Revised Is as Ff	factive
					ogn Disord 2012; 34:		ion itevised is as Li	1001116
Study type	Prospective cohort							
Country	Belgium							

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Inclusion criteria	People examined a had an MMSE scor			ovember 2007 a	nd October 2011 that h	nad been fo	ollowed at least 6 mor	nths and		
Exclusion criteria					umas; people with pos avernoma; people beir			erosis,		
Sex	0.4% male									
Age	Mean age 79.0 yea	ars (SD 13.0)							
Presentation	Suspected dement	Suspected dementia								
Reference standard	was based on the I Disorders Associat	National Instion criteria.	itute of Neurologica The patients who we	I and Communicere diagnosed a	diagnosis of dementia cative Disorders, Strok s having FTLD fulfilled of DLB was based on t	e-Alzheime the clinica	er's Disease and Rela I criteria of the Work (ted Group or		
Dementia versus n	ot dementia (includi	ng MCI)								
	prooke's Cognitive Enitive Examination ReTrue positives:	vised (ACE-	R), French version, False	83/100	False positives:	60	True negatives:	132		
Addenbrooke's Cogr Results	nitive Examination Re	vised (ACE- 118	R), French version,	83/100 10	False positives: Reference standard:	60 Low	True negatives: Flow and timing:	132 Low		
Addenbrooke's Cogr Results Risk of bias	True positives: Patient selection:	vised (ACE- 118 Low	R), French version, False negatives: Index test:	83/100 10	Reference		Flow and			
Addenbrooke's Cogr	True positives: Patient selection:	vised (ACE- 118 Low I test cut-offs	R), French version, False negatives: Index test:	83/100 10	Reference		Flow and			
Addenbrooke's Cogr Results Risk of bias Overall risk of bias	True positives: Patient selection: Serious (Optimised Patient	vised (ACE- 118 Low I test cut-offs	R), French version, False negatives: Index test:	83/100 10 High	Reference standard:	Low	Flow and			
Addenbrooke's Cogr Results Risk of bias Overall risk of bias Indirectness	Patient selection: Serious (Optimised Patient selection: Not serious	vised (ACE- 118 Low I test cut-offs	R), French version, False negatives: Index test:	83/100 10 High	Reference standard:	Low	Flow and			

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Country

Setting

Sex

Inclusion criteria

Exclusion criteria

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							
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	Not serious							

Germany

not stated

51.7% male

University of Ulm memory clinic.

People seeking first time advice on subjective memory complaints at the outpatient clinic

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Age	mean age 64.7 yea	ars (SD 7.5)						
Presentation	subjective memory	complaints						
Reference standard	disorder according	to DSM-IV o I, clinical, ra	criteria. Subjects we diological, and labor	re considered a	according to the criter s healthy controls (HC ons were normal and i) only when	findings on extensive	e .
Dementia versus no	dementia							
Index Test: Clock D								
Clock Drawing Test,		_			· ,			
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			re-specified thresho d independently of e		veen tests was unclea	and it was	unclear whether the	index and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Clock D			• • • • • • • • • • • • • • • • • • • •	-10004-11	0/0 (5.4)			
Clock Drawing Test, (·	J			, ,	00	T	4.40
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			re-specified threshod independently of e		veen tests was unclea	and it was	unclear whether the	index and
Indirectness	Patient		Index test:		Reference	Low		

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Beinhoff U, Hilbert V Cognitive Disorders			MW. Screening for	cognitive imp	airment: a triage for o	out patient	care. Dementia and	Geriatr
	selection:				standard:			
Overall indirectness	Not serious							
Index Test: Clock Di Clock Drawing Test, (• • • • • • • • • • • • • • • • • • • •	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			re-specified thresho d independently of e		veen tests was unclea	r and it was	unclear whether the	index a
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Letter So LST (letter sorting tes	•		etter word forwards, l	oackwards and i	n alphabetical order. C	One point pe	er 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			re-specified threshod independently of e		veen tests was unclea	r and it was	unclear whether the	index a
Indirectness	Patient	Low	Index test:	Low	Reference	Low		
	selection:				standard:			

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Beinhoff U, Hilbert V Cognitive Disorders			MW. Screening for	cognitive impa	airment: a triage for c	out patient o	care. Dementia and	Geriatric
indirectness								
Index Test: Letter So LST (letter sorting tes	•	•	tter word forwards	hackwards and i	n alphabetical order. ()ne noint ne	r correct answer	
Results	True positives:		False negatives:		False positives:		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			re-specified thresho d independently of e		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 So LST (letter sorting tes	•	•	etter word forwards,	backwards and i	n alphabetical order. C	one point pe	r correct answer.	
Results	True positives:		False negatives:		False positives:		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			re-specified thresho d independently of e		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: Orientati	on, OR (<8)							

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Results	True positives:	43	False	23	False positives:	16	True negatives:	150
			negatives:					
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	,		re-specified threshord independently of e		een 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: Orientat	ion, OR (<7)							
OR (Orientation), <7.	Eight questions abou	ut time, plac	e and situation withi	in about a minute	e. Score out of 8. Uses	s a subsection	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			re-specified threshord independently of e		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	n, MIS (<8)						
MIS (Memory Impairn	nent Screen), 8. Test	ts delaved f	ree and cued recall of	of 4 items. Score	out of 12.			
(//	,						

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			negatives:					
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias			re-specified thresho d independently of e		veen tests was unclea	r and it was	unclear whether the	index an
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
	/ Impairment Screen ment Screen), 7. Test		ree and cued recall o	of 4 items. Score	e out of 12.			
Results	True positives:		False		False positives:	78	True negatives:	88
			negatives:		i alloo pooliii ool	, 0	True negativee.	00
			negatives:		T who poolin oo.		True negativee.	00
Additional comme nts Risk of bias	Patient selection:	Low	negatives:		Reference standard:	Low	Flow and timing:	Low
nts	selection: Serious (Use of mu	ıltiple non-p	Index test:	High lds; interval betw	Reference	Low	Flow and timing:	Low
nts Risk of bias	selection: Serious (Use of mu	ultiple non-p re interprete	Index test:	High lds; interval betweach other.)	Reference standard:	Low	Flow and timing:	Low
nts Risk of bias Overall risk of bias	selection: Serious (Use of mureference tests were patient)	ultiple non-p re interprete	Index test: re-specified thresho d independently of e	High lds; interval betweach other.)	Reference standard: ween tests was unclear	Low r and it was	Flow and timing:	Low
nts Risk of bias Overall risk of bias Indirectness Overall indirectness Index Test: Memory	selection: Serious (Use of mureference tests were patient selection:	ultiple non-pre interprete Low a, MIS (<6)	Index test: re-specified thresho d independently of e Index test:	High lds; interval betweach other.) Low	Reference standard: veen tests was unclear Reference standard:	Low r and it was	Flow and timing:	Low

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nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias			re-specified threshol d independently of e		veen tests was unclea	r and it was	unclear whether the	index an
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Memory MIS (Memory Impairr			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			re-specified threshold independently of e		veen tests was unclea	r and it was	unclear whether the	index an
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Boston Boston Naming Test,	<u> </u>	•	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

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	selection:				standard:		timing:	
Overall risk of bias			re-specified thresho d independently of e		veen tests was unclea	and it wa	s unclear whether the	index and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Boston	Naming Test, BNT (<14)						
Boston Naming Test	, 14. Tests ability to 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			re-specified thresho d independently of e		veen tests was unclea	and it wa	s unclear whether the	index and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
	Naming Test, BNT (, 13. Tests ability to n		drawings. Score ou	t of 15.				
Results	True positives:	26	False negatives:	40	False positives:	11	True negatives:	155
Additional comme								
IIIS								

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	reference tests wer	e interprete	d independently of e	each other.)				
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall ndirectness	Not serious							
	category fluency (an ncy, <24. Tests ability			names in given	time. In this case the o	category w	as animals and time o	luration
Results	True positives:	65	False negatives:	1	False positives:	115	True negatives:	51
Additional comme								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	`		re-specified threshod independently of e		veen tests was unclea	r and it wa	s unclear whether the	index ar
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
	category fluency (an ncy, <23. Tests ability		• , ,	names in given	time. In this case the	category w	as animals and time d	uration
Results	True positives:	64	False negatives:	2	False positives:	102	True negatives:	64
Additional comme								
nts								

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	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							
Index Test: Verbal	category fluency (an	imal namin	g), VF (<22)					
Verbal category fluerwas 60 secs.	ncy, <22. Tests ability	y to generate	e as many category	names in given	time. In this case the	category w	as animals and time d	luration
Results	True positives:	63	False negatives:	3	False positives:	90	True negatives:	76
Additional comme								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	`		re-specified thresho d independently of e		veen tests was unclea	r and it wa	s unclear whether the	index a
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
ndex Test: Verbal	category fluency (an	imal namin	g), VF (<21)					
Verbal category flue was 60 secs.	ncy, <21. Tests ability	y to generate	e as many category	names in given	time. In this case the	category w	as animals and time d	luration
Results	True positives:	62	False negatives:	4	False positives:	79	True negatives:	87
Additional comme								
Risk of bias	Patient	Low	Index test:	High	Reference	Low	Flow and	Low

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	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							
	category fluency (anncy, <20. Tests ability		• , ,	names in given	time. In this case the o	category w	as animals and time d	uration
Results	True positives:	62	False negatives:	4	False positives:	70	True negatives:	96
Additional comme								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	`		re-specified thresho d independently of e		veen tests was unclea	r and it wa	s unclear whether the	index a
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
	rategory fluency (ani ncy, <19. Tests ability			names in given	time. In this case the o	category w	as animals and time d	uration
Results	True positives:	56	False negatives:	10	False positives:	61	True negatives:	105
Additional comme								
Risk of bias	Patient	Low	Index test:	High	Reference	Low	Flow and	Low

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	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							
	., Weber B, Pantel J. iatr Pscych and Neur			ne clock drawin	ng test: the relevance	of "Time s	etting" in screenin	g
Study type	Prospective cohort							
Country	Germany							
Setting	Memory clinic of th	e University	of Frankfurt am Ma	in				
Inclusion criteria	People vising the r	nemory clini	c with suspected de	mentia.				
Exclusion criteria	People who receive	ed a final dia	agnosis 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	g the DSM-IV criteria	a and AD using I	NINCDS-ADRDA; VaD	using NINI	OS-AIREN.	
Dementia versus n	ot dementia							
	Drawing Test, CDT, S							
			` ' / '	•	fect, 6 no reasonable r			
Results	True positives:	301	False negatives:	33	False positives:	56	True negatives:	72
			Index test:	Low	Reference	Low	Flow and	Low
Risk of bias	Patient selection:	High	muex test.	LOW	standard:		timing:	2011
Risk of bias Overall risk of bias	selection:	J				the study.)		Low

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Overall	Not serious		; 21: 250-260.					
indirectness	1401 0011040							
	rawing Test, CDT, L		• •					
Clock Drawing Test,	CDT (Lin method), cu		,		,			
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 wl	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 D	rawing Test, CDT, N	lanos and \	Wu scoring method					
	CDT (Manos and Wu	ı method),cu	it-off 8/7 (<8), time s	etting included,	(0 to 10, higher better)		
	CDT (Manos and Wu True positives:		it-off 8/7 (<8), time s False negatives:		(0 to 10, higher better False positives:	1	True negatives:	77
Clock Drawing Test,	•		False			1	True negatives:	77
Clock Drawing Test, Results Additional comme	•	271	False	63		1	True negatives: Flow and timing:	77 Low
Clock Drawing Test, Results Additional comme nts	True positives: Patient selection:	271 High	False negatives:	63	False positives:	51 Low	Flow and	
Clock Drawing Test, Results Additional comme nts Risk of bias	True positives: Patient selection:	271 High no received	False negatives:	63 Low TD, DLB or MC	False positives: Reference standard:	51 Low	Flow and	

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•	•		` ,		(0 to 10, higher better	1		
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 diagnosi	s of FTD, DLB o	or MCI were excluded	from the stu	dy and an optimised	threshol
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Clock Dr Clock Drawing Test, C			•	<i>-</i>	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 wh	no received	a final diagnosis of F	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	•	,	` '	•	•			
Results	True positives:	240	False negatives:	94	False positives:	46	True negatives:	82

Results

Overall risk of bias Indirectness	Patient selection:	High	Index test:					
	erious (People wh			Low	Reference standard:	Low	Flow and timing:	Low
Indirectness	erious (i copie wi	o received	a final diagnosis of I	FTD, DLB or MC	I were excluded from	the study.)		
	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall N indirectness	ot serious							
Bergman H, Chertkow				Dixon R. HM-PA	O (CERETEC) SPEC	T brain scaı	nning in the diagno	osis of
Alzheimer's disease. J		1997; 45: 1	5–20					
, ,,	rospective cohort							
	anada	onital (MaCi	III I win caraitus Maraa	m., alimialaaa m	wincer of traction is AD	diamania		
			iii University) Memo	ry clinic whose p	orimary function is AD	diagnosis.		
	eferral to the men	nory clinic.						
	Not stated							
	0.0% male							
	iean age 75.4 yea	` ,						
	uspected dementi							
standard so	cans. Diagnosis w neeting the AD crit	as repeated eria after 1	l after 12 months an	nd then 6 monthl as cognitive im	nd neurological evalua y. Diagnostic criteria u pairment no dementia; having VaD.	sed: NINCD	S-ADRDA for AD; p	atients n
AD versus non-AD (Val	D and cognitive i	mpairment	no dementia grou	ps)				

True positives: 39

False positives: 29

True negatives: 13

False 19

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			negatives:					
Additional comme nts	on a subset of SPE	CT patterns		efore we exclud	ot have suspected dem led them all due to risk 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							
			oisord 1999; 10: 40	–46 .				
			Disord 1999; 10: 40	– 46.				
Study type	Prospective cohort France		isord 1999; 10: 40	–46.				
Study type Country	Prospective cohort France		ed by the French na		eillance network			
Study type Country Setting	Prospective cohort France	nples provid			eillance network			
Study type Country Setting Inclusion criteria	Prospective cohort France Not stated, but san	nples provid			eillance network			
Study type Country Setting Inclusion criteria Exclusion criteria	Prospective cohort France Not stated, but sam People with suspec	nples provid			eillance network			
Study type Country Setting Inclusion criteria Exclusion criteria Sex	Prospective cohort France Not stated, but san People with suspect Not stated	nples provid			eillance network			
Study type Country Setting Inclusion criteria Exclusion criteria Sex Age Presentation	Prospective cohort France Not stated, but san People with suspect Not stated 47.3% male Not stated	nples providented CJD		tional CJD surve	eillance network			
Study type Country Setting Inclusion criteria Exclusion criteria Sex Age Presentation Reference	Prospective cohort France Not stated, but san People with suspect Not stated 47.3% male Not stated	nples provide eted CJD	ed by the French na	tional CJD surve	eillance network			
Study type Country Setting Inclusion criteria Exclusion criteria Sex Age Presentation Reference standard	Prospective cohort France Not stated, but sam People with suspect Not stated 47.3% male Not stated Rapidly progressive Criteria for CJD base	nples providented CJD e dementia I	ed by the French na eading to suspected ters et al. (1979)	tional CJD surve	eillance network			
Study type Country Setting Inclusion criteria Exclusion criteria Sex Age	Prospective cohort France Not stated, but sam People with suspect Not stated 47.3% male Not stated Rapidly progressive Criteria for CJD base stelle and possible) v 3-3 immunoblotting	nples providented CJD e dementia I sed on Mastersus not C	ed by the French na eading to suspected ters et al. (1979)	tional CJD surve	eillance network			

Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Unclear	Flow and timing:	Low
Overall risk of bias	inappropriate exclu	sions avoide	ed; the index test re	sults were interp	ther: a consecutive or preted without knowled ge of the results of the	ge of the re	sults of the reference	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
CJD (excluding pos	sible CJD) versus n	ot CJD						
	3-3 immunoblotting letected by immunobl							
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
	selection: Serious (Optimised inappropriate exclu or the reference sta	I test cut-offs sions avoide andard resul	s were used and it wed; the index test re	vas unclear whe sults were interp without knowled		random san	timing: uple of patients was sults of the reference	enrolled o
Risk of bias Overall risk of bias Indirectness	selection: Serious (Optimised inappropriate exclu or the reference sta	I test cut-offs sions avoide andard resul o not downg	s were used and it wed; the index test rests were interpreted	vas unclear where sults were interpwithout knowled s.)	standard: ther: a consecutive or preted without knowled	random san	timing: uple of patients was sults of the reference	enrolled o
Overall risk of bias	selection: Serious (Optimised inappropriate excluor the reference states 10% population serious Patient	I test cut-offs sions avoide andard resul o not downg	s were used and it wed; the index test rest ts were interpreted traded for risk of bia	vas unclear where sults were interpwithout knowled s.)	standard: ther: a consecutive or preted without knowled ge of the results of the Reference	random san ge of the re index test.	timing: uple of patients was sults of the reference	enrolled o
Overall risk of bias Indirectness Overall	selection: Serious (Optimised inappropriate excluor the reference states <10% population selection: Not serious	I test cut-offs sions avoide andard resul o not downg	s were used and it wed; the index test rest ts were interpreted traded for risk of bia	vas unclear where sults were interpwithout knowled s.)	standard: ther: a consecutive or preted without knowled ge of the results of the Reference	random san ge of the re index test.	timing: uple of patients was sults of the reference	enrolled o
Overall risk of bias Indirectness Overall indirectness CJD versus not CJE	selection: Serious (Optimised inappropriate excluor the reference state) <10% population serious Patient selection: Not serious	I test cut-offs sions avoide andard resul o not downg Low	s were used and it wed; the index test rets were interpreted traded for risk of bia	vas unclear where sults were interpwithout knowled s.)	standard: ther: a consecutive or preted without knowled ge of the results of the Reference	random san ge of the re index test.	timing: uple of patients was sults of the reference	enrolled o

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nts								
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Unclear	Flow and timing:	Low
Overall risk of bias	inappropriate exclu	sions avoid	ed; the index test re	sults were interp	ther: a consecutive or preted without knowled ge of the results of the	ge of the re	sults of the reference	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
CJD (excluding pos	sible CJD) versus n	ot CJD						
Index Test: Neuron- neuron-specific enola	• • • • • • • • • • • • • • • • • • •	detected by	/ ELISA					
Results	True positives:	55	False negatives:	14	False positives:	4	True negatives:	43
Additional comme nts	NSE was not meas	ure in 1 san	nple					
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Unclear	Flow and timing:	Low
Overall risk of bias	inappropriate exclu or the reference sta	sions avoide andard resul	ed; the index test re	sults were interp without knowled	ther: a consecutive or preted without knowled ge of the results of the	ge of the re	sults of the reference	standar
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
CJD versus not CJD								

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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		
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 pos	sible CJD) versus n	ot CJD								
Index Test: S100B, 2	2.5ng/ml									
S-100 glial protein, >2	2.5ng/ml, measured i	using an imr	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	inappropriate exclu or the reference sta	sions avoido andard resul	ed; the index test re	sults were interp without knowled	ther: a consecutive or preted without knowled ge of the results of the	ge of the re	sults of the reference	standar		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									
	or A.I. Annlauso sig	n: ecroonin	a utility for demon	tia and cognitiv	ve impairment Posto	raduato Ma	dicina 2016: 128: 2	50_253		
	er AJ. Applause sig		g utility for demen	tia and cognitiv	ve impairment. Postg	raduate Me	edicine 2016; 128: 2	50–253.		

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Setting	Cognitive disorders	clinic								
Inclusion criteria	New referrals to the	e cognitive of	disorders clinic seen	over a 12-mo	onth period (January 201	4–January	/ 2015).			
Exclusion criteria	None	None								
Sex	49.2% male									
Age	Median age 61 yea	Median age 61 years (range 18-91)								
Presentation	Cognitive impairme	ent								
Reference standard	Clinician diagnosis	Clinician diagnosis using DSM-IV for dementia and Petersen (1999) for mild cognitive impairment.								
Dementia versus no	t dementia									
Index Test: Applaus 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	Not serious									

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

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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.

30.	
	NINCDS-ADRDA criteria
Exclusion criteria	1) Clinical symptoms at inclusion fulfilling existing criteria for FTD, VaD, PD, LBD, progressive supranuclear palsy/corticobasal degeneration spectrum; 2) a major depressive disorder based on DSM-IV-TR criteria that is not being treated; 3) rapidly progressing dementia (<1 year since symptoms onset); 4) neoplastic, inflammatory, infectious, toxic or metabolic causes as evidenced by imaging and routine blood tests; 5) abnormal CSF (>5.109 leukocytes/mL and/or total protein level >1g/L); 6) advanced or unstable disease; 7) contraindications to MRI or SPECT imaging; 8) investigators unable to obtain CSF.
Sex	61.7% male
Age	Mean age 63.9 years (SD 9.4)
Presentation	Clinically ambiguous dementia (CAD) as defined by CAD criteria at baseline
Reference standard	Clinician diagnosis at 24 month follow up based on: Neary 1998 (FTD); NINCDS-ADRDA (AD); NINDS-AIREN (VaD); McKeith consensus criteria (DLB); psychiatric disorders using DSM-IV-TR; AD based on 4 criteria. AD criteria: 1) patients did not fit into either of the aforementioned criteria for non-AD dementia; 2) patients fulfilled NINCDS-ADRDA criteria I and II for probable AD; 3) 2-years follow-up evidenced a deterioration in memory impairment (drop in FCSRT total recall score ≥4) and in global cognitive functioning (drop in MMSE score ≥3); 4) initial atypical features did not appear meaningful in retrospect (i.e., gait disturbances that did not evolve into overt parkinsonism, or initial psychiatric, cognitive and/or behavioural symptoms that were relegated to the background in hindsight).

FTD versus non-FTD

Index Test: 99mTc-HMPAO SPECT

99mTc-HMPAO SPECT. Images taken with a multiple headed camera. Threshold is pre-specified; visual interpretation of the SPECT images. Details: Sixty-four 20 s views over a 360° elliptical orbit taken using a three-headed gamma camera and reformatted into a matrix of 128×128. 99 mTc-HMPAO fixation was analysed regionally for frontal, parietal, temporal and occipital regions on the left and right. According to the pattern of 99mTc-HMPAO fixation, results were classified in four categories: Hypoperfusion of the AD type (temporoparietal hypoperfusion, whatever the perfusion of the frontal lobes); hypoperfusion of the FTD type (frontal±temporal hypoperfusion, no posterior defect); hypoperfusion of another type; normal SPECT. FTD type pattern used for analysis here.

Results	True positives:	8	False negatives:	_	False positives:	10	True negatives:	39
Additional comme nts	Calculations for FT	D versus no	on -FTD used inform	ation in Archer 2	t 24 months follow up. 2015 Cochrane review alyses as the study or	that was ob		

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	resulting in a high r	isk of report	ing bias.					
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	High
Overall risk of bias					ive versus random en and again at 24 mont			agnosis
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
FTD versus AD								
Sixty-four 20 s views fixation was analysed fixation, results were	over a 360∘ elliptical regionally for frontal classified in four cate	orbit taken u , parietal, te gories: Hyp	using a three-heade mporal and occipita operfusion of the AI	d gamma came I regions on the D type (temporo	a and reformatted into left and right. Accordin parietal hypoperfusion	a matrix of ng to the pa , whatever t	ttern of 99mTc-HMP he perfusion of the fr	IMPAO AO rontal
Sixty-four 20 s views fixation was analysed fixation, results were lobes); hypoperfusion pattern used for analy	over a 360° elliptical regionally for frontal classified in four cate of the FTD type (frossis here.	orbit taken u , parietal, te gories: Hyp ntal±tempor	using a three-heade mporal and occipita operfusion of the AI	d gamma came I regions on the D type (temporo p posterior defec	a and reformatted into left and right. According parietal hypoperfusion t); hypoperfusion of an	o a matrix of ng to the pa , whatever t nother type;	128×128. 99 mTc-H ttern of 99mTc-HMP/ he perfusion of the fr normal SPECT. FTI	IMPAO AO rontal
Sixty-four 20 s views fixation was analysed fixation, results were lobes); hypoperfusion pattern used for analy	over a 360° elliptical regionally for frontal classified in four cate of the FTD type (fro	orbit taken u , parietal, te gories: Hyp ntal±tempor	using a three-heade mporal and occipita operfusion of the AI al hypoperfusion, no	d gamma came I regions on the D type (temporo p posterior defec	a and reformatted into left and right. Accordin parietal hypoperfusion	o a matrix of ng to the pa , whatever t nother type;	f 128×128. 99 mTc-H ttern of 99mTc-HMP, he perfusion of the fr	IMPAO AO rontal O type
Sixty-four 20 s views fixation was analysed fixation, results were lobes); hypoperfusion pattern used for analy Results Additional comme	over a 360° elliptical regionally for frontal classified in four cate of the FTD type (from sis here. True positives:	orbit taken u , parietal, te gories: Hyp ntal±tempor	using a three-heade mporal and occipita operfusion of the AI al hypoperfusion, no False negatives:	d gamma came I regions on the D type (temporor o posterior defect	a and reformatted into left and right. According parietal hypoperfusion t); hypoperfusion of an	o a matrix of ng to the pa , whatever t nother type;	128×128. 99 mTc-H ttern of 99mTc-HMP/ he perfusion of the fr normal SPECT. FTI	IMPAO AO rontal O type
Sixty-four 20 s views fixation was analysed fixation, results were lobes); hypoperfusion pattern used for analy Results Additional comments	over a 360° elliptical regionally for frontal classified in four cate of the FTD type (from sis here. True positives:	orbit taken u , parietal, te egories: Hyp ntal±tempor 8	using a three-heade mporal and occipita operfusion of the AI al hypoperfusion, no False negatives:	d gamma camed I regions on the D type (temporop o posterior defect 3 agnosis made a	a and reformatted into left and right. According parietal hypoperfusion t); hypoperfusion of an False positives:	o a matrix of ng to the pa , whatever t nother type;	128×128. 99 mTc-H ttern of 99mTc-HMP/ he perfusion of the fr normal SPECT. FTI	IMPAO AO rontal O type
Sixty-four 20 s views fixation was analysed fixation, results were clobes); hypoperfusion pattern used for analy Results Additional comments Risk of bias	over a 360° elliptical regionally for frontal classified in four cate of the FTD type (from sis here. True positives: Patients tested at be patient selection: Very serious (Loss diagnosis made at the patient selection)	orbit taken u, parietal, te gories: Hypntal±tempor 8 caseline and Unclear to follow up 24 month fo	using a three-heade mporal and occipita operfusion of the AI al hypoperfusion, no False negatives: formal reference di Index test: of 6/69 patients; un	d gamma camed regions on the D type (temporor posterior defects a gamma camed a Low release a carried out a gamma camed a gamma	a and reformatted into left and right. According parietal hypoperfusion of an arrival properfusion of arrival p	o a matrix of a g to the pa , whatever t nother type; 1 Low m enrolmen	tern of 99mTc-Hetern of 99mTc-HMP/ tern of 99mTc-HMP/ the perfusion of the fr normal SPECT. FTD True negatives: Flow and timing:	IMPAO AO rontal O type 17 High
Sixty-four 20 s views fixation was analysed fixation, results were	over a 360° elliptical regionally for frontal classified in four cate of the FTD type (from sis here. True positives: Patients tested at be patient selection: Very serious (Loss diagnosis made at the patient selection)	orbit taken u, parietal, te egories: Hypntal±tempor 8 asseline and Unclear to follow up 24 month fo >10% study	using a three-heade mporal and occipita operfusion of the AI al hypoperfusion, no False negatives: formal reference di Index test: of 6/69 patients; un Illow up with index test	d gamma camed regions on the properties of type (temporor of posterior defects) agnosis made a low local region about consects carried out a red.)	ra and reformatted into left and right. According the parietal hypoperfusion of an arietal hypoperfusion of arietal hypoperfusion of arietal hypoperfusion of arietal hypoperfusion arie	o a matrix of a g to the pa , whatever t nother type; 1 Low m enrolmen	tern of 99mTc-Hetern of 99mTc-HMP/ tern of 99mTc-HMP/ the perfusion of the fr normal SPECT. FTD True negatives: Flow and timing:	IMPAO AO rontal O type 17 High

Boutoleau-Bretonniere C, Lebouviera T, Delaroche O, Lamy E, Evrard C, Charriau T, et al. Value of neuropsychological testing, imaging, and CSF biomarkers for the differential diagnosis and prognosis of clinically ambiguous dementia. Journal of Alzheimer's Disease 2012; 28(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 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	diagnosis made at	24 month fo		ests carried out a	secutive versus randor at baseline and again a						
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										

FTD versus non-FTD dementia plus unclassifiable

Index Test: 99mTc-HMPAO SPECT

99mTc-HMPAO SPECT. Images taken with a multiple headed camera. Threshold is pre-specified; visual interpretation of the SPECT images. Details: Sixty-four 20 s views over a 360° elliptical orbit taken using a three-headed gamma camera and reformatted into a matrix of 128×128. 99 mTc-HMPAO fixation was analysed regionally for frontal, parietal, temporal and occipital regions on the left and right. According to the pattern of 99mTc-HMPAO fixation, results were classified in four categories: Hypoperfusion of the AD type (temporoparietal hypoperfusion, whatever the perfusion of the frontal lobes); hypoperfusion of the FTD type (frontal±temporal hypoperfusion, no posterior defect); hypoperfusion of another type; normal SPECT. FTD type pattern used for analysis here.

Results True	e positives: 8	False 3	False positives:	10	True negatives:	35
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Boutoleau-Bretonniere C, Lebouviera T, Delaroche O, Lamy E, Evrard C, Charriau T, et al. Value of neuropsychological testing, imaging, and CSF biomarkers for the differential diagnosis and prognosis of clinically ambiguous dementia. Journal of Alzheimer's Disease 2012; 28(2):323-36. negatives: Patients tested at baseline and formal reference diagnosis made at 24 months follow up. Additional comme nts Patient Unclear Risk of bias Index test: Low Reference Low Flow and High selection: standard: timing: Overall risk of bias Serious (Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used but <10% study population discarded) Patient Low Index test: Low Reference Low Indirectness selection: standard: Overall Not serious indirectness AD versus non-AD dementia plus unclassifiable Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT. Images taken with a multiple headed camera. Threshold is pre-specified; visual interpretation of the SPECT images. Details: Sixty-four 20 s views over a 360 elliptical orbit taken using a three-headed gamma camera and reformatted into a matrix of 128×128. 99 mTc-HMPAO fixation was analysed regionally for frontal, parietal, temporal and occipital regions on the left and right. According to the pattern of 99mTc-HMPAO fixation, results were classified in four categories: Hypoperfusion of the AD type (temporoparietal hypoperfusion, whatever the perfusion of the frontal lobes); hypoperfusion of the FTD type (frontal±temporal hypoperfusion, no posterior defect); hypoperfusion of another type; normal SPECT. FTD type pattern used for analysis here. Results True positives: 14 False 4 False positives: 13 True negatives: 25 negatives: Additional comme Patients tested at baseline and formal reference diagnosis made at 24 months follow up. nts Risk of bias Index test: Low Patient Unclear Reference Flow and High Low selection: standard: timing: Serious (Loss to follow up of 6/69 patients: unclear about consecutive versus random enrolment of patients: reference diagnosis Overall risk of bias made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used but <10% study population discarded) **Indirectness** Patient Low Index test: Low Reference Low

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

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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):323lobes); 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 4 False positives: 3 True negatives: 8 negatives: Patients tested at baseline and formal reference diagnosis made at 24 months follow up. Additional comme nts Risk of bias Patient Unclear Index test: Low Reference Low Flow and High selection: standard: timing: Very serious (Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference Overall risk of bias 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 Low Index test: Low Reference Low selection: standard: Overall Not serious indirectness

	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.
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

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CC. Diomarkolo loi			O, Lamy E, Evrard prognosis of clinic		s dementia. Journal o		er's Disease 2012; 2	
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	consensus criteria either of the aforem 2-years follow-up e functioning (drop in	Clinician diagnosis at 24 month follow up based on: Neary 1998 (FTD); NINCDS-ADRDA (AD); NINDS-AIREN (VaD); McKeith consensus criteria (DLB); psychiatric disorders using DSM-IV-TR; AD based on 4 criteria. AD criteria: 1) patients did not fit into either of the aforementioned criteria for non-AD dementia; 2) patients fulfilled NINCDS-ADRDA criteria I and II for probable AD; 3) 2-years follow-up evidenced a deterioration in memory impairment (drop in FCSRT total recall score ≥4) and in global cognitive functioning (drop in MMSE score ≥3); 4) initial atypical features did not appear meaningful in retrospect (i.e., gait disturbances that did not evolve into overt parkinsonism, or initial psychiatric, cognitive and/or behavioural symptoms that were relegated to the						
AD versus non-AD	dementia plus uncla	<u> </u>	oun.					
					LA was rated visually v			
sequence was availa averaged. The degree	able (55/60 patients), i	using Schelt erintensities from grade (ens score ranging fr severity was rated	om 0 (no atrophyisually on axial e 3 (confluent le	ny) to 4 (severe atroph T2-weighted or fluid-a	y). Scores attenuated i	of the left and right sid	de were _AIR)
sequence was availa averaged. The degre images using the Fa	able (55/60 patients), the of white matter hypoteness scale, ranging for the positives:	using Schelt erintensities from grade (6	ens score ranging fr severity was rated (no lesion) to grade False negatives:	rom 0 (no atroph visually on axial e 3 (confluent le 12	ny) to 4 (severe atroph T2-weighted or fluid-asions).	y). Scores attenuated i	of the left and right sid inversion recovery (Fl	de were _AIR)
sequence was availa averaged. The degree images using the Fat Results Additional comme	able (55/60 patients), the of white matter hypoteness scale, ranging for the positives:	using Schelt erintensities from grade 0 6 oaseline and	ens score ranging fr severity was rated (no lesion) to grade False negatives:	rom 0 (no atroph visually on axial e 3 (confluent le 12 agnosis made a	ny) to 4 (severe atroph T2-weighted or fluid-a sions). False positives:	y). Scores attenuated i	of the left and right sid inversion recovery (Fl	de were _AIR)
sequence was availa averaged. The degre images using the Fax Results Additional comme nts	able (55/60 patients), the of white matter hypoteness scale, ranging for the positives: Patients tested at the position: Serious (Loss to for the patients)	using Schelt erintensities from grade 0 6 paseline and Unclear	ens score ranging fr severity was rated 0 (no lesion) to grade False negatives: formal reference dia Index test:	rom 0 (no atroph visually on axial e 3 (confluent le 12 agnosis made a Low	ry) to 4 (severe atroph T2-weighted or fluid-asions). False positives: t 24 months follow up. Reference	y). Scores attenuated in the state of particular to the state of particular	of the left and right sicinversion recovery (Fl True negatives: Flow and timing: patients; reference dia	de were _AIR) 25 High
sequence was availa averaged. The degree images using the Far Results Additional comments Risk of bias	able (55/60 patients), the of white matter hypoteness scale, ranging for the positives: Patients tested at the position: Serious (Loss to for the patients)	using Schelt erintensities from grade 0 6 paseline and Unclear llow up of 6/ follow up wit	ens score ranging fr severity was rated 0 (no lesion) to grade False negatives: formal reference dia Index test:	rom 0 (no atroph visually on axial e 3 (confluent le 12 agnosis made a Low	ry) to 4 (severe atroph T2-weighted or fluid-assions). False positives: t 24 months follow up. Reference standard: tive versus random en	y). Scores attenuated in the state of particular to the state of particular	of the left and right sicinversion recovery (Fl True negatives: Flow and timing: patients; reference dia	de were _AIR) 25 High
sequence was availa averaged. The degree images using the Far Results Additional comments Risk of bias Overall risk of bias	Patients Serious (Loss to formade at 24 month) able (55/60 patients), the period of t	using Schelt erintensities from grade 0 6 paseline and Unclear llow up of 6/ follow up wit	ens score ranging fr severity was rated of (no lesion) to grade False negatives: formal reference dis Index test:	rom 0 (no atroph visually on axial e 3 (confluent le 12 agnosis made a Low about consecut d out at baseline	ry) to 4 (severe atroph T2-weighted or fluid-asions). False positives: t 24 months follow up. Reference standard: tive versus random en and again at 24 months.	y). Scores attenuated in 13 Low rolment of purchasin some	of the left and right sicinversion recovery (Fl True negatives: Flow and timing: patients; reference dia	de were _AIR) 25 High

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Boutoleau-Bretonniere C, Lebouviera T, Delaroche O, Lamy E, Evrard C, Charriau T, et al. Value of neuropsychological testing, imaging, and CSF biomarkers for the differential diagnosis and prognosis of clinically ambiguous dementia. Journal of Alzheimer's Disease 2012; 28: 323-36.

Index Test: MRI

MRI scans were made on different 1.0 and 1.5 Tesla scanners across several clinics. MTLA was rated visually when a coronal T1-weighted gradient echo sequence was available (55/60 patients), using Scheltens score ranging from 0 (no atrophy) to 4 (severe atrophy). Scores of the left and right side were averaged. The degree of white

matter hyperintensities severity was rated visually on axial T2-weighted or fluid-attenuated inversion recovery (FLAIR) images using the Fazekas scale, ranging from grade 0 (no lesion) to grade 3 (confluent lesions).

Results	True positives:	10	False negatives:	8	False positives:	4	True negatives:	22			
Additional 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										

FTD versus non-FTD dementia plus unclassifiable group

Index Test: MRI

MRI scans were made on different 1.0 and 1.5 Tesla scanners across several clinics. MTLA was rated visually when a coronal T1-weighted gradient echo sequence was available (55/60 patients), using Scheltens score ranging from 0 (no atrophy) to 4 (severe atrophy). Scores of the left and right side were averaged. The degree of white

matter hyperintensities severity was rated visually on axial T2-weighted or fluid-attenuated inversion recovery (FLAIR) images using the Fazekas scale, ranging from grade 0 (no lesion) to grade 3 (confluent lesions).

Results	True positives:	2	False	9	False positives:	17	True negatives:	28
			negatives:					
Additional comme nts	Patients tested at t	aseline and	I formal reference di	agnosis made a	t 24 months follow up.			
Risk of bias	Patient	Unclear	Index test:	Low	Reference	Low	Flow and	High

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	selection:				standard:		timing:	
Overall risk of bias					ive versus random en and again at 24 mont			agnosis
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
VaD versus non-Val) dementia plus und	classifiable	group					
sequence was availal averaged. The degre	ole (55/60 patients), ole of white es severity was rated	using Schelt	ens score ranging for axial T2-weighted or	rom 0 (no atroph	A was rated visually viry) to 4 (severe atrophisms) to 4 inversion recovery (F	y). Scores o	f the left and right sid	de were
Results	True positives:	•	False negatives:	1	False positives:	12	True negatives:	36
Additional comme	Patients tested at h	aseline and	formal reference di	agnosis made a	t 24 months follow up.			
	r anomo tootoa at a				•			
nts	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	High
nts Risk of bias	Patient selection: Serious (Loss to fo	llow up of 6/	69 patients; unclear	about consecut	Reference	Low rolment of pa	timing: atients; reference dia	Ū
nts Risk of bias Overall risk of bias	Patient selection: Serious (Loss to fo	llow up of 6/ follow up wi	69 patients; unclear	about consecut d out at baseline	Reference standard: ive versus random en	Low rolment of pa	timing: atients; reference dia	Ū
nts Risk of bias Overall risk of bias Indirectness Overall	Patient selection: Serious (Loss to fo made at 24 month Patient	llow up of 6/ follow up wi	69 patients; unclear th index tests carried	about consecut d out at baseline	Reference standard: ive versus random enterence and again at 24 monto	Low rolment of paths in some	timing: atients; reference dia	Ū
nts Risk of bias Overall risk of bias Indirectness Overall indirectness	Patient selection: Serious (Loss to fo made at 24 month Patient selection: Not serious	llow up of 6/ follow up wi	69 patients; unclear th index tests carried Index test:	about consecut d out at baseline	Reference standard: ive versus random enterence and again at 24 monto	Low rolment of paths in some	timing: atients; reference dia	Ū
nts Risk of bias Overall risk of bias Indirectness Overall indirectness AD versus non AD o	Patient selection: Serious (Loss to fo made at 24 month Patient selection: Not serious lementia (FTD, VaD Beta 1-42	llow up of 6/follow up wi	69 patients; unclear th index tests carried Index test: c disease)	about consecut d out at baseline Low	Reference standard: ive versus random ente and again at 24 monto Reference standard:	Low rolment of pa hs in some of Low	timing: atients; reference dia cases.)	Ů
nts Risk of bias Overall risk of bias Indirectness Overall indirectness AD versus non AD o	Patient selection: Serious (Loss to fo made at 24 month Patient selection: Not serious lementia (FTD, VaD Beta 1-42	llow up of 6/follow up wind Low , psychiatrically available	69 patients; unclear th index tests carried Index test: c disease)	about consecut d out at baseline Low Low	Reference standard: ive versus random enterence and again at 24 monto	Low rolment of particle in some of the come of the com	timing: atients; reference dia cases.)	Ů

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Boutoleau-Bretonnie	ere C, Lebouviera T	, Delaroche	O, Lamy E, Evrard	d C, Charriau T	, et al. Value of neuro	psychologi	ical testing, imagin	g, and	
			prognosis of clinic		s dementia. Journal d				
			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	diagnosis made at	Very serious (Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.)							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								
Index Test: Total tau	l								
CSF Total tau measu	red by commercially	available sa	andwich ELISAs (Inn	otest, Innogene	tics,Ghent, Belgium). I	Jsual test cu	ut off >350 pg/ml pre	specifie	
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	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	diagnosis made at	24 month fo		ests carried out a	secutive versus randor at baseline and again				
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								
Index Test: Total tau									
CSF Total tau measu	red by commercially	available sa	andwich ELISAs (Inn	otest, Innogene	tics, Ghent, Belgium).	Optimised to	est cut off of > 480po	g/ml her	
Results	True positives:	16	False	2	False positives:	3	True negatives:	23	

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					, et al. Value of neuro s dementia. Journal o			
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	diagnosis made at	24 month fo		ests carried out a	secutive versus randor at baseline and again a			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: p-tau 18 CSF P- tau measured		ailable sand	lwich ELISAs (Innote	est, Innogenetics	s, 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	d 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	diagnosis made at	24 month fo		ests carried out a	secutive versus randor at baseline and again a			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: p-tau 18°		ailable sand	lwich FLISAs (Innote	est. Innogenetics	s, Ghent, Belgium). Op	timised test	cut off >68 pg/ml	
Results	True positives:		False		False positives:		True negatives:	22

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			negatives:					
Additional comme nts	Patients tested at b	paseline 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	diagnosis made at	24 month fo		ests carried out a	secutive versus randor at baseline and again a			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall	Not serious							
Index Test: Amyloid The INNOTEST Amyl	oid Tau Index (IATI)			Beta 42/(240 + [1	.18×T-tau]) ratio. Mea	sured by co	mmercially available	sandwid
Index Test: Amyloid The INNOTEST Amyl ELISAs (Innotest, Inno	oid Tau Index (IATI) ogenetics, Ghent, Be	elgium). Cut	off <0.8.					
ELISAs (Innotest, Inno Results Additional comme	oid Tau Index (IATI) ogenetics, Ghent, Be True positives:	elgium). Cut 17	off <0.8. False negatives:	1	.18×T-tau]) ratio. Mea False positives: t 24 months follow up.	8	mmercially available True negatives:	sandwid
Index Test: Amyloid The INNOTEST Amyl ELISAs (Innotest, Inno Results Additional comme nts	oid Tau Index (IATI) ogenetics, Ghent, Be True positives: Patients tested at b	elgium). Cut 17 paseline and	off <0.8. False negatives: I formal reference di	1 agnosis made a	False positives: t 24 months follow up.	8	True negatives:	18
Index Test: Amyloid The INNOTEST Amyl ELISAs (Innotest, Inno Results	oid Tau Index (IATI) ogenetics, Ghent, Be True positives:	elgium). Cut 17 paseline and	off <0.8. False negatives:	1 agnosis made a	False positives:	8		
Index Test: Amyloid The INNOTEST Amyl ELISAs (Innotest, Inno Results Additional comme nts	oid Tau Index (IATI) ogenetics, Ghent, Be True positives: Patients tested at be Patient selection: Very serious (Loss diagnosis made at	elgium). Cut 17 paseline and Unclear to follow up 24 month fo	off <0.8. False negatives: I formal reference di Index test: of 6/69 patients; ur	agnosis made a Low clear about consests carried out a	False positives: t 24 months follow up. Reference	8 Low	True negatives: Flow and timing:	18 High
Index Test: Amyloid The INNOTEST Amyl ELISAs (Innotest, Inno Results Additional comme nts Risk of bias	oid Tau Index (IATI) ogenetics, Ghent, Be True positives: Patients tested at be Patient selection: Very serious (Loss diagnosis made at	elgium). Cut 17 paseline and Unclear to follow up 24 month fo >10% study	False negatives: I formal reference di Index test: Of 6/69 patients; ur	agnosis made a Low clear about consests carried out a	False positives: t 24 months follow up. Reference standard: secutive versus randor	8 Low	True negatives: Flow and timing:	18 High

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					, et al. Value of neuro s dementia. Journal o			
Results	True positives:	18	False negatives:	0	False positives:	8	True negatives:	18
Additional comme nts	Patients tested at b	aseline and	formal reference dia	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	diagnosis made at	24 month fo		ests carried out	secutive versus randor at baseline and again a			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: CSF 14-3 ≥2 abnormal CSF bio	•		loid beta 1-42 500pg	g/ml, total tau 48	0pg/ml, P-tau 68pg/m	I		
Results	True positives:	17	False negatives:	1	False positives:	3	True negatives:	23
Additional comme nts	Patients tested at b	aseline and	formal reference dia	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	diagnosis made at	24 month fo		ests carried out	secutive versus randor at baseline and again a			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

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Brandel JP, Delasne incidence estimates				vitch A. Diagnos	sis of Creutzfeldt-Jak	cob disease	e: effect of clinical o	riteria on	
Study type	Retrospective coho								
Country	France								
Setting	Not stated, but san	nples provid	led by the French na	itional CJD surve	eillance network				
Inclusion criteria	Suspicion of spora	• •	,						
Exclusion criteria	Genetic or iatroger								
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 case	s was excluded as t	he clinician diag	nosis used the index to	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 CJ									
Results	True positives:	173	False negatives:	23	False positives:	20	True negatives:	20	

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Brandel JP, Delasne incidence estimates				ritch A. Diagnos	sis of Creutzfeldt-Jak	ob disease	: effect of clinical o	riteria o
Additional comme nts	Data for the non-au	utopsy cases	s was excluded as the	ne clinician diagr	nosis used the index to	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 European criteria for								
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 to	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 versu	s not CJD (possible	CJD exclu	ıded)					
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	utopsy case:	s was excluded as the	ne clinician diagr	nosis used the index to	est		

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Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Serious (Unclear ri	sk of bias fo	r patient selection a	s we could only	use data for autopsied	l patients; si	ubgroup analysis tha	t exclude
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: French of French criteria for CJ								
Results	True positives:	99	False negatives:	52	False positives:	1	True negatives:	21
Additional comme nts	Data for the non-au	utopsy cases	s was excluded as th	ne clinician diagi	nosis used the index to	est		
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Serious (Unclear ri	sk of bias fo	r patient selection a	s we could only	use data for autopsied	l patients; sı	ubgroup analysis tha	t exclude
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Europea European criteria for								
Results	True positives:	99	False negatives:	52	False positives:	1	True negatives:	21
Additional comme nts	Data for the non-au	utopsy cases	s was excluded as th	ne clinician diagi	nosis used the index to	est		
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	High

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incidence estimates Overall risk of bias	Serious (Unclear ri	sk of bias fo	r patient selection a	s we could only	use data for autopsied	patients; su	bgroup analysis tha	t exclude
	>10% population.)							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Brandt C, Bahl JC, F Geriatr Cogn Disord		emar G, Joh	nannsen P. Usabilit	ty of cerebrosp	inal fluidbiomarkers	in a tertiary	memoryclinic. Dei	ment
Study type	Retrospective coho	ort						
Country	Denmark							
Setting	Copenhagen Mem	ory Clinic , C	Copenhagen Univers	sity Hospital				
Inclusion criteria	Participants underg	joing initial o	diagnosis 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	ırs (no SD d	ata provided, but ag	es of participant	s ranged from 27-86 y	ears old)		
Presentation	suspected dementi	а						
Reference standard	FTD consensus cri	teria (Neary		e DLB consensu	s diagnosed using NINs criteria (McKeith et a pecified.			
AD versus non-AD (including depression	on, MCI, oth	ner forms of demer	ntia and unspec	ified diagnoses)			
Index Test: Amyloid Beta Amyloid 1–42 ir		etermined u	using 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	Low	Index test:	Low	Reference	Low		

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Overall indirectness	Not serious							
Index Test: Total T Total -tau in CSF. <	au 51 years >300pg/ml, 5	1-70 vears	>450pg/ml. >70 vea	rs >530pa/ml. de	etermined using an EL	JSA assav	v (Innotest hTau Aɑ)	
Results	True positives:	•	False negatives:		False positives:		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 1 p-tau 181 in CSF, >		sing an ELI	SA assay (Innotest	Phospho-tau 18°	1)			
	81 80pg/ml, determined u True positives:		SA assay (Innotest False negatives:		1) False positives:	8	True negatives:	92
p-tau 181 in CSF, >	80pg/ml, determined u		False			8	True negatives:	92
p-tau 181 in CSF, > Results Additional comme	80pg/ml, determined u		False			8 Low	True negatives: Flow and timing:	92 Low
p-tau 181 in CSF, > Results Additional comme nts	80pg/ml, determined u True positives: Patient selection:	16	False negatives:	32	False positives:		Flow and	
p-tau 181 in CSF, > Results Additional comme nts Risk of bias	80pg/ml, determined u True positives: Patient selection:	16	False negatives:	32 Low	False positives:		Flow and	

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Results	True positives:	20	False negatives:	28	False positives:	10	True negatives:	89
Additional comme								
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: Amyloid	d Beta 1-42, Total Ta	•		cut offs were <5	1 vears >300ng/ml 51	-70 vears	>450ng/ml >70 years	
Index Test: Amyloid 3 out of 3 abnormal (>530pg/ml; Beta Am	· ·	Γotal- tau, p- ml; p-tau 18	-tau). For total -tau c		1 years >300pg/ml, 51-	·	>450pg/ml, >70 years True negatives:	98
Index Test: Amyloid 3 out of 3 abnormal (>530pg/ml; Beta Am	Beta Amyloid 1–42, 7 yloid 1–42 , < 400pg/	Γotal- tau, p- ml; p-tau 18	tau). For total -tau c 1, >80pg/ml		, ,	·		98
3 out of 3 abnormal (Beta Amyloid 1–42, 7 yloid 1–42 , < 400pg/	Γotal- tau, p- ml; p-tau 18	tau). For total -tau c 1, >80pg/ml False		, ,	·		98
ndex Test: Amyloid 3 out of 3 abnormal (>530pg/ml; Beta Amg Results Additional comments	Beta Amyloid 1–42, 7 yloid 1–42 , < 400pg/	Fotal- tau, p- ml; p-tau 18 13	tau). For total -tau c 1, >80pg/ml False		, ,	·		98 Low
Index Test: Amyloid 3 out of 3 abnormal (>530pg/ml; Beta Amg Results Additional comme	Beta Amyloid 1–42, 7 yloid 1–42, < 400pg/ True positives: Patient	Fotal- tau, p- ml; p-tau 18 13	tau). For total -tau o 1, >80pg/ml False negatives:	35	False positives:	1	True negatives:	
ndex Test: Amyloid 3 out of 3 abnormal (>530pg/ml; Beta Amg Results Additional comments Risk of bias	Beta Amyloid 1–42, 7 yloid 1–42, < 400pg/ True positives: Patient selection:	Fotal- tau, p- ml; p-tau 18 13 Low	tau). For total -tau o 1, >80pg/ml False negatives:	35 Low	False positives:	1	True negatives:	

Study type

Prospective cohort

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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	rith 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	Not stated							
Sex	59.0% male								
Age	Mean age 66 years	(range 17-	85)						
Presentation	Patients with ongoi	ng cognitive	impairment						
Reference standard	Criteria not specifie	ed							
CJD versus not CJD									
Index Test: CSF 14-3-3 protein, in	_								
Results	True positives:	2	False negatives:	0	False positives:	12	True negatives:	86	
Risk of bias	Patient selection:	Low	Index test:	Yes	Reference standard:	Unclear	Flow and timing:	Low	
Overall risk of bias	Not serious								
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low			
Overall indirectness	Serious (Patients d	o not have s	suspected CJD at ba	aseline)					

P.1.3 C

	zagt FW, Hui SL, et al. Six-item screener to identify cognitive impairment among potential subjects for clinical research.
Study type	Prospective cohort
Country	USA
Setting	Indiana Alzheimer's Disease Centre

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Inclusion criteria	People referred to	the Indiana	Alzheimer's Disease	Centre for eval	uation 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	ırs (SD not p	provided)					
Presentation	Suspected dement	ia						
Reference standard	informant reported cognition; or (3) the impairment in the p	a clinically see participant performance	significant decline in 's scores on cognitive of activities of daily	cognition; (2) the testing fell bell living.17 The 7tl	were diagnosed as contempts of the physician detected a contempts ow the 7th percentile; high percentile is approximately Mayo Clinic in their	a clinically si and if there mately equiv	gnificant impairment was no clinically imp valent to 1.5 standard	in `´ oortant d
Dementia versus no Index Test: 6 item s								
6 item screener, ≥ 0	(20)							
Results	True positives:	345	False negatives:	0	False positives:	306	True negatives:	0
Results Additional comme	The data for cohort have suspected de	one was ex mentia at ba	negatives: scluded as the peoplaseline. For the anal	le consisted of a lysis presented t	False positives: community- based sa he paper does not state e non-dementia group	ample scree te whether t	ned for dementia and	I did not
Additional comme	The data for cohort have suspected de	one was ex mentia at ba ognitive imp	negatives: scluded as the peoplaseline. For the anal	le consisted of a lysis presented t a or if it is just th	community- based sa he paper does not sta	ample scree te whether t	ned for dementia and	I did not
Additional comme	The data for cohort have suspected de no dementia and consequence Patient selection: Serious (It was uno	one was ex mentia at ba ognitive imp Low lear whethe	negatives: Accluded as the people aseline. For the analysisment no demention index test: er a consecutive or research.	le consisted of a ysis presented t a or if it is just the High andom sample o	community- based sa he paper does not sta e non-dementia group Reference	ample scree te whether t alone. Low d in the stud	ned for dementia and he comparator group Flow and timing:	I did not include Low
Additional comments	The data for cohort have suspected de no dementia and consequence Patient selection: Serious (It was uno	one was exmentia at bacognitive implement Low	negatives: Accluded as the people aseline. For the analysisment no demention index test: er a consecutive or research.	le consisted of a ysis presented t a or if it is just the High andom sample of d the test thresh	community- based sa he paper does not state e non-dementia group Reference standard:	ample scree te whether t alone. Low d in the stud	ned for dementia and he comparator group Flow and timing:	I did not include Low

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Results	True positives:	334	False negatives:	11	False positives:	143	True negatives:	163
Additional comme nts	have suspected de	mentia at ba	aseline. For the anal	lysis presented t	community- based sa he paper does not sta e non-dementia group	te whether tl		
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias					f patients was enrolled old was not pre-specif		y; whether the index	and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: 6 item s 6 item screener, ≥ 2	creener (≥2)							
Dogulto	True positivos:							
Results	True positives:	309	False negatives:	36	False positives:	63	True negatives:	243
Additional comme	The data for cohort have suspected de	one was ex mentia at b	negatives: xcluded as the peop aseline. For the anal	le consisted of a lysis presented t	False positives: community- based sa he paper does not sta e non-dementia group	imple screer te whether t	ned for dementia and	I did not
Additional comme	The data for cohort have suspected de	one was ex mentia at bo ognitive imp	negatives: xcluded as the peop aseline. For the anal	le consisted of a lysis presented t a or if it is just th	community- based sa he paper does not sta	imple screer te whether t	ned for dementia and	I did not
Additional comme nts	The data for cohort have suspected de no dementia and concent and concent selection: Serious (It was uno	one was exmentia at boognitive imple Low	negatives: Accluded as the people aseline. For the analysisment no demention index test: er a consecutive or research	le consisted of a lysis presented t a or if it is just th High andom sample o	community- based sa he paper does not sta e non-dementia group Reference	imple screer te whether the alone. Low d in the stud	ned for dementia and he comparator group Flow and timing:	I did not include Low
Additional comme nts Risk of bias	The data for cohort have suspected de no dementia and concent and concent selection: Serious (It was uno	one was exmentia at be ognitive implement Low steel the independent control on the control of th	negatives: Accluded as the people aseline. For the analysisment no demention index test: er a consecutive or research	le consisted of a lysis presented t a or if it is just the High andom sample of d the test thresh	community- based sa he paper does not sta e non-dementia group Reference standard: of patients was enrolled	imple screer te whether the alone. Low d in the stud	ned for dementia and he comparator group Flow and timing:	I did not include Low

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Results	True positives:	278	False negatives:	67	False positives:	28	True negatives:	278
Additional comme nts	have suspected de	mentia at ba	aseline. For the anal	ysis presented t	community- based sa he paper does not sta e non-dementia group	te whether t		
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias					of patients was enrolled hold was not pre-specif		y; whether the index	and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: 6 item s 6 item screener, ≥ 4	creener (≥4)							
Results	True positives:	233	False negatives:	112	False positives:	12	True negatives:	294
Additional comme nts	have suspected de	mentia at ba	aseline. For the anal	ysis presented t	community- based sa he paper does not sta e non-dementia group	te whether t		
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias					of patients was enrolled nold was not pre-specif		y; whether the index	and
	Patient	Low	Index test:	Low	Reference	Low		
ndirectness	selection:				standard:			

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Results	True positives:	169	False negatives:	176	False positives:	4	True negatives:	302
Additional comme nts	have suspected de	mentia at ba	aseline. For the anal	ysis presented t	community- based sa he paper does not sta e non-dementia group	te whether th		
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias					f patients was enrolled old was not pre-specif		y; whether the index	and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: 6 item s 6 item screener, 6	creener (≥6)							
Results	True positives:	105	False	240	False positives:	2	True negatives:	304
			negatives:					
Additional comme nts	have suspected de	mentia at ba	xcluded as the peop aseline. For the ana	ysis presented t	community- based sa he paper does not sta e non-dementia group	te whether t		
nts	have suspected de	mentia at ba ognitive imp	xcluded as the peop aseline. For the ana	ysis presented t a or if it is just the	he paper does not sta	te whether t		
	have suspected de no dementia and converse Patient selection: Serious (It was und	mentia at ba ognitive imp Low clear whethe	ccluded as the peop aseline. For the anal airment no dementian Index test:	ysis presented to a or if it is just the High andom sample c	he paper does not sta e non-dementia group Reference	te whether the alone. Low d in the stud	he comparator group Flow and timing:	include Low
nts Risk of bias	have suspected de no dementia and converse Patient selection: Serious (It was und	mentia at ba ognitive imp Low clear whether re independ	ccluded as the peop aseline. For the anal airment no dementian Index test:	ysis presented to a or if it is just the High andom sample of the test thresh	he paper does not stare non-dementia group Reference standard: If patients was enrolled	te whether the alone. Low d in the stud	he comparator group Flow and timing:	include Low

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Results	True positives:	338	False negatives:	7	False positives:	107	True negatives:	199
Additional comme nts	have suspected de	mentia at ba	aseline. For the anal	ysis presented t	community- based sa he paper does not sta e non-dementia group	te whether th		
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias					f patients was enrolled old was not pre-specif		y; whether the index	and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
ndex Test: MMSE (MMSE, ≤ 26	<27)							
Results	True positives:	326	False	19	False positives:	67	True possitives:	239
		5_5	negatives:		i aise positives.	67	True negatives:	239
Additional comme	The data for cohort have suspected de	t one was ex mentia at ba	negatives: ccluded as the peop aseline. For the anal	le consisted of a ysis presented t	community- based sa he paper does not sta e non-dementia group	imple screer te whether t	ned for dementia and	I did not
Additional comme	The data for cohort have suspected de	one was ex mentia at ba ognitive imp	negatives: ccluded as the peop aseline. For the anal	le consisted of a lysis presented t a or if it is just the	community- based sa he paper does not sta	imple screer te whether t	ned for dementia and	I did not
Additional comme	The data for cohort have suspected de no dementia and considerable Patient selection: Serious (It was und	t one was ex mentia at ba ognitive imp Low clear whether	negatives: coluded as the people aseline. For the analysisment no demention index test: er a consecutive or reserved.	le consisted of a lysis presented to a or if it is just the High andom sample c	community- based sa he paper does not sta e non-dementia group Reference	imple screer te whether the alone. Low d in the stud	ned for dementia and he comparator group Flow and timing:	I did not include Low
Additional comments	The data for cohort have suspected de no dementia and considerable Patient selection: Serious (It was und	t one was ex mentia at be ognitive imp Low clear whether re independ	negatives: coluded as the people aseline. For the analysisment no demention index test: er a consecutive or reserved.	le consisted of a ysis presented t a or if it is just the High andom sample of d the test thresh	community- based sa he paper does not sta e non-dementia group Reference standard: of patients was enrolled	imple screer te whether the alone. Low d in the stud	ned for dementia and he comparator group Flow and timing:	I did not include Low

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Results	True positives:	308	False negatives:	37	False positives:	49	True negatives:	257
Additional comme nts	have suspected de	mentia at ba	aseline. For the anal	ysis presented t	community- based sa he paper does not sta e non-dementia group	te whether t		
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias					of patients was enrolled old was not pre-specif		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	53	False positives:	30	True pegatives:	276
		202	negatives:		i alse positives.	30	True negatives:	276
Additional comme	The data for cohort have suspected de	one was ex mentia at ba	negatives: xcluded as the peop aseline. For the anal	le consisted of a lysis presented t	community- based sa he paper does not sta e non-dementia group	ample screer te whether t	ned for dementia and	I did not
Additional comme	The data for cohort have suspected de	one was ex mentia at ba ognitive imp	negatives: xcluded as the peop aseline. For the anal	le consisted of a lysis presented t a or if it is just the	community- based sa he paper does not sta	ample screer te whether to alone.	ned for dementia and	I did not
Additional comme nts	The data for cohort have suspected de no dementia and considerable Patient selection: Serious (It was uno	one was ex mentia at ba ognitive imp Low lear whethe	negatives: Accluded as the people aseline. For the analysisment no demention index test: er a consecutive or research	le consisted of a ysis presented t a or if it is just the High andom sample c	community- based sa he paper does not sta e non-dementia group Reference	ample screer te whether to alone. Low d in the stud	ned for dementia and he comparator group Flow and timing:	I did not include Low
Additional comme nts Risk of bias	The data for cohort have suspected de no dementia and considerable Patient selection: Serious (It was uno	one was ex mentia at ba ognitive imp Low lear whether e independ	negatives: Accluded as the people aseline. For the analysisment no demention index test: er a consecutive or research	le consisted of a ysis presented t a or if it is just the High andom sample of d the test thresh	community- based sa he paper does not sta e non-dementia group Reference standard: of patients was enrolled	ample screer te whether to alone. Low d in the stud	ned for dementia and he comparator group Flow and timing:	I did not include Low

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Results	True positives:	281	False negatives:	64	False positives:	20	True negatives:	286
Additional comme nts	have suspected de	mentia at ba	aseline. For the anal	ysis presented t	community- based sa he paper does not sta e non-dementia group	te whether t		
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias					f patients was enrolled old was not pre-specification.		y; whether the index	and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (4 MMSE, ≤ 22	<23)							
Results	True positives:	265	False negatives:	80	False positives:	14	True negatives:	292
				la capaiated of a	., .		and for domantic and	
Additional comme nts		mentia at ba	aseline. For the anal	ysis presented t	community- based sa he paper does not sta e non-dementia group	te whether t		
	have suspected de	mentia at ba ognitive imp	aseline. For the anal	ysis presented to a or if it is just the	he paper does not sta	te whether t alone.		
nts	have suspected de no dementia and converse Patient selection: Serious (It was und	mentia at ba ognitive imp Low lear whethe	aseline. For the analyairment no demention index test: er a consecutive or researched.	ysis presented to a or if it is just the High andom sample o	he paper does not sta e non-dementia group Reference	te whether to alone. Low d in the stud	he comparator group Flow and timing:	include Low
nts Risk of bias	have suspected de no dementia and converse Patient selection: Serious (It was und	mentia at ba ognitive imp Low clear whether e independ	aseline. For the analyairment no demention index test: er a consecutive or researched.	ysis presented to a or if it is just the High andom sample of d the test thresh	he paper does not sta e non-dementia group Reference standard: f patients was enrolled	te whether to alone. Low d in the stud	he comparator group Flow and timing:	include Low

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Callahan CM, Unvers Med Care. 2002;40(9			n screener to identi	fy cognitive im	pairment among pot	ential subje	cts for clinical rese	earch.
Results	True positives:	252	False negatives:	93	False positives:	9	True negatives:	297
Additional comme nts	have suspected de	mentia at ba	aseline. For the anal	ysis presented t	community- based sa he paper does not sta e non-dementia group	te whether th		
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias					of patients was enrolled sold was not pre-specif		y; whether the index	and
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

	spejo-Martinez B, Lopez-Alcalde S, Espinosa-Garcia M, Saez-Zea C, Vilchez-Carrillo R, et al. Effectiveness and costs of tia 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	o dementia

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Carnero-Pardo C, Es phototest in dement						R, et al. E	ffectiveness and cos	ts of
Index Test: phototes		pairinent S	creening. Divid Net	irology zu i i, i	1. 92.			
phototest ≤ 26. Spani								
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 MIS (Memory Impairn			h					
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 indirectness	Not serious							
Index Test: Memory	Impairment Screen	, MIS (<5)						
MIS (Memory Impairn	nent Screen), cut off	4/5. Spanisl	h					
Results	True positives:	29	False negatives:	1	False positives:	25	True negatives:	62
Additional comme								

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Carnero-Pardo C, Es phototest in dement nts						R, et al. Eff	ectiveness and cos	ts of
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							

Vilchez-Carrillo R, e Creavin S. Solicitud	t al. Effectiveness a	nd costs of a la revisió	f phototest in demo n Cochrane : Efect	entia and cogni tividad del Mini	rtinez B, Lopez-Alca tive impairment scre -Mental en la detecci	ening. BM0	C Neurology 2011;1	1: 92.]		
Study type	Prospective cohort									
Country	Spain									
Setting	Four primary care of	entres in th	e Metropolitan Distr	ict of North Gran	ada plus 1 health cen	tre in Madrid	b			
Inclusion criteria		•		•	ve complaints of memo	•	•	milar		
Exclusion criteria	Previous enrolment in this study or previous diagnosis of cognitive or dementia.									
Sex	29.2% male									
Age	Mean age 72.6 yea	rs (SD not s	stated)							
Presentation	Memory loss compl general observation		he patient, the famil	y or the person a	accompanying them, o	or suspected	by the doctor on the	basis of		
Reference standard	Clinician diagnosis DSM-IVR criteria fo		e Cognitive-Behavio	oural Neurology	Unit evaluations and a	a detailed cli	inical assessment us	ing the		
Dementia versus no	dementia									
Index Test: MMSE (<25)									
MMSE (Folstein 1975	version), cut off 24/2	25, Spanish	version							
Results	True positives:	77	False	0	False positives:	175	True negatives:	108		

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			negatives:					
Additional comme nts	Granada data from	February 2	008 to January 2009). ´	h centre between April sented here as these c		•	
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 selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE (Folstein 1975	•	24, Spanish	version					
Results	True positives:	77	False negatives:	0	False positives:	153	True negatives:	130
Additional comme nts	Granada data from	February 2	008 to January 2009). [']	h centre between April sented here as these c			
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 selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<	•							
MMSE (Folstein 1975	,.							
Results	True positives:	76	False	1	False positives:	122	True negatives:	161

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			negatives:					
Additional comme nts	Granada data from	February 2	008 to January 2009). ´	h centre between Apri sented here as these c		•	
Risk of bias	Patient selection:		Index test:	•	Reference standard:	Low	Flow and timing:	
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							
Index Test: MMSE (•							
MMSE (Folstein 1975	version), cut off 21/	22, Spanish						
Results	True positives:	74	False negatives:	3	False positives:	93	True negatives:	190
Additional comme nts	Granada data from	February 2	008 to January 2009). [']	h centre between Apri sented here as these c		·	
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							
Index Test: MMSE (<21)							
	(version) out off 20/	21 Spanish	version					
MMSE (Folstein 1975 Results	True positives:		False		False positives:		True negatives:	

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			negatives:					
Additional comme nts	Granada data from	February 2	008 to January 2009). ´	h centre between Apri sented here as these c		•	
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							
Index Test: MMSE (< MMSE (Folstein 1975	•	20, Spanish	version.					
Results	True positives:	72	False negatives:	5	False positives:	51	True negatives:	232
Additional comme nts	Granada data from	February 2	008 to January 2009). [']	h centre between Apri sented here as these c			
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		
	Not serious							
Overall risk of bias Indirectness Overall indirectness Index Test: MMSE (<	selection: Serious (Multiple te Patient selection: Not serious	est threshold	s were used)		standard:			
MSE (Folstein 1975	version), cut off 18/	19, Spanish	version					
Results	True positives:	60	False	0	False positives:	27	True negatives:	246

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			negatives:					
Additional comme nts	Granada data from	February 20	008 to January 2009). ´	h centre between Apri sented here as these c		•	
Risk of bias	Patient selection:		Index test:		Reference standard:	Low	Flow and timing:	
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							
Index Test: MMSE (< MMSE (Folstein 1975	•	/18, Spanish	version					
Results	True positives:	62	False negatives:	15	False positives:	23	True negatives:	260
Additional comme nts	Granada data from	February 20	008 to January 2009). ´	h centre between Apri sented here as these c		•	
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							
Index Test: MMSE (<	(17)							
MMSE (Folstein 1975	*							
Results	True positives:	54	False	23	False positives:	20	True negatives:	263

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

	ruz-Orduña I, Espejo-Martínez B, Martos-Aparicio C, López-Alcalde S, Olazarán J. Utility of the Mini-Cog for detection of nt 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	o dementia (including MCI)
Index Test: Mini-Co	g (≤2)

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Carnero-Pardo C, Cr cognitive impairmen								on of
Mini-Cog data extract	ed from MMSE and	clock drawir	ng test (Spanish vers	sion), ≤ 2 cut off				
Results	True positives:	49	False negatives:	0	False positives:	56	True negatives:	37
Additional comme nts	primary study. The to the Granada studentum has been known by the indiving was only available. The data for the CI	The data presented here was obtained from an unpublished Cochrane review using published and unpublished data from the primary study. The published primary study includes data from 2 study sites, but the Cochrane review authors used data confined to the Granada study sites as part of the Mini-Cog test (the CDT) was included as part of the reference standard in Madrid and was known by the individuals completing the reference standard. Also, the diagnosis of dementia separate from cognitive impairment was only available in the Granada sample and the data was made available to the CR group by the authors. The data for the CDT and MMSE were not extracted here as the primary study authors grouped mild cognitive impairment and dementia together in their analysis and we could not separate them with the information provided.						
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (The test 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							

	Ho H-F, Ho K-M, Lam ET-K, Leung W-L, Kam K-M. Use of cerebrospinal fluid enzyme immunoassay for diagnosis of national 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

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

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	nentia

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(normal + MCI)								
Index Test: Montrea	l Cognitive Assess	ment, MoCA	A (<19)					
Montreal Cognitive As	ssessment (MoCA),	18/19, Singa	porean version					
Results	True positives:	162	False negatives:	10	False positives:	49	True negatives:	95
Additional comme nts	published and unp	ublished dat	a from the Chen 201	11 authors. Chei	was obtained from Da n 2011 is a conference studies were exclude	e abstract ar		
Risk of bias	Patient selection:	Unclear	Index test:	Unclear	Reference standard:	Unclear	Flow and timing:	High
Overall risk of bias					led or if a pre-specified ach other and whether			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall	Not serious							
indirectness								
Chohan G, Penningt other proteins in the 1243-8.	diagnosis of spor	adic Creutz			RS, Green AJ. The r 0-year review. J Neu			
Chohan G, Penningt other proteins in the 1243-8. Study type		adic Creutz						
Chohan G, Penningtother proteins in the 1243-8. Study type Country	Retrospective coho	adic Creutz	feldt-Jakob diseas					
Chohan G, Penningtother proteins in the 1243-8. Study type Country Setting	Retrospective coho	ort eillance Unit	feldt-Jakob diseas	e in the UK: a 1				
Chohan G, Penningtother proteins in the 1243-8. Study type Country Setting Inclusion criteria	Retrospective coho	ort eillance Unit	feldt-Jakob diseaso	e in the UK: a 1				
Chohan G, Penningt	Retrospective cond UK National CJD surve People referred to	ort eillance Unit	feldt-Jakob diseaso	e in the UK: a 1				

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Presentation	Rapidly progressive	Rapidly progressive dementia leading to suspected CJD								
Reference standard		Confirmed CJD based on neuropathological data, non-CJD diagnosis based on neuropathology or alternative clinical diagnosis, asis for probable CJD diagnosis is unclear.								
confirmed CJD vers	us not CJD									
Index Test: CSF 14-3 Presence of a detecta	_									
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					the included groups pependently of each ot		issing without explar	nation; it i		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									
Index Test: Total Ta) - 4000/	1							
CSF Total Tau (Innote Results	True positives:	,	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		
	0	analysis with	h > 100/ nonulation	ovaludad and in	the included groups of	oonlo ara m	icaina without avalar	otion: it		
Overall risk of bias	Serious (Subgroup unclear whether the				ependently of each ot		issing without explai	iation, it		

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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 Not serious indirectness Index Test: S100B, 1.0ng/ml CSF S100b assayed using an ELISA, >1.0ng/ml True positives: 158 False 85 False positives: 17 True negatives: 152 Results negatives: Age range was 28-89 years old. Analysis excludes people diagnosed with probable CJD, but lacking neuropathological Additional comme confirmation. nts Patient Low Hiah Risk of bias Index test: Low Reference Low Flow and standard: selection: timing: Overall risk of bias Serious (Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.) Indirectness Patient Low Index test: Low Reference Low selection: standard: Overall Not serious indirectness Index Test: CSF 14-3-3 (presence) and S100b (>1.0ng/ml) Presence of a detectable 14-3-3 band in CSF sample and CSF S100b assayed using an ELISA, >1.0ng/ml False 91 False positives: 9 True negatives: 160 Results True positives: 151 negatives: Age range was 28-89 years old. Analysis excludes people diagnosed with probable CJD, but lacking neuropathological Additional comme confirmation. nts Risk of bias Patient Low Index test: Low Reference Flow and High Low selection: standard: timina: Serious (Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is Overall risk of bias unclear whether the reference and index tests were interpreted independently of each other.) Indirectness Patient Low Index test: Low Reference Low selection: standard:

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Overall indirectness	Not serious	Not serious								
Index Test: Total Ta	u and S100b									
CSF Total Tau (Innote	est h-TAU -Ag assay), >1260pg/ı	ml and CSF S100b	assayed using a	n 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	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). >1260pg/i	ml and presence of	a detectable 14-	3-3 band in CSF sam	ole.				
Results	True positives:	162	False negatives:		False positives:		True negatives:	119		
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					the included groups p ependently of each otl		nissing without explar	nation; it		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				

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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. True positives: 123 False positives: 6 True negatives: 129 Results False 93 negatives: Age range was 28-89 years old. Analysis excludes people diagnosed with probable CJD, but lacking neuropathological Additional comme confirmation. nts Risk of bias Patient Low Index test: Low Hiah Reference Flow and Low selection: standard: timing: Overall risk of bias Serious (Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.) **Indirectness** Patient Low Index test: Low Reference Low selection: standard: Overall Not serious indirectness Christensen IT, Larsson E-M, Holm IE, Nielsen OBF, Andersen S. Olfactory testing in consecutive patients referred with suspected dementia. BMC Geriatrics 2017; 17: 129-135. Study type Prospective cohort Denmark Country Aalborg University Hospital geriatric outpatient clinic Settina Patients referred to the geriatric outpatient clinic at Aalborg University Hospital for evaluation of cognitive decline. Inclusion criteria A history of nose-throat pathology with increasing sinusitis or chronic sinusitis, a flue condition, previous brain trauma, concussion **Exclusion criteria** of the brain with unconsciousness, and cerebral surgery. Sex 52% male Mean age 79.1 years (no SD provided) Age **Presentation** Suspected dementia

Reference

Clinician diagnosis of probable AD according to the ICD-10 criteria suported by other criteria

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Chohan G, Pennington C, Mackenzie JM, Andrews M, Everington D, Will RG, Knight RS, Green AJ. The role of cerebrospinal fluid 14-3-3 and other proteins in the diagnosis of sporadic Creutzfeldt-Jakob disease in the UK: a 10-year review. J Neurol Neurosurg Psychiatry. 2010; 81: 1243-8.

standard

AD versus non-AD

Index Test: Olfactory test, ≥ 3 errors

Olfactory test, ≥ 3 errors. Using Pocket Smell Test pads that released odours when scratched. Each included three different scents, with each patient exposed to 6 different scents. In the case of uncertainty the test was repeated and the patient was given one additional opportunity to complete the test. The patient had to match the scent to one of four named choices.

Results	True positives:	19	False negatives:	5	False positives:	14	True negatives:	12
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Not serious (Althou	igh the thres	shold was not pre-sp	pecified data was	presented for all pos	sible cut offs	S.)	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

Index Test: Olfactory test, ≥ 4 errors

Olfactory test, ≥ 4 errors. Using Pocket Smell Test pads that released odours when scratched. Each included three different scents, with each patient exposed to 6 different scents. In the case of uncertainty the test was repeated and the patient was given one additional opportunity to complete the test. The patient had to match the scent to one of four named choices

Results	True positives:	12	False negatives:	12	False positives:	7	True negatives:	19
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Not serious (Althou	gh the thres	shold was not pre-sp	ecified data was	presented for all pos	sible cut offs	S.)	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Olfactory	y test, ≥ 5 errors							

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Chohan G, Pennington C, Mackenzie JM, Andrews M, Everington D, Will RG, Knight RS, Green AJ. The role of cerebrospinal fluid 14-3-3 and other proteins in the diagnosis of sporadic Creutzfeldt-Jakob disease in the UK: a 10-year review. J Neurol Neurosurg Psychiatry. 2010; 81: 1243-8.

Olfactory test, ≥ 5 errors. Using Pocket Smell Test pads that released odours when scratched. Each included three different scents, with each patient exposed to 6 different scents. In the case of uncertainty the test was repeated and the patient was given one additional opportunity to complete the test. The patient had to match the scent to one of four named choices.

Results	True positives:	5	False negatives:	19	False positives:	4	True negatives:	22
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Not serious (Althou	igh the thres	shold was not pre-sp	ecified data was	presented for all pos	sible cut offs	S.)	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

Coulthart M, Jansen GH, Olsen E, Godal D, Connolly, T, Choi BCK, Wang Z, Cashman NR. Diagnostic accuracy of cerebrospinal fluid protein markers for sporadic Creutzfeldt-Jakob disease in Canada: a 6-year prospective study. BMC Neurology 2011, 11:133.

Study type	Prospective cohort
Country	Canada
Setting	CJD surveillance system laboratory
Inclusion criteria	People with suspected CJD.
Exclusion criteria	Not stated
Sex	51.4% male
Age	Median age ranged from 63-66 years across CJD and not CJD groups.
Presentation	Rapidly progressive dementia leading to suspected CJD
Reference standard	Neuropathology was carried out on 170/1000 participants, with clinician diagnosis of non-CJD for the remaining participants.

CJD versus not CJD

Index Test: CSF 14-3-3 immunoblotting

14-3-3 in CSF, detection by immunoblotting at threshold of approximately 1.5ng control 14-3-3 protein per lane.

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Results	True positives:	112	False negatives:	15	False positives:	244	True negatives:	629
Additional comme nts	duplicate samples; diagnostic classifica	(iii) unconfir ation was ge a criterion t	med suspected CJE enetic prion disease; o classify such case	o at sample sub (vi) final diagno	e sample was technica mission; (iv) the 14-3-3 estic classification was t be included in the va	assay resu probable s0	ult was indeterminate CJD (as a positive 14	; (v) fina -3-3
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Not serious (Not do	owngraded 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 Ta tau in CSF, INNOTES	·	ut off 976pg	ı/ml					
Results	True positives:	109	False negatives:	11	False positives:	99	True negatives:	727
Additional comme nts	duplicate samples; diagnostic classifica	(iii) unconfir ation was ge a criterion t	med suspected CJE enetic prion disease; o classify such case	o at sample sub (vi) final diagno	e sample was technica mission; (iv) the 14-3-3 estic classification was t be included in the va	assay resu probable s0	ılt was indeterminate CJD (as a positive 14	; (v) fina -3-3
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias					whether the reference data analysis as <10%			ify non-
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall	Not serious				Standard.			

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tau in CSF, INNOTES	ST hTau-Ag ELISA, c	ut off 1300p	og/ml					
Results	True positives:	101	False negatives:	19	False positives:	66	True negatives:	760
Additional comme nts	duplicate samples; diagnostic classific	(iii) unconfir ation was ge a criterion t	rmed suspected CJE enetic prion disease; o classify such case	at sample sub (vi) final diagno	e sample was technical mission; (iv) the 14-3-3 estic classification was t be included in the val	assay resu probable s0	It was indeterminate CJD (as a positive 14	; (v) final -3-3
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias					ctly classify non-CJD o			graded fo
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: S100B, 3 S100B, Sangtec 100	2.5ng/ml ELISA kit, cut off 2.5	ng/ml						
Results	True positives:	106	False negatives:	16	False positives:	104	True negatives:	698
Additional comme nts	duplicate samples; diagnostic classific	(iii) unconfir ation was ge a criterion t	rmed suspected CJE enetic prion disease; o classify such case	o at sample sub (vi) final diagno	e sample was technical mission; (iv) the 14-3-3 ostic classification was t be included in the va	assay resu probable s0	It was indeterminate CJD (as a positive 14	; (v) final -3-3
Risk of bias	Patient	Low	Index test:	High	Reference	Low	Flow and	Low

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Coulthart M, Jansen	GH, Olsen E, Goda	l D, Conno	lly, T, Choi BCK, W	lang Z, Cashma	an NR. Diagnostic ac	curacy of c	erebrospinal fluid լ	orotein	
markers for sporadio	c Creutzfeldt-Jakob	disease in	Canada: a 6-year	prospective stu	idy. BMC Neurology	2011, 11:13	3.		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								
Index Test: S100B, 4 S100B, Sangtec 100		ng/ml							
Results	True positives:	63	False negatives:	59	False positives:	24	True negatives:	778	
Additional comme nts	duplicate samples; diagnostic classific result was used as	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 prior 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					ctly classify non-CJD o			graded fo	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								
Coutinho G, De Olive Alzheimer's disease	•	•	· · · · · · · · · · · · · · · · · · ·	•	entify individuals with 2013;40:139-43	n mild cogn	itive impairment ar	nd	
Study type	Prospective cohort								
Country	Brazil								
Setting	Private clinic								

Not stated

Inclusion criteria

Exclusion criteria

People referred by their physicians because of memory complaints.

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Sex	38.2% male	38.2% male								
Age	Mean age 73.9 yea	Mean age 73.9 years (7.1)								
Presentation	Memory complaint	s								
Reference standard	(Logical Memory fr Vocabulary from W	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, /ocabulary 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 (includir	ig MCI)								
	Neuropsychological T ts (The brief battery cor SE)	_		e Wechsler Me	mory Scale III, digit spa	an, clock dr	awing, verbal categor	y fluen		
Results	True positives:	48	False negatives:	5	False positives:	13	True negatives:	65		
	Patient	Low	Index test:	Unclear	Reference	Low	Flow and	Low		
Risk of bias	selection:				standard:		timing:			
	selection:				standard:		uming:			
Risk of bias Overall risk of bia Indirectness	selection:	Low	Index test:	Low	Reference standard:	Low	uming:			

Cruz-Orduna I, Bellon JM, Torrero P, Aparicio E, Sanz A, Mula N, et al. Detecting MCI and dementia in primary care: effectiveness of the MMS,	
the FAQ and the IQCODE. Family Practice 2012; 29: 401-6.	

Study type	prospective cohort
Country	Spain
Setting	Seven medical clinics of the Pena Prieta Primary Care Centre (Health District 1, Autonomous Community of Madrid).
Inclusion criteria	
	Age >49 years; any complaint or suspicion raised by the patient, an informant or primary care physician related to cognition; a reliable informant

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Exclusion criteria	Not stated	Not stated								
Sex	29.1% male	29.1% male								
Age	Mean age 72.2 yea	Mean age 72.2 years (SD 8.9)								
Presentation	Complaint or suspi-	Complaint or suspicion of cognitive 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	ore-specified but we	re calculated to	give optimum sensitivi	ty and spec	ificity.)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									
Index Test: Informar Informant Questionna			· · · · · · · · · · · · · · · · · · ·	•						
Results	True positives:	12	False negatives:	3	False positives:	34	True negatives:	111		
Additional comme nts										
D: 1 (1)	Patient	Low	Index test:	High	Reference	Low	Flow and	Low		
Risk of bias	selection:				standard:		timing:			
Overall risk of bias		ls were not p	ore-specified but we	re calculated to	standard: give optimum sensitivi	ty and spec				

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Cruz-Orduna I, Bello the FAQ and the IQC				I. Detecting MC	I and dementia in pr	imary care:	effectiveness of th	e MMS,
Overall indirectness	Not serious							
Index Test: Function FAQ (Functional Activ		•		ce). Spanish. Cı	ut 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 p	ore-specified but we	re calculated to	give optimum sensitivi	ty and spec	ificity.)	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

	N, Jiménez-Huete A, Albo C, Hortigüela R, Vega L, Cerrato L, Sierra-Moros M, Rábano A, de Pedro-Cuesta J, Calero M. al 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

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CJD versus not CJD								
Index Test: CSF 14-3 CSF 14-3-3 protein, ir	_							
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 sampl	es; <10 % exclu	ded from analysis for	possible CJ	D so not downgraded	d for th
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

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	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 assesssment
Exclusion criteria	A history of head trauma or loss of consciousness; curent diagnosis of active brain neoplasm or infection.
Sex	66.7% male
Age	Median age 39 years (range 33-47)
Presentation	Neurological issues
Reference standard	Clinician diagnosis using the American Academy of Neurology criteria
HAND versus other	neurological disorder in HIV+ people

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vioaitiea HIV aement	ia scale (m-HDS), cu	e (m-HDS) (t-off <7.5	(~1.5)					
Results	True positives:		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			s used; unclear whe r random patients w		est was interpreted with	nout knowle	dge of the reference	test;
ndirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low		
Overall ndirectness	Serious (Study par	ticipants we	re aged from 33-47	years, median 3	9 years.)			
ndex Test: Grooved Grooved pegboard te	d pegboard test est, cut-off 1.5SD belo	ow the expe	cted age-and educa	tion- adjusted m	ean.			
Results	True positives:	102	False negatives:	42	False positives:	168	True negatives:	143
Additional comments								
Risk of bias	Patient selection:	Unclear	Index test:	Unclear	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (Unclear was random patients we		-	reted without kn	owledge of the referer	nce test; und	clear whether consec	utive or
ndirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low		
Overall	Serious (Study par	ticipants we	re aged from 33-47	years, median 3	9 years.)			
ndirectness								

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Davis HF, Skolasky grooved pegboard.				ssing HIV-asso	ciated dementia: mo	dified HIV d	ementia scale vers	us the
			negatives:					
Additional comme nts								
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias			s used; unclear whe r random patients w		est was interpreted with	nout knowle	dge of the reference	test;
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low		
Overall indirectness	Serious (Study par	ticipants we	re aged from 33-47	years, median 3	9 years.)			

Dobert N, Pantel J, F	rolich L, Hamscho N, Menzel C, Grunwald F. Diagnostic value of FDG-PET and HMPAO-SPET in patients with mild									
dementia and mild c	ementia 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 Dementia diagnosed based on all available information apart from PET and SPET index test results and using NINCDS-ADRDA for Standard 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.

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Results	True positives:	102	False negatives:	41.76	False positives:	167.94	True negatives:	143.06	
Additional comme	Additional subgrou	p analyses v	were not carried out	as the numbers	of study participants v	was very sm	nall (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 Not serious Not serious									
Index Test: FDG-PE FDG-PET. Carried ou coronal images were	it using a whole body reconstructed with a	n iterative re	econstruction algorit	hm (slice thickne	cquisition starting 45 ress 3.49mm, pixel size	• 1.03mm). S	Scans assess qualita	tively by	
Index Test: FDG-PE FDG-PET. Carried ou coronal images were by 2 experienced nuc	it using a whole body reconstructed with a lear medicine physic	n iterative re ians and for	econstruction algoriter quantitative analysi	hm (slice thickne is the MI was me	ess 3.49mm, pixel size easure based on a sta	• 1.03mm). S	Scans assess qualita	tively by	
Index Test: FDG-PE FDG-PET. Carried ou coronal images were	it using a whole body reconstructed with a lear medicine physic	n iterative re ians and for ge patterns	econstruction algority quantitative analyst are described in det	hm (slice thickne is the MI was me	ess 3.49mm, pixel size easure based on a sta	• 1.03mm). S	Scans assess qualita	tively by	
Index Test: FDG-PE FDG-PET. Carried ou coronal images were by 2 experienced nuc consisting of 16 ROIs Results Additional comme	It using a whole body reconstructed with a lear medicine physic The qualitative ima True positives:	n iterative re ians and for ge patterns 111	econstruction algoritic quantitative analysic are described in det False negatives:	hm (slice thickness the MI was metail the methods.	ess 3.49mm, pixel size easure based on a sta	e 1.03mm). s ndardized re	Scans assess qualita egion of interest (RO	tively by I) analysi	
Index Test: FDG-PE FDG-PET. Carried ou coronal images were by 2 experienced nuc consisting of 16 ROIs Results Additional comme nts	It using a whole body reconstructed with a lear medicine physic The qualitative ima True positives:	n iterative re ians and for ge patterns 111 p analyses v	econstruction algoritic quantitative analysic are described in det False negatives:	hm (slice thickness the MI was me tail the methods. 33.12 as the numbers	ess 3.49mm, pixel size easure based on a sta	e 1.03mm). s ndardized re	Scans assess qualita egion of interest (RO	tively by I) analysi	
Index Test: FDG-PE FDG-PET. Carried outcoronal images were by 2 experienced nuctoonsisting of 16 ROIs Results Additional comments Risk of bias	at using a whole body reconstructed with a clear medicine physic. The qualitative image True positives: Additional subgroup Patient selection:	n iterative reians and for ge patterns 111 p analyses v	econstruction algority r quantitative analysis are described in det False negatives: were not carried out Index test:	hm (slice thickness the MI was mediail the methods. 33.12 as the numbers	False positives: of study participants v	e 1.03mm). Sindardized re 186.6 was very sm	Scans assess qualitategion of interest (RO True negatives: all (n=24) Flow and timing:	tively by I) analysi 124.4 Low	
Index Test: FDG-PE FDG-PET. Carried ou coronal images were by 2 experienced nuc consisting of 16 ROIs	reconstructed with a reconstructed with a reconstructed with a relear medicine physic. The qualitative image True positives: Additional subgroup Patient selection: Serious (It is unclear	n iterative reians and for ge patterns 111 p analyses v Unclear ar whether a	econstruction algority r quantitative analysis are described in det False negatives: were not carried out Index test:	hm (slice thickness the MI was mediail the methods. 33.12 as the numbers Low dom sample of page 1.55 thickness the number of page 1.55 thi	False positives: of study participants v Reference standard:	e 1.03mm). Sindardized re 186.6 was very sm	Scans assess qualitategion of interest (RO True negatives: all (n=24) Flow and timing:	tively by I) analysi 124.4 Low	

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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. 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 0 False positives: 1 True negatives: 5 negatives: Additional comme Additional subgroup analyses were not carried out as the numbers of study participants was very small (n=24) nts Risk of bias Patient Unclear Index test: Reference Flow and Low Low Low selection: standard: timing: Serious (It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were Overall risk of bias avoided.) Patient Low **Indirectness** Index test: Low Reference Low selection: standard: Overall Not serious indirectness Index Test: 99mTc-HMPAO SPECT (all dementia patterns) 99mTc-HMPAO SPECT. Transaxial, saggital and coronal images were reconstructed by a filtered back projection method using a Butterworth filter. Scans assess qualitatively by 2 experienced nuclear medicine physicians and for quantitative analysis a perfusion index was measured based on a standardised ROI analysis. The qualitative image patterns are described in detail the methods. True negatives: 2 Results True positives: 16 False 2 False positives: 4 negatives: Additional comme Subgroup analysis was not carried out as the numbers of study participants was very small (n=24) nts Risk of bias Patient Unclear Index test: Low Reference Low Flow and Low selection: standard: timina: Overall risk of bias Serious (It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided.) Patient Low Index test: Low Reference Low Indirectness selection: standard:

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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.

Overall indirectness

Not serious

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	ot stated									
Sex	54.4% male										
Age	Mean age 67.1 year	rs (SD 7.5)									
Presentation	Suspected dementia	а									
Reference standard	Aging– Alzheimer's	Association y, 1998), M NINDS–Soc	n (NIA-AA) criteria. (cKeith criteria (2005 iety for Progressive	Other criteria inc 5) for DLB, NIND Supranuclear	eria, and all patients r lude: the consensus c S-AIREN for VaD; crit	riteria for fro	ontotemporal lobar				
AD versus no deme	ntia (SMC, excludes	MCI)									
Index Test: Amyloid	l Beta 1-42										
Amyloid Beta 1-42, IN	NOTEST ELISA, cut	off < 550 p	g/ml								
Results	True positives:	517	False	114	False positives:	33	True negatives:	218			

7 milyiola Bota 1 12, iii		. o ooo p	9,					
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			excluded; uncle	ar whether consecutiv	e or random	n patients were enrol	led or
Indirectness	Patient	Low	Index test:	Low	Reference	Low		

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	selection:				standard:			
Overall ndirectness	Not serious							
AD versus other de	mentias (excluding	MCI)						
ndex Test: Amyloid								
Amyloid Beta 1-42, II	NNOTEST ELISA, cu	t-off < 550 p	og/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 inappropria			excluded; uncle	ear whether consecutiv	e or rando	m patients were enrol	led or
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus not AD (SMC and other dem	entias, exc	luding MCI)					
de voicae not ite (
Index Test: Amyloid	i Beta 1-42 NNOTEST ELISA, cu	t-off < 550 p	og/ml					
Index Test: Amyloid			og/ml False negatives:	114	False positives:	107	True negatives:	411
Index Test: Amyloid Amyloid Beta 1-42, IN	NNOTEST ELISA, cu		False	114 Low	False positives: Reference standard:	107 Low	True negatives: Flow and timing:	411 Low
ndex Test: Amyloid Amyloid Beta 1-42, If Results Risk of bias	NNOTEST ELISA, cui True positives: Patient	517	False negatives:		Reference		Flow and	
ndex Test: Amyloic Amyloid Beta 1-42, IN Results	NNOTEST ELISA, cui True positives: Patient selection:	517 Unclear	False negatives:		Reference		Flow and	

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Index Test: Total tar	u							
t-tau, INNOTEST ELI	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.)							led or
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus other de	mentias (excluding	MCI)						
Index Test: Total tau t-tau, INNOTEST ELI		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			excluded; uncle	ar whether consecutiv	e or random	n patients were enrol	led or
	Patient	Low	Index test:	Low	Reference	Low		
Indirectness	selection:				standard:			
Overall					standard:			
Overall indirectness	selection: Not serious	entias, exc	luding MCI)		standard:			
Overall indirectness AD versus not AD (selection: Not serious SMC and other dem	entias, exc	luding MCI)		standard:			
Overall indirectness AD versus not AD (Sindex Test: Total tag Total tau, INNOTEST	selection: Not serious SMC and other dem		luding MCI)		standard:			

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			negatives:					
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus no deme	entia (SMC, excludes	MCI)						
Index Test: p-tau 18 p-tau 181, INNOTES	<mark>31</mark> 3T 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			excluded; uncle	ar whether consecutiv	e or rando	m patients were enrol	led or
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus other de	mentias (excluding	MCI)						
Index Test: p-tau 18	31							
p-tau 181, INNOTES	T 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

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	whether inappropri		ns were avoided.)					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus not AD (SMC and other dem	entias, exc	luding MCI)					
Index Test: p-tau 18 p-tau 181, INNOTES		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 deme	ntia (SMC, excludes	MCI)						
375 pg/ml; p-tau 181,	nd t-tau and/or p-tau , INNOTEST ELISA,	181 abnorm cut-off > 52	al. Amyloid Beta 1-4 pg/ml.				INNOTEST ELISA, cu	
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
	Serious (Subgroup	analysis wi	th > 35% population	excluded; uncle	ear whether consecutive	e or rando	om patients were enrol	led or
Overall risk of bias	whether inappropri			,			, 	

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Overall indirectness	Not serious							
AD versus other de	mentias (excluding	MCI)						
Index Test: Amyloid	l Beta 1-42 and t-taι	and/or p-ta	au abnormal					
Amyloid Beta 1-42 ar 375 pg/ml; p-tau 181				2, INNOTEST E	ELISA, cut-off < 550 pg	g/ml; t-tau,	INNOTEST ELISA, cu	ıt-off >
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 inappropri	-	• •	excluded; uncle	ear whether consecutive	e or rando	om patients were enrol	led or
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall	Not serious							
indirectness								
indirectness AD versus not AD (\$	SMC and other dem	entias, excl	uding MCI)					
AD versus not AD (\$ Index Test: Amyloid	Beta 1-42 and t-tau	and/or p-ta	au abnormal al. Amyloid Beta 1-4	2, INNOTEST E	ELISA, cut-off < 550 pç	ŋ/ml; t-tau,	INNOTEST ELISA, cu	ıt-off >
AD versus not AD (\$ Index Test: Amyloid Amyloid Beta 1-42 ar 375 pg/ml; p-tau 181	Beta 1-42 and t-tau	and/or p-ta 181 abnorma cut-off > 52	au abnormal al. Amyloid Beta 1-4	2, INNOTEST E 164	ELISA, cut-off < 550 pg False positives:	g/ml; t-tau, 71	INNOTEST ELISA, cu	ut-off > 447
AD versus not AD (\$ Index Test: Amyloid Amyloid Beta 1-42 ar	Beta 1-42 and t-taund t-taund t-tau and/or p-taunNNOTEST ELISA,	and/or p-ta 181 abnorma cut-off > 52 467	au abnormal al. Amyloid Beta 1-4 pg/ml. False					
AD versus not AD (Solution Index Test: Amyloid Amyloid Beta 1-42 ar 375 pg/ml; p-tau 181; Results Risk of bias	Beta 1-42 and t-taund t-taund t-taund t-taund/or p-taund INNOTEST ELISA, True positives: Patient	and/or p-ta 181 abnorma cut-off > 52 467	au abnormal al. Amyloid Beta 1-4 pg/ml. False negatives:	164	False positives:	71	True negatives:	447
AD versus not AD (Sindex Test: Amyloid Amyloid Beta 1-42 ar 375 pg/ml; p-tau 181 Results	Beta 1-42 and t-tau nd t-tau and/or p-tau INNOTEST ELISA, True positives: Patient selection:	and/or p-ta 181 abnorma cut-off > 52 467	au abnormal al. Amyloid Beta 1-4 pg/ml. False negatives:	164	False positives:	71	True negatives:	447

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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.

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 whether inappropri			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 other dementias (excluding MCI)

Index Test: ≥ 2 of 3 biomarkers abnormal (Amyloid Beta 1-42, t-tau, p-tau)

≥ 2 of 3 biomarkers abnormal (Amyloid Beta 1-42, t-tau, p-tau 181). Amyloid Beta 1-42, INNOTEST ELISA, cut-off < 550 pg/ml; t-tau, INNOTEST ELISA, cut-off > 375 pg/ml; p-tau 181, INNOTEST ELISA, cut-off > 52 pg/ml.

Results	True positives:	543	False negatives:	88	False positives:	93	True negatives:	174		
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	High		
Overall risk of bias		rious (Subgroup analysis with > 35% population excluded; unclear whether consecutive or random patients were enrolled or ether inappropriate exclusions were avoided.)								
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									

AD versus not AD (SMC and other dementias, excluding MCI)

Index Test: ≥ 2 of 3 biomarkers abnormal (Amyloid Beta 1-42, t-tau, p-tau)

≥ 2 of 3 biomarkers abnormal (Amyloid Beta 1-42, t-tau, p-tau 181). Amyloid Beta 1-42, INNOTEST ELISA, cut-off < 550 pg/ml; t-tau, INNOTEST ELISA,

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cut-off > 375 pg/ml; p			-off > 52 pg/ml.					
Results	True positives:	543	False negatives:	88	False positives:	144	True negatives:	374
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus no deme	ntia (SMC, excludes	MCI)						
Index Test: Total Ta t-tau/ Amyloid Beta 1-			-42, INNOTEST ELI	SA; t-tau, INNO	TEST 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 inapproprise			excluded; uncle	ear 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 other der	mentias (excluding	MCI)						
Index Test: Total Ta	u/Amyloid Beta 1-42	2						
t-tau/ Amyloid Beta 1-	-42, cut-off 0.71. Amy	loid Beta 1	-42, INNOTEST ELI	SA; t-tau, INNO	TEST ELISA.			
Results	True positives:	536	False	95	False positives:	67	True negatives:	200

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					ow K et al. The cereb	rospinal flu	iid "Alzheimer prof	ile":
Easily said, but wha	t does it mean?Alzi	neimer's &	negatives:	: /13–/23.				
Additional comme nts	Cut-off determined	for sensitivi						
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Serious (Subgroup whether inappropri			excluded; uncle	ear 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, exc	luding MCI)					
Index Test: Total Tar Total tau/ Amyloid Be			eta 1-42, INNOTEST	ELISA; t-tau, IN	INOTEST 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 demei	ntia (SMC, excludes	MCI)						
Index Test: Total Tart-tau/ Amyloid Beta 1-			-42. INNOTEST FI I	SA: t-tau. INNO	TEST ELISA.			
Results	True positives:		False		False positives:	43	True negatives:	208

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			negatives:					
Additional comme nts	Cut-off determined	for sensitivi	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 inappropri			excluded; uncle	ear whether consecutiv	e or randon	n patients were enro	lled or
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus other der	mentias (excluding	MCI)						
Index Test: Total Ta t-tau/ Amyloid Beta 1			-42, INNOTEST ELI	SA; t-tau, INNO	TEST ELISA.			
Results	True positives:	587	False negatives:	44	False positives:	91	True negatives:	176
Additional comme nts	Cut-off determined	for sensitivi	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 inappropri			excluded; uncle	ear whether consecutiv	e or randor	n patients were enrol	lled or
	Patient	Low	Index test:	Low	Reference standard:	Low		
Indirectness	selection:				·			
Indirectness Overall indirectness								

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Easily said, but wha Results	True positives:		False		False positives:	133	True negatives:	385
results	True positives.	301	negatives:	77	r disc positives.	100	True negatives.	303
Additional comme nts	Cut-off determined	for sensitivi	ty 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 deme	ntia (SMC, excludes	MCI)						
Index Test: p-tau/An p-tau 181/ Amyloid Bo		. Amyloid Be	eta 1-42, INNOTEST	Γ ELISA; p-tau 1	81, INNOTEST ELISA	١.		
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 inappropri	•	• •	excluded; uncle	ar whether consecutiv	e or random	n patients were enro	led or
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus other der	mentias (excluding	MCI)						
Index Test: p-tau/An p-tau 181/ Amyloid Bo		. Amyloid Be	eta 1-42, INNOTEST	Γ ELISA; p-tau 1	81, INNOTEST ELISA	١.		
Results	True positives:	536	False negatives:	95	False positives:		True negatives:	214

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Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Serious (Subgroup whether inappropri			excluded; uncle	ear whether consecutive	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	SMC and other dem	entias, exc	luding MCI)					
Index Test: p-tau/An		Amyloid R	eta 1-42 INNOTEST	Γ FI ISA: n-tau 1	81, INNOTEST ELISA			
Results	True positives:		False negatives:		False positives:		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 deme	ntia (SMC, excludes	MCI)						
Index Test: p-tau/An p-tau 181/ Amyloid Be		. Amyloid Be	eta 1-42, INNOTES	Γ ELISA; p-tau 1	81, INNOTEST ELISA	١.		
Results	True positives:	587	False negatives:	44	False positives:	48	True negatives:	203
Risk of bias	Patient	Unclear	Index test:	Low	Reference	Low	Flow and	High

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Duits FH, Teunissen Easily said, but wha					ow K et al. The cereb	rospinal flu	ıid "Alzheimer profi	ile":
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus other der	mentias (excluding	MCI)						
Index Test: p-tau/An		. Amvloid Be	eta 1-42. INNOTES	Γ ELISA: p-tau 1	81, INNOTEST ELISA			
Results	True positives:		False negatives:		False positives:		True negatives:	179
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Serious (Subgroup whether inappropri			excluded; uncle	ear 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	SMC and other dem	entias, exc	luding MCI)					
Index Test: p-tau/An p-tau 181/ Amyloid Be		. Amyloid Be	eta 1-42, INNOTES ⁻	Γ ELISA; p-tau 1	81, INNOTEST ELISA	١.		
Results	True positives:	_	False negatives:		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							

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AD versus no deme	ntia (SMC, excludes	MCI)						
Index Test: Formula	•							
Formula Hulstaert, 19								
Results	True positives:	587	False negatives:	44	False positives:	43	True negatives:	208
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Serious (Subgroup whether inappropri			excluded; uncle	ear whether consecutiv	e or rando	om 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: 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			excluded; uncle	ear whether consecutiv	e or rando	om patients were enrol	led or
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
	Not serious							
Overall indirectness								

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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 deme	ntia (SMC, excludes	MCI)						
Index Test: Formula Formula Mulder, 373		s)						
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 inappropri			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 other de	mentias (excluding	MCI)						
Index Test: Formula	Mulder (biomarker	s)						
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

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Overall risk of bias	Serious (Subgroup whether inappropri			excluded; uncle	ear whether consecutive	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 not AD (SMC and other dem	entias, exc	luding MCI)					
Index Test: Formula Formula Mulder, 373	•	s)						
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 deme	ntia (SMC, excludes	MCI)						
Index Test: Formula Formula Mattson, 3.6	· · · · · · · · · · · · · · · · · · ·	•						
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 whether inappropri			excluded; uncle	ear whether consecutive	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 other de	mentias (excluding	MCI)						
Index Test: Formula	a Mattson (biomarke	rs)						
Formula Mattson, 3.6	694 + 0.0105 x tau = 7	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			excluded; uncle	ar whether consecutiv	e or rando	m patients were enrol	led or
Indirectness	Patient	Low	Index test:	Low	Reference	Low		
	selection:				standard:			
Overall indirectness	selection: Not serious				standard:			
indirectness		entias, excl	luding MCI)		standard:			
indirectness AD versus not AD (Index Test: Formula	Not serious	rs)	luding MCI)		standard:			
indirectness AD versus not AD (Index Test: Formula	Not serious SMC and other dem a Mattson (biomarke	r s) Ab42/p-tau	luding MCI) False negatives:	26	standard:	79	True negatives:	440
indirectness AD versus not AD (Index Test: Formula Formula Mattson, 3.6	Not serious SMC and other dem a Mattson (biomarke 694 + 0.0105 x tau = 7	r s) Ab42/p-tau	False	26 Low		79 Low	True negatives: Flow and timing:	440 Low
indirectness AD versus not AD (Index Test: Formula Formula Mattson, 3.6 Results	Not serious SMC and other dem a Mattson (biomarke 694 + 0.0105 x tau = 7 True positives: Patient	rs) Ab42/p-tau 505	False negatives:		False positives:		Flow and	
indirectness AD versus not AD (Index Test: Formula Formula Mattson, 3.6 Results Risk of bias	Not serious SMC and other dem Mattson (biomarke 694 + 0.0105 x tau = 7 True positives: Patient selection:	Ab42/p-tau 505 Unclear	False negatives:		False positives:		Flow and	

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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 whether inappropri			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 other der	mentias (excluding	MCI)						
Index Test: Formula	Schoonenboom (b	iomarkers)						
Formula Schoonenbo	om, 152+8.25x p-tau	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	•	• •	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	SMC and other dem	entias, exc	luding MCI)					
Index Test: Formula	Schoonenboom (b	iomarkers)						
Formula Schoonenbo	om, 152+8.25x p-tau	ı = Ab42						
Results	True positives:	574	False negatives:	57	False positives:	115	True negatives:	403
			nogun voor					

	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, Lange HIV-Infected Patients						tion and D	Diagnosis of Neurosy	philis
Study type	Retrospective coho	rt						
Country	Canada							
Setting	Centre Hospitalier	de l' Univers	ite de Montreal (CH	IUM)				
Inclusion criteria	Early syphilis plus of cell count of < 350			1:32, neurologic	al and/or ophthalmic s	igns or syr	nptoms of neurosyphil	is or C
Exclusion criteria	Syphilis of unknow	n duration, h	istory of neurosyph	ilis, treatment wi	th penicillin prior to lur	nbar punc	ture.	
Sex	99.2% male							
Age	Median age 42 year	rs (range 22	2-66)					
	Suspected neurosy	philis						
Presentation								
Presentation Reference standard	CSF-VDRL test rea	ctive						
Reference								
Reference standard	s not neurosyphilis		7, and bmp.					
Reference standard Neurosyphilis versus Index Test: PCR for 1	s not neurosyphilis Γ. pallidum genes:	polA, Tpp4	7, and bmp.					
Reference standard Neurosyphilis versus	s not neurosyphilis Γ. pallidum genes:	polA, Tpp4 .nd bmp.	7, and bmp. False negatives:	9	False positives:	36	True negatives:	57

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Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low		
Overall indirectness	Serious (>99% me	n who have	sex with men)					
ndex Test: FTA-Al								
	nt treponemal antibod	•	•					
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)					
ndex Test: TPPA								
TPPA, Treponema ر	oallidum particle agglu	tination assa	ay.					
Results	True positives:	10	False negatives:	5	False positives:	45	True negatives:	40
Additional comme								
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		

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Dummaresq J, Lang HIV-Infected Patients						tion and Dia	agnosis of Neurosy	philis in
Index Test: INNO-LIA	4							
INNO-LIA Syphilis ass	say.							
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)					

	en S, Gabelle A, Vercruysse O, Bombois S, Laplanche J-L, Peoc'h K et al. Cerebrospinal fluid amyloid-β 42/40 ratio in Jemory 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/Ar	myloid Beta 1-42

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					'h K et al. Cerebrosp erapy 2015; 7:30-38.		myloid-β 42/40 ratio	in
CSF p-tau181 and An	nyloid Beta 1-42 con	nbined						
Results	True positives:	114	False negatives:	12	False positives:	9	True negatives:	150
Additional comme nts	CSF was taken 1 n	nonth after o	liagnosis.		ard diagnosis included for the use of combina			s, but the
Risk of bias	Patient selection:	High	Index test:	High	Reference standard:	High	Flow and timing:	High
Overall risk of bias	patients with unknown	own clinical	diagnoses or MCI w	ere excluded fro	ation of the CSF result m the study; the timing 0% population (with inc	g of the refe	rence and index test	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: p-tau and CSF p-tau181 and An			vined					
Results	True positives:	118	False negatives:	17	False positives:	15	True negatives:	153
Additional comme nts	CSF was taken 1 n	nonth after o	liagnosis.		ard diagnosis included for the use of combina			s, but the
Risk of bias	Patient selection:	High	Index test:	High	Reference standard:	High	Flow and timing:	High
Overall risk of bias	patients with unkno	own clinical	diagnoses or MCI w	ere excluded fro	ation of the CSF result m the study; the timing 0% population (with inc	g of the refe	rence and index test	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
	Sciection.				Staridard.			

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indirectness								
			d then in case of di	screpancy betw	veen p-tau and Amyl	oid Beta 1-	42 the Amyloid Beta	a 42/40
	lace of Amyloid Beta		in case of discrepar	nov hotwoon n to	au181 and Amyloid Be	to 1 12 tho	Amyloid Rota 1 42/1	40 ratio
was used in place of		iibiiieu tiieii	iii case oi discrepar	icy between p-ta	iu io i anu Amylolu be	ia 1-42 liic	Alliyiolu bela 1-42/1-	40 Tallo
Results	True positives:	125	False negatives:	17	False positives:	16	True negatives:	171
Additional comme nts	CSF was taken 1 n	nonth after o	ming is unclear: the diagnosis.		ard diagnosis included			s, but th
Risk of bias	Patient selection:	High	Index test:	High	Reference standard:	High	Flow and timing:	High
Overall risk of bias	patients with unknown	own clinical	diagnoses or MCI w	ere excluded fro	ation of the CSF result m the study; the timing 0% population (with inc	of the refe	rence and index test	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Total Total Total Total Tau in CSF me	au easured using an INN	OTEST ELIS	SA kit. optimal cut o	ff calculated as 3	389pg/ml			
Results	True positives:		False negatives:		False positives:	9	True negatives:	42
Additional comme	The study descripti			reference standa	ard diagnosis included	considerati	ion of the CSF results	s, but th
nts	Patient	High	Index test:	High	Reference standard:	High	Flow and timing:	Low
Additional comme	CSF was taken 1 n	month after o	ming is unclear: the diagnosis.		Reference		Flow ar	nd

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clinical setting of mo								
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		OTEST ELI	SA kit, optimal cut of	f calculated as 6	64pg/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			reference standa	ard diagnosis included	considerati	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					ation of the CSF result m the study and the ti			
Indirectness						_		
muneciness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall		Low	Index test:	Low		Low		
Overall indirectness Index Test: Amyloid	selection: Not serious Beta 1-42				standard:	Low		
Overall indirectness Index Test: Amyloid Amyloid Beta 1–42 in	selection: Not serious Beta 1-42 CSF measured usin	g an INNO	ΓEST ELISA kit, opti	mal cut off calcu	standard: lated as 836pg/ml			
Overall indirectness	selection: Not serious Beta 1-42	g an INNO		mal cut off calcu	standard:	Low 15	True negatives:	36
Overall indirectness Index Test: Amyloid Amyloid Beta 1–42 in Results	selection: Not serious Beta 1-42 CSF measured usin True positives:	g an INNO	TEST ELISA kit, opti False negatives: ming is unclear: the	mal cut off calcu 7	standard: lated as 836pg/ml	15		
Overall indirectness Index Test: Amyloid Amyloid Beta 1–42 in Results Additional comme	selection: Not serious Beta 1-42 CSF measured usin True positives: The study descripti	g an INNO 66 on of test til nonth after (TEST ELISA kit, opti False negatives: ming is unclear: the	mal cut off calcu 7	standard: lated as 836pg/ml False positives:	15		

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ves: 66 scription of test en 1 month afte ient High ion:	r diagnosis. Index test:	7 reference stand	False positives: ard diagnosis included Reference standard: ration of the CSF result	High	Flow and timing:	Low specified;
ves: 66 scription of test en 1 month afte ient High ion:	False negatives: timing is unclear: the r diagnosis. Index test: standard diagnosis in	7 reference stand	False positives: ard diagnosis included Reference standard: ration of the CSF result	considerat High as; the test of	ion of the CSF results Flow and timing: cut offs were not pre-	s, but the Low specified
scription of test en 1 month afte ient High ion: (The reference	negatives: timing is unclear: the r diagnosis. Index test: standard diagnosis in	reference standard High	ard diagnosis included Reference standard: ration of the CSF result	considerat High as; the test of	ion of the CSF results Flow and timing: cut offs were not pre-	s, but the Low specified
en 1 month afte ient High ion: (The reference	r diagnosis. Index test: standard diagnosis ir	High	Reference standard:	High	Flow and timing:	Low
ion: (The reference	standard diagnosis ir	cluded consider	standard: ration of the CSF result	s; the test of	timing: cut offs were not pre-	specified
		oro oxoladod iro	om the study and the til	ming of the	reference and index	tests is
ient Low ion:	Index test:	Low	Reference standard:	Low		
INNOTEST EI	_ISA kit, optimal cut o	ff calculated as :	343pg/ml			
	_			26	True negatives:	85
		reference stand	ard diagnosis included	considerat	ion of the CSF results	s, but the
	Index test:	High	Reference standard:	High	Flow and timing:	Low
t	n INNOTEST Eleves: 37 scription of testen 1 month aftetient Hightion:	n INNOTEST ELISA kit, optimal cut of ves: 37 False negatives: scription of test timing is unclear: the en 1 month after diagnosis. tient High Index test: timing: (The reference standard diagnosis in	n INNOTEST ELISA kit, optimal cut off calculated as a negatives: scription of test timing is unclear: the reference standen 1 month after diagnosis. tient High Index test: High tion: (The reference standard diagnosis included consider	tion: INNOTEST ELISA kit, optimal cut off calculated as 343pg/ml ves: 37 False negatives: scription of test timing is unclear: the reference standard diagnosis included en 1 month after diagnosis. tient High Index test: High Reference standard: (The reference standard diagnosis included consideration of the CSF result)	tion: INNOTEST ELISA kit, optimal cut off calculated as 343pg/ml ves: 37 False 13 False positives: 26 scription of test timing is unclear: the reference standard diagnosis included considerate 1 month after diagnosis. tient High Index test: High Reference standard: (The reference standard diagnosis included consideration of the CSF results; the test of the constant of the CSF results; the test of the constant of the CSF results; the test of the constant of the CSF results; the test of the constant of the CSF results; the test of the constant of the CSF results; the test of the constant of the CSF results; the test of the constant of the CSF results; the test of the constant of the CSF results; the test of the constant of the CSF results; the test of the constant of	tion: INNOTEST ELISA kit, optimal cut off calculated as 343pg/ml ves: 37 False negatives: scription of test timing is unclear: the reference standard diagnosis included consideration of the CSF results en 1 month after diagnosis. tient High Index test: High Reference High Flow and

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					'h K et al. Cerebrosp	inal fluid an	nyloid-β 42/40 ratio	in
Indirectness	emory centers: a m Patient		Index test:		erapy 2015; 7:30-38. Reference	Low		
	selection:				standard:			
Overall indirectness	Not serious							
Index Test: p-tau 18	1							
p-tau 181 in CSF mea	asured using an INN	OTEST ELI	SA kit, optimal cut of	f calculated as 6	32pg/ml			
Results	True positives:	36	False negatives:	14	False positives:	9	True negatives:	102
Additional comme nts	The study descripti CSF was taken 1 n			reference standa	ard diagnosis included	consideration	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					ation of the CSF result m the study and the ti			
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 INNO	ΓEST ELISA kit, opti	mal cut off calcu	lated as 737pg/ml			
Results	True positives:	35	False negatives:	15	False positives:	22	True negatives:	89
Additional comme nts	The study descripti CSF was taken 1 n			reference standa	ard diagnosis included	consideration	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					ation of the CSF result m the study and the ti			

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Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Amyloid Amyloid Beta 1-42/1-		using an IN	INOTEST ELISA kit	, optimal cut off	calculated as 0.050.			
Results	True positives:	32	False negatives:	18	False positives:	23	True negatives:	88
Additional comme nts	The study descripti CSF was taken 1 m			reference standa	ard diagnosis included	consideration	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					ation of the CSF result m the study and the ti			
Indirectness	Patient	Low	Index test:	Low		Lave		
	selection:	20	muex test.	LOW	Reference standard:	Low		
	selection: Not serious	2011	muex test.	LOW		LOW		
indirectness Index Test: Total Ta	Not serious u				standard:	Low		
Overall indirectness Index Test: Total Ta Total Tau in CSF mea	Not serious u	OTEST ELI		ff calculated as 3	standard:		True negatives:	43
ndirectness ndex Test: Total Ta Total Tau in CSF mea Results Additional comme	Not serious u asured using an INNO	OTEST ELI	SA kit, optimal cut of False	ff calculated as 3	standard:		True negatives:	43
indirectness Index Test: Total Ta Total Tau in CSF mea	Not serious u asured using an INNO	OTEST ELI	SA kit, optimal cut of False	ff calculated as 3	standard:		True negatives: Flow and timing:	43 Low

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Indirectness	Patient		Index test:		erapy 2015; 7:30-38. Reference	Low		
indirectness	selection:	LOW	index test:	LOW	standard:	LOW		
Overall indirectness	Not serious							
Index Test: p-tau 1		OTEST ELIG	CA kit antimal out of	ff coloulated as F	50ng/ml			
	easured using an INN				. •		_	
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			andard diagnosis in diagnoses or MCI w		ation of the CSF result			
	unclear.)				are stady and the th		reference and mack	10313 13
Indirectness	unclear.) Patient selection:	Low	Index test:		Reference standard:	Low	relevence and index	10313 13
Overall	Patient	Low	Index test:		Reference	J	Telefonde and index	10010 10
Overall indirectness	Patient selection: Not serious	Low	Index test:		Reference	J	Telefonde and index	15315
Overall indirectness Index Test: Amyloi	Patient selection: Not serious			Low	Reference standard:	J	Telefonde and index	16313 13
Overall indirectness Index Test: Amyloi Amyloid Beta 1–42 i	Patient selection: Not serious d Beta 1-42	g an INNOT		Low mal cut off calcu	Reference standard:	Low	True negatives:	36
Overall indirectness Index Test: Amyloi Amyloid Beta 1–42 i Results Additional comme	Patient selection: Not serious d Beta 1-42 n CSF measured usin	g an INNOT	EST ELISA kit, opti False	Low mal cut off calcu	Reference standard:	Low		
Indirectness Overall indirectness Index Test: Amyloi Amyloid Beta 1–42 i Results Additional comments Risk of bias	Patient selection: Not serious d Beta 1-42 n CSF measured usin	g an INNOT	EST ELISA kit, opti False	Low mal cut off calcu 6	Reference standard:	Low		

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Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Amyloid Amyloid Beta 1-42/1-4		using an IN	INOTEST ELISA kit,	optimal cut off	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 m		•	reference standa	ard diagnosis included	consideration	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					ation of the CSF result m the study and the ti			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

P.1.5 E

	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.
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.

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	al J, Hoegh P, Jelic V, Bo Andersen B, Naik M, Wahlund LO, Oeksengaard AR. Quantitative EEG applying the statistical n 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 he population of interes		duals that were recr	uited separately	from our analysis as t	hey do not r	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-DLB

Index Test: EEG

EEGs were recorded using NicoletOne EEG Systems (Natus). For each EEG channel, 20 spectral features were extracted; coherence was estimated for 37 chosen channel pairs, and the same spectral features were extracted as for each individual channel. All EEGs in this study were resampled to 256 Hz in order to make them comparable. The data are analysed applying the statistical pattern recognition technique, which is used to construct a classifier

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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 h population of interes	•	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, Camacho V, Paredes P, et al. Cardiac (123)I-metaiodobenzylguanidine imaging allows early identification of dementia with Lewy bodies during life. Eur J Nucl Med Mol Imaging 2008; 35: 1636-1641.

Study type	Prospective cohort
Country	Spain
Setting	Memory Unit in a Department of Neurology
Inclusion criteria	All patients with neurodegenerative diseases and cognitive impairment, and meeting the clinical international criteria of probable DLB
Exclusion criteria	None stated
Sex	46.2% male
Age	Mean age 77 years (range 60-89)
Presentation	People have previously been diagnosed with a neurodegenerative disease and meet the International Consensus Criteria for probable DLB (when two of fluctuating cognition, well-structured visual hallucinations and/or motor symptoms of parkinsonism are present)
Reference standard	Final clinical diagnosis 4 years after MIBG imaging

Estorch M, Camacho V, Paredes P, et al. Cardiac (123)I-metaiodobenzylguanidine imaging allows early identification of dementia with Lewy bodies during life. Eur J Nucl Med Mol Imaging 2008; 35: 1636-1641.

DLB vs no-DLB

Index Test: 123I-MIBG cardiac scintigraphy

Myocardial 123I-MIBG activity was semi-quantified, obtaining the heart-to-mediastinuim ratio (HMR) and myocardial washout rate. Normal HMR defined for patients older than 60 years as >1.56

ioi pationito oraci tinai								
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	t proportion	of people not given	a final reference	standard diagnosis)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

P.1.6 F

Ferman TJ, Boeve BF, Smith GE, Lin S-C, Silber MH, Wszolek Z et al. Inclusion of RBD improves the diagnostic classification of dementia with Lewy bodies. Neurology200; 77: 876-882.

Lewy bodies. Neuro	logy200, 77. 676-662.
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	

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Index Test: Two or r	logy200; 77: 876-88		nd concentration, v	risual hallucina	tions and Parkinson	ism		
Two or more of fluctu								
Results	True positives:	83	False negatives:	15	False positives:	37	True negatives:	99
Additional comme nts	Features are very	similar to the	e DLB consensus cri	iteria, 2004.				
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Two or r Two or more of visual		•	•		n and concentration n or RBD	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							
				•	ting attention and co	ncentration		
RBD or two or more of			,					
Results	True positives:	00	False	10	False positives:	27	True negatives:	99

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			negatives:					
Additional comme								
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 I		•		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							
	D Carlin IB Ames	D The pre	dictive value of de	mentia screeni	ng instruments in cli	nical nonu	lations Internationa	uol. le
of Geriatric Psychia								
Study type	prospective cohort							
Country	Australia							
Setting	Memory clinic							

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Inclusion criteria	Patients attending tinterpreter.	the memory	clinic who were abl	e to complete th	e 3 assessments (MM	SE, IQCOE	E and AMT) without	an
Exclusion criteria	Not stated							
Sex	37.8% male							
Age	Mean age 73.4 yea	rs (SD 9.3)						
Presentation	Memory problems							
Reference standard	Clinician diagnosis	based on D	SM -III-R criteria.					
Dementia versus no	dementia							
Index Test: Informa	nt Questionnaire on	Cognitive	Decline, IQCODE (26 item, >3.5)				
Informant Questionna	aire on Cognitive Dec	line, IQCOD	DE (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			care assessmer	nt team were excluded	from analy	rsis 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		uded in the a			number of patients ex standard results were i			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
muneciness	Sciection.							
Overall indirectness	Not serious							
Overall indirectness	Not serious nt Questionnaire on	Cognitive	Decline, IQCODE (26 item, >3.6)				

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nts	suspected dementia	a at baselin	e.					
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias		ided in the a			number of patients ex standard results were i			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Informa IQCODE (26 item, 3.	nt Questionnaire on 8)	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 demention			care assessmer	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		ided in the a			number of patients ex standard results were i			
			Index test:		Reference	Low		
Indirectness	Patient selection:	Low	index test:	Low	standard:	LOW		
Overall		Low	index test.	Low		LOW		
Overall ndirectness	selection: Not serious nt Questionnaire on					Low		

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Risk of bias		a at baselin	G .					
	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias		ided in the a			number of patients ex standard results were			
ndirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall ndirectness	Not serious							
ndex Test: Informar QCODE (26 item, 4.0		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 dementi			care assessmen	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		ided in the a			number of patients ex standard results were i			
ndirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall ndirectness	Not serious							
ndex Test: Informar QCODE (26 item, 4.1		Cognitive	Decline, IQCODE (26 item, >4.0)				
Results	True positives:	140	False negatives:	76	False positives:	17	True negatives:	66

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nts	suspected dementi	a at baselin	e.					
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias		ided in the a			number of patients ex standard results were i			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Information IQCODE (26 item, 4.2		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			care assessmer	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		ided in the a			number of patients ex standard results were i			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
	-10\							
Index Test: MMSE (< MMSE (17/18)	· 10)							

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nts	suspected dementia	a at baselin	e.					
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias		ided in the a			number of patients ex standard results were i			
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 demention			care assessmer	nt team were excluded	from analys	sis as they did not ha	ve
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias		ided in the a			number of patients ex standard results were i			
						Laur		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Indirectness Overall indirectness		Low	Index test:	Low		LOW		
Overall	selection: Not serious	Low	Index test:	Low		Low		

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nts	suspected dementi	a at baselin	e.					
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias		ided in the a			number of patients ex standard results were i			
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			care assessmer	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		ided in the a			number of patients ex standard results were i			
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 renders are un	of motionts :	referred to the aged			£		

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nts	suspected dementia	a at baselin	e.					
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias		uded in the a			number of patients ex standard results were i			
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 demention			care assessmer	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
	_						atudy: look of clarity	-14
Overall risk of bias	Very serious (Due to patient groups inclures ults of the index	uded in the a			number of patients ex standard results were i			
Overall risk of bias	patient groups inclu	uded in the a test.)						
	patient groups incluresults of the index Patient	uded in the a test.)	analysis and whethe	r the reference s	standard results were i	nterpreted v		
Indirectness Overall	patient groups incluresults of the index Patient selection: Not serious	uded in the a test.)	analysis and whethe	r the reference s	standard results were i	nterpreted v		

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nts	suspected dementia	a at baselin	e.					
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias		ided in the a			number of patients ex standard results were i			
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 demention			care assessmer	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		ided in the a			number of patients ex standard results were i			
	. Julius of the mack					1		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Indirectness Overall Indirectness	Patient	Low	Index test:	Low		LOW		
Overall	Patient selection:	Low	Index test:	Low		Low		

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nts	suspected dementi	a at baselin	e.					
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias		uded in the a			number of patients ex standard results were			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Abbrevi 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			care assessmer	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		uded in the a			number of patients ex standard results were			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
	Not serious							
Overall indirectness	Not serious							
indirectness	ated Mental Test, A	MT (<8)						

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nts	suspected dementia	a at baseline	e.					
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias		uded in the a			number of patients ex standard results were i			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Abbrevi AMT (8/9)	ated Mental Test, Al	ИТ (<9)						
Results	True positives:	189	False negatives:	27	False positives:	39	True negatives:	44
Additional comme nts	The random group suspected demention			care assessmer	nt team were excluded	I 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					number of patients ex standard results were			
Overall fisk of blas	results of the index	test.)						
Indirectness		,	Index test:	Low	Reference standard:	Low		
	results of the index Patient	,	Index test:	Low		Low		
Indirectness Overall indirectness	results of the index Patient selection: Not serious ated Mental Test, Al	Low	Index test:	Low		Low		

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Flicker L, Logiudice of Geriatric Psychia			dictive value of de	mentia screeni	ng instruments in cli	nical popula	ations. Internationa	al Journal
nts	suspected dementi	ia at baselin	e.					
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias		uded in the a			number of patients ex standard results were			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

	Perret-Liauder A, Quadro I. Detection of CSF 14-3-3 Protein in Sporadic Creutzfeldt-Jakob Disease Patients Using a New y Western Assay.Mol Neurobiol, [epub ahead of print]
Study type	Retrospective cohort
Country	France
Setting	Neurochemistry Laboratory (Hospices Civils de Lyon, France)
Inclusion criteria	Patients undergoing a lumbar puncture for the evaluation of CSF 14-3- 3 protein who have suspected CJD.
Exclusion criteria	None stated
Sex	47.3% male
Age	Median age sCJD 71.0 years, non-CJD 72.0 years (range 54.1-86.7)
Presentation	Rapidly progressive dementia leading to suspected CJD
Reference standard	Clinician diagnosis using WHO criteria, with definite sCJD confirmed using neuropathology. For non-CJD patients the probable clinical diagnosis was proposed by neurologists based on clinical data, imaging/biological markers, and disease evolution.
CJD versus not CJI	

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.

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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 (Unclea	ar whether t	he threshold was pr	e-specified)				
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	nmunoblotting. The 1	4-3-3 protei	n band in CSF samp	oles was opticall	y observed and compa	ared to kno	wn specimen to perm	it a
14-3-3 detected by im characterization as ne	nmunoblotting. The 1	4-3-3 protei	n band in CSF samp False negatives:		y observed and compa		wn specimen to perm True negatives:	it a 162
14-3-3 detected by im characterization as ne Results	nmunoblotting. The 1 egative or positive sa	4-3-3 protei Imple 71	False				· ·	
14-3-3 detected by im characterization as ne Results Risk of bias	nmunoblotting. The 1 egative or positive sa True positives: Patient	4-3-3 protei Imple 71	False negatives:	6	False positives:	29	True negatives:	162
	nmunoblotting. The 1 egative or positive sa True positives: Patient selection:	4-3-3 proteinmple 71 Low	False negatives:	6 Low	False positives:	29	True negatives:	162

	Ann Neurol 2017; 81: 79-92.
Study type	Prospective cohort
0	LICA

CountryUSASettingNational 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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Sex	Not stated							
Age	Nor stated							
Presentation	Suspected CJD							
Reference standard	Neuropathology							
CJD versus not 0	CJD							
Index Test: Real-	time quaking-induced	prion conv	ersion, RT-QuIC.					
	-induced prion conversi				ples considered positiv	ve if >1 wel	I in the first round or >	2 wells
•	epeat rounds) were posi							
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 bia	as Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: CSF	14-3-3 immunoblotting							
14-3-3 detected by	y immunoblotting.							
Results	True positives:	53	False negatives:	12	False positives:	8	True negatives:	6
Additional comm	ie –							
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bia	as Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		

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Setting

Sex

Age

Inclusion criteria

Exclusion criteria

Presentation

Reference

Overall indirectness	Not serious							
Index Test: Total T Total tau, ELISA, cu								
Results	True positives:	62	False negatives:	3	False positives:	4	True negatives:	10
Additional comme								
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							
					etti G, Bocchio L, Paç memory clinic. Alzho			l,Benus
317.							,	
Study type	Prospective cohort							
Country	Italy							

37.0% male

physical, psychiatric, or metabolic diseases.

Mean age 73.1 years (SD 7.4)

Translational out-patient memory clinic at the Scientific Institute for the Research and Care of Alzheimer's disease

Patients whose cognitive deficit reverted (regarded as primarily depressed with secondary cognitive impairment)

Patients referred to the memory clinic with memory complaints or other cognitive disturbances unaccounted for by focal cerebral,

Memory complaints or other cognitive disturbances unaccounted for by focal cerebral, physical, psychiatric, or metabolic diseases.

AD was diagnosed according to NINCDS-ADRDA criteria; LDLB using the consensus criteria reported in McKeith et al. 2006, FTD

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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. based on Knopman et al. 2003, VaD according to NINDS-AIREN. standard 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. True positives: 59 False positives: 20 True negatives: 28 Results False 26 negatives: Risk of bias Patient Low Index test: Low Reference Unclear Flow and Low selection: standard: timing: Overall risk of bias Not serious Patient Low Indirectness Index test: Low Reference Low selection: standard: Not serious Overall indirectness 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		condary cog	nitive impairment) w		its whose cognitive de om the study; unclear v			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

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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	excluded from the	study; uncle		e test was interp	marily depressed with reted without knowled t.)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall	Not serious							

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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	depressed with sec	condary cog	nitive impairment) w	ere excluded fro	patients whose cognition om the study; unclear we ex test interpreted with	vhether refe	rence test was interp	oreted
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

AD versus non-AD (including other dementias and MCI)

Index Test: FDG-PET

24-ring, three dimensional PET/CT device with an isotropic resolution of 5.99 mm, a 15.7-cm axial field of view (FOV), a 70-cm transaxial FOV.

Test assessed cortical hypometabolism on 18F-FDG-PET. Score of 8/36 or higher on visual rating scale assessing metabolism in six bilateral brain areas (frontal, temporal pole, medial temporal, superior parietal, inferior parietal, and posterior cingulate). For each area, glucose metabolism is rated as 0 for normal, 0.5 for uncertain, 1 for mild, 2 for moderate, and 3 for severe.

Results	True positives:	22	False	12	False positives:	10	True negatives:	34		
			negatives:							
Risk of bias	Patient	Low	Index test:	High	Reference	Unclear	Flow and	Low		
	selection:				standard:		timing:			
Overall risk of bias	Serious (Patients v	Serious (Patients whose cognitive deficit reverted (regarded as primarily depressed with secondary cognitive impairment) were								

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			ar whether reference without knowledge		reted without knowled t.)	ge of index	test and unclear whe	ether
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Dementia versus no	dementia (MCI incl	uded)						
Amyloid Beta 1-42, < INNOTEST ELISAs.		tau > 450 pզ	•	•	d >500pg/ml in 71–93-	-		
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	excluded from the	study; uncle		e test was interp	marily depressed with reted without knowled t.)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus non-AD	dementias (excludir	g MCI)						
	d Beta 1-42 and total :500 pg/mL and total		g/mL in 51–70-year-	old subjects, and	d >500pg/ml in 71–93-	year-old sul	ojects. Assayed usin	g
Results	True positives:	27	False negatives:	11	False positives:	1	True negatives:	27
			negatives.					

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					etti G, Bocchio L, Pag memory clinic. Alzh			l,Benussi				
Overall risk of bias	depressed with sec	ery serious (Subgroup analysis with >10% population excluded; patients whose cognitive deficit reverted (regarded as primarily expressed with secondary cognitive impairment) were excluded from the study; unclear whether reference test was interpreted thout 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 den	nentias and	I MCI)									
Index Test: Amyloid Amyloid Beta 1-42, <br INNOTEST ELISAs.			g/mL in 51–70-year-	old subjects, and	d >500pg/ml in 71–93-	-year-old su	bjects. Assayed usin	9				
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	excluded from the	study; uncle		e test was interp	marily depressed with preted without knowled t.)							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low						
Overall	Not serious											

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 biomarkers in research memory center: the PLM Study. J. Alzheimers Dis. 2013; 34: 7–305.

Study type

Prospective cohort

Study type	i rospective conort
Country	France
Setting	Memory centres in Lille and Paris-North

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					mpact of the 2008-20		Aizneimer plan on t	the use c				
cerebrospinai fiuid i Inclusion criteria			y center: the PLM ioural disorders atte		imers Dis. 2013; 34:	7–305.						
Exclusion criteria	'			• '	pating cirries.							
Sex	•	People with unclear, unknown or postponed clinical diagnosis 4.2% male										
Age		Median age varies from 61-73 years across diagnostic groups.										
Presentation		Suspected dementia										
Reference standard		AD was diagnosed using NINCDS-ADRDA; patients with MCI had to meet the Petersen criteria, McKhann and Neary consensus criteria was used for FTLD; McKeith criteria for LBD.										
AD versus non-AD (MCI excluded from	analysis)										
Index Test: Amyloid												
Amyloid Beta 1-42, IN	INOTEST Amyloid B	eta 1-42 EL	ISA, 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	random or consecu	itive people		riate exclusions	ed on the data; it was . A subgroup analysis							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low						
Overall indirectness	Not serious											
indirectness	u	: off >301pg	/ml									
indirectness Index Test: Total Ta	u		/ml False negatives:	66	False positives:	48	True negatives:	161				
indirectness Index Test: Total Ta Total tau, INNOTEST	u hTau-Ag ELISA, cut		False	66	False positives:	48	True negatives:	161				

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					mpact of the 2008-20 imers Dis. 2013; 34:		Alzheimer plan on t	he use of
	selection:				standard:		timing:	
Overall risk of bias	random or consecu	itive people		riate exclusions	ed on the data; it was . A subgroup analysis			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: p-tau 18 ^o p-tau, INNOTEST tau		าไ						
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	random or consecu	itive people		riate exclusions	ed on the data; it was . A subgroup analysis			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Amyloid Amyloid Beta 1-42/tot		1						
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

					mpact of the 2008-20 imers Dis. 2013; 34:		Alzheimer plan on t	he use o
	selection:				standard:		timing:	
Overall risk of bias	random or consecu	ıtive people		riate exclusions	ed on the data; it was . A subgroup analysis			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Amyloid Amyloid Beta 1-42/p-	· · · · · · · · · · · · · · · · · · ·	1						
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	random or consecu	ıtive people		riate exclusions	ed on the data; it was . A subgroup analysis			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Amyloid Amyloid Beta 1-42, IN		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

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	selection:				standard:		timing:	
Overall risk of bias	random or consecu	ıtive people		riate exclusions	ed on the data; it was . A subgroup analysis			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Total Ta Total tau, INNOTES	au Γ hTau-Ag ELISA, cu	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	random or consecu	ıtive people		riate exclusions	ed on the data; it was . A subgroup analysis			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: p-tau 18 p-tau 181, INNOTES	<mark>31</mark> T ELISA, cut off >61ր	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

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Gabelle A Dumurgio	er .I. Vercriivsse O	Paguet C. I	Rombois S. Lanlan	che la etall	mpact of the 2008-20	12 French	Δlzheimer nlan on t	he use o
					imers Dis. 2013; 34:			iic usc o
	selection:				standard:		timing:	
Overall risk of bias	random or consecu	ıtive people		riate exclusions	ed on the data; it was . A subgroup analysis			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Amyloid Amyloid Beta 1-42/tot		u						
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	random or consecu	itive people		riate exclusions	ed on the data; it was . A subgroup analysis			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Amyloid Amyloid Beta 1-42/ p-								
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

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

g the clinical detection of Lewy body dementia with the Lewy body composite risk score. Alzheimer's & Dementia: nent & Disease Monitoring, 2015; 1: 316-324.
Prospective cohort
USA
Pearl I. Barlow Centre for Memory Evaluation and Treatment, a dementia specialty practice at NYU Medical Center.
Consecutive memory clinic referrals
Not stated
47.0% male
Mean age 77.8 years (8.2)
Suspected dementia
AD was diagnosed according to the NINCDS-ADRDA criteria; FTD according to Rascovsky (2011) revised diagnostic criteria for the behavioural variant of frontotemporal dementia; PPA according to Gorno-Tempini (2011); VaD according to the VASCOG statement (Sachdev 2014).

DLB versus AD

Index Test: Lewy body composite risk score, LBCRS, ≥3

Lewy body composite risk score (LBCRS) which consists of items from Movement Disorders Society-Unified Parkinson's Disease Rating Scale, motor subscale part III (UPDRS), the neuropsychiatric inventory (NPI), Mayo fluctuation questionnaire (MFQ), Epworth Sleepiness Scale (EES), the Mayo sleep questionnaire (MSQ) and from physical findings and complaints of the patient. The operationalization of physical findings as being present for at least 6 months or symptoms permitted the scoring of the LBCRS by totalling the sum of signs and symptoms rated as present occurring at least three times over the past 6 months. Cut off ≥3.

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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	s carried out exclud	ing >30% study	population.)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

DLB versus non-DLB dementias

Index Test: Lewy body composite risk score, LBCRS, ≥3

Lewy body composite risk score (LBCRS) which consists of items from Movement Disorders Society-Unified Parkinson's Disease Rating Scale, motor subscale part III (UPDRS), the neuropsychiatric inventory (NPI), Mayo fluctuation questionnaire (MFQ), Epworth Sleepiness Scale (EES), the Mayo sleep questionnaire (MSQ) and from physical findings and complaints of the patient. The operationalization of physical findings as being present for at least 6 months or symptoms permitted the scoring of the LBCRS by totalling the sum of signs and symptoms rated as present occurring at least three times over the past 6 months. Cut off ≥3.

Results	True positives:	52	False negatives:	1	False positives:	17	True negatives:	107
Risk of bias	Patient selection:	Low	Index test:	Unclear	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Serious (Subgroup	analysis wa	as carried out exclud	ling >30% study	population.)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

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

Study type Prospective cohort

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Forcano Garcia M, P consultations. Revis					ort version of the Inf	ormant Tes	t (IQCODE) in the g	eriatrics
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	deterioration	١.	
Exclusion criteria			ed dementia. The C here may be other a		v has marked this stud ed groups.	ly as having	inappropriate exclus	sions at
Sex	Not stated in Coch	rane Review	1					
Age	Not stated in Coch	rane Review						
Presentation	Memory loss, beha	vioural diso	rder and/or cognitive	e deterioration.				
Reference standard	Clinician diagnosis	based on D	SM -III-R					
Dementia versus no	dementia							
Index Test: Informar IQCODE (Spanish, 16		_	•	16 item, >3.5)				
Results	True positives:	83	False negatives:	7	False positives:	4	True negatives:	19
Additional comme nts	The random group suspected dement			care assessme	nt team were excluded	I from analy	sis as they did not ha	ave
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

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Country	Switzerland							
Setting	University of General	va Hospitals	Belle-Idée					
Inclusion criteria					cally evaluated, includi			
Exclusion criteria	Patients with major	neuropsycl	niatric illness, alcoho	olism, or Parkins	on's disease were exc	luded.		
Sex	61.8% male							
Age	Mean age 84.7 yea	ars (SD 6.4)						
Presentation	Dementia							
Reference standard	on the presence of	both macro		opic vascular pa	al Institute on Aging-Ro thology. Cases that sa g mixed dementias.			
VaD versus AD and	mixed dementia (A	D plus VaD)					
Index Test: NINDS-A NINDS-AIREN, possi	``							
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	cted as updated	d versions of these crit	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							
ndex Test: NINDS-A	••							
Results	True positives:	4	False negatives:	16	False positives:	5	True negatives:	64

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Gold G, Bouras C, C of Four Sets of Clini					J-P, Giannakopoulos 2–87.	P. Clinicop	atnological Validat	ion Stu
Additional comme nts	The data for the IC	D-10 and D	SM-IV was not extra	cted as updated	I versions of these crit	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: ADDTC ADDTC, possible diag	`• ′							
Results	True positives:	14	False negatives:	6	False positives:	15	True negatives:	54
Additional comme nts	The data for the IC	D-10 and D	SM-IV was not extra	cted as updated	I versions of these crit	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: ADDTC ADDTC, probable dia	``							
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	cted as updated	I versions of these crit	eria exist.		
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	Low

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Overall risk of bias	Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
					treal Cognitive Asse ol 2014; 27; 199-203.	ssment as	a screen for mild co	gnitiv
Study type	Prospective cohort		ournal of Geriati F	Sych and Neuro	n 2014, 21, 199-203.			
Country	USA							
Setting	Memory disorders	clinic at Gra	dy memorial Hospita	al, Atlanta.				
Inclusion criteria	African American,	≥ 50 years c	old, cognitive assess	ment at the clini	c.			
Exclusion criteria				, ,	substance abuse, and imary neurodegenerat			ould
Sex	30.1% male							
Age	Mean age 70.2 (SI	9.5)						
Presentation	Suspected dement	ia						
Reference standard	Clinician diagnosis	based on n	europsychological b	attery				
Dementia versus no	dementia (MCI incl	uded						
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:	High	Index test:	Low	Reference standard:	Low		

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Overall indirectness	Serious (Study only	y recruited A	frican Americans ≥	50 years old.)				
Index Test: Montrea MoCA ≤24	I Cognitive Assess	ment, MoCA	A (<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, Arno setting. Internationa				mentia: compai	rative utility of three I	orief instru	uments in the memo	ry clinic
Study type	Prospective cohort							
Country	Australia							
Setting	Memory clinic in a							

setting. Internationa	Il Psychogeriatrics 2011; 23: 788–96.
Study type	Prospective cohort
Country	Australia
Setting	Memory clinic in a city hospital
Inclusion criteria	Participants were referred by their primary care physicians.
Exclusion criteria	Patients lacking an informant to complete the IQCODE for them.
Sex	44.0% male
Age	Mean age 76.9 years (SD 8.9)
Presentation	Memory problems.
Reference standard	Clinician diagnosis based on DSM-IV-TR criteria plus all available information (including index tests)
Dementia versus no	dementia (includes MCI)

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QCODE (16 item), op								
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 diagno	sis was not indepen	dent of the index	tests; optimised test	thresholds	were used.)	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< SMMSE (Molloy, 199		Optimised to	threshold 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 diagno	sis was not indepen	dent of the index	tests; optimised test	thresholds	were used.)	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Goncalves DC, Arno	old E, Appadurai K,	Byrne GJ.	Case finding in der	nentia: compar	ative utility of three I	orief instru	ments in the memo	ry clinic
setting. Internationa			88–96.					
Study type	Prospective cohort							
Country	Australia							

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Study type

Inclusion criteria

Country

Setting

Setting	Memory clinic in a	city hospital						
Inclusion criteria	Participants were re	eferred by th	neir primary care ph	ysicians.				
Exclusion criteria	Patients lacking an	informant to	complete the IQC	ODE for them				
Sex	44.0% male							
Age	Mean age 76.9 yea	ars (SD 8.9)						
Presentation	Memory problems							
Reference standard	DSM-IV-TR criteria	ı plus all ava	nilable information (in	ncluding index	x tests)			
Dementia verus no	dementia (incluldes	MCI)						
Index Test: Rowland Rowland Universal D			· ·	(<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 in	dex tests; optimised test	thresholds	were used.)	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall	Not serious							

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USA

New referrals to the specialist clinics with cognitive impairment, memory problems or suspected dementia for the diagnosis of

8 speciality memory/ dementia/ cognitive impairment clinics across 8 US states.

dementia; ≥ 45 years old; subsequent clinical diagnosis.

Exclusion criteria	Inability to provide morning urine).	a suitable fir	st morning urine sa	mple (contamina	ated sample with bacte	eria etc., ren	al disease or not the	first
Sex	61.0% male							
Age	Mean age 69.6 yea	ars (SD 11.7)					
Presentation	People had cognitive	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	Quality Standards Subo	committee o	f the AAN (AAN MCI	criteria
AD (probable and po	ossible) versus non	-AD (includ	ling MCI)					
Index Test: Urinary AUT: Urinary AD7c-NTP (22)	•)						
Results	True positives:	52	False negatives:	36	False positives:	22	True negatives:	58
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Probable AD versus	non-AD (including	MCI)						
Index Test: Urinary AUrinary AD7c-NTP (22	•)						
Results	True positives:	32	False negatives:	3	False positives:	22	True negatives:	58
					(n= 2F)			
Additional comme nts	The probable AD g	roup was ex	cluded from this sui	ogroup analysis	(n= 35).			

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Overall risk of bias	Serious (Subgroup of the index test res		cluding >10% popul	ation; it is unclea	ar whether the referen	ce test was	carried out without k	nowledge
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Possible AD versus	non-AD (including	MCI)						
Index Test: Urinary AD7c-NTP (2	•)						
Results	True positives:	20	False negatives:	33	False positives:	22	True negatives:	58
Additional comme nts	The possible AD gr	oup was ex	cluded from this sub	ogroup analysis	(n= 53).			
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Serious (Subgroup of the index test res		cluding >10% popul	ation; it is unclea	ar whether the referen	ce test was	carried out without k	nowledge
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
					. The Accuracy of Sh iatry 2010; 18: 810-8		Rating Scales in	
Study type	Prospective cohort			ochamic i sych	iad y 2010, 10. 010-0	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,		
	·							
Country	Sweden							

Inclusion criteria

Individuals with DSM-III and ICD-10 diagnosed dementia who were referred to the department and followed up for subtype diagnosis.

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Guetafeon I Englur	nd F Brunnetrom U	Brun A E	rikeon C. Warkonti	in S. Dassant II	. The Accuracy of Sh	ort Clinical	Pating Scales in	
					iatry 2010; 18: 810-8		Nating Scales in	
Exclusion criteria					ead injury, addiction, scation of the three clini			
Sex	41.1% male							
Age	Mean age at onset	64.0 years	(no SD stated)					
Presentation	Dementia with subt	type diagnos	sis required					
Reference standard	Diseases (Wallin, 1	994) and in		iteria for AD (Bra	me with reference to that, 1991; CERAD), D			
AD (including mixed	VaD and AD) versi	us FTD and	VaD alone					
Index Test: AD scale AD scale, cut-off ≥ 6	e (≥6)							
Results	True positives:	84	False	21	False positives:	11	True negatives:	74
			negatives:					
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 no	t downgraded for su	bgroup analysis	as <10% population v	vas exclude	d.)	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
FTD versus AD and	VaD							
Index Test: FTD sca FTD scale, cut- off ≥ 6								
Results	True positives:	48	False negatives:	4	False positives:	11	True negatives:	127
Risk of bias	Patient selection:	Low	Index test:	Unclear	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Not serious (The st	udy was no	t downgraded for su	bgroup analysis	as <10% population v	vas exclude	d.)	
Indirectness	Patient	Low	Index test:	Low	Reference	Low		

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	selection:				standard:			
Overall indirectness	Not serious							
VaD (including mixe	ed VaD and AD) vers	sus AD aloi	ne and FTD					
Index Test: Hachins	ki Ischemic score,	HIS (≥7)						
Hachinski Ischemic s	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 st	tudy was no	t downgraded for su	bgroup analysis	as <10% population v	vas exclude	d.)	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

P.1.8 H

п	
Hamlin C, Puoti G, E Neurology, 2012; 79	Berri S, Sting E, Harris C et al. A comparison of tau and 14-3-3 protein in the diagnosis of Creutzfeldt-Jakob disease. :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

Reference standard	Criteria not specifie	ed						
Prion disease versu	s no prion disease							
Index Test: Total Ta	u							
Tau, >1000 pg/ml (In	vitrogen 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			ere tested and uncle owledge of index tes		archers were blind to	eference t	est results or that the	referenc
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Total Ta Tau, >1150 pg/ml (In								
Results	True positives:	213	False negatives:	32	False positives:	57	True negatives:	118
Additional comme								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias			ere tested and uncle owledge of index tes		archers were blind to i	eference t	est results or that the	referenc
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
	Not serious							

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researchers were blind to reference test results or that the reference test was interpreted without knowledge of index test.) Indirectness Patient selection: Not serious Not serious Not serious Not serious Patient selection: Not serious Not serious Not serious Not serious Patient selection: Not serious Not serious	14-3-4, Immunoblottii	ng with ambiguous re	sults ignore	d					
Risk of bias Patient selection:	Results	True positives:	183		10	False positives:	76	True negatives:	30
Selection: Overall risk of bias Very serious (> 28% population excluded as 14-3-3 results were ambiguous; multiple thresholds were tested and unclear whether researchers were blind to reference test results or that the reference test was interpreted without knowledge of index test.) Indirectness Patient selection: Not serious Not serious Not serious 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: 52: 30. Study type Prospective cohort Country UK Setting Memory clinics in a psychiatric hospital and cognitive function clinic based in a regional neuroscience centre Inclusion criteria Patients attending memory/cognitive function clinics with an informant. Patients attending memory/cognitive function clinics with an informant. Patients lacking an informant to complete the IQCODE for them. Sex 49.0% male Median age 67 years (range 29-94) Presentation Memory problems. Clinician diagnosis based on DSM-IV criteria									
researchers were blind to reference test results or that the reference test was interpreted without knowledge of index test.) Indirectness Patient selection: Not serious Not serious 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: 52: 30. Study type Prospective cohort UK Setting Memory clinics in a psychiatric hospital and cognitive function clinic based in a regional neuroscience centre Patients attending memory/cognitive function clinics with an informant. Exclusion criteria Patients lacking an informant to complete the IQCODE for them. Sex 49.0% male Median age 67 years (range 29-94) Presentation Memory problems. Clinician diagnosis based on DSM-IV criteria	Risk of bias		Low	Index test:	High		Low		High
Not serious 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: 52: 30. Study type Prospective cohort Country UK Setting Memory clinics in a psychiatric hospital and cognitive function clinic based in a regional neuroscience centre Inclusion criteria Patients attending memory/cognitive function clinics with an informant. Exclusion criteria Patients lacking an informant to complete the IQCODE for them. Sex 49.0% male Age Median age 67 years (range 29-94) Presentation Memory problems. Reference Clinician diagnosis based on DSM-IV criteria	Overall risk of bias								
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: 52: 30. Study type Prospective cohort UK Setting Memory clinics in a psychiatric hospital and cognitive function clinic based in a regional neuroscience centre Inclusion criteria Patients attending memory/cognitive function clinics with an informant. Exclusion criteria Patients lacking an informant to complete the IQCODE for them. Sex 49.0% male Age Median age 67 years (range 29-94) Presentation Memory problems.	Indirectness		Low	Index test:	Low		Low		
the Addenbrooke's Cognitive Examination-Revised (ACE-R) in a memory clinic-based population. International Psychogeriatrics 2009; 21: 52: 30. Study type Prospective cohort Country UK Setting Memory clinics in a psychiatric hospital and cognitive function clinic based in a regional neuroscience centre Inclusion criteria Patients attending memory/cognitive function clinics with an informant. Exclusion criteria Patients lacking an informant to complete the IQCODE for them. Sex 49.0% male Age Median age 67 years (range 29-94) Presentation Memory problems. Reference Clinician diagnosis based on DSM-IV criteria		Not serious							
Country Setting Memory clinics in a psychiatric hospital and cognitive function clinic based in a regional neuroscience centre Inclusion criteria Patients attending memory/cognitive function clinics with an informant. Exclusion criteria Patients lacking an informant to complete the IQCODE for them. Sex 49.0% male Age Median age 67 years (range 29-94) Presentation Memory problems. Reference Clinician diagnosis based on DSM-IV criteria									
Memory clinics in a psychiatric hospital and cognitive function clinic based in a regional neuroscience centre Inclusion criteria Patients attending memory/cognitive function clinics with an informant. Exclusion criteria Patients lacking an informant to complete the IQCODE for them. Sex 49.0% male Age Median age 67 years (range 29-94) Presentation Memory problems. Reference Clinician diagnosis based on DSM-IV criteria	Hancock P, Larner Athe Addenbrooke's 30.	Cognitive Examinat							
centre Inclusion criteria Patients attending memory/cognitive function clinics with an informant. Exclusion criteria Patients lacking an informant to complete the IQCODE for them. Sex 49.0% male Age Median age 67 years (range 29-94) Presentation Memory problems. Reference Clinician diagnosis based on DSM-IV criteria	Hancock P, Larner <i>i</i> the Addenbrooke's 30.	Cognitive Examinat Prospective cohort							
Exclusion criteria Patients lacking an informant to complete the IQCODE for them. 49.0% male Age Median age 67 years (range 29-94) Presentation Memory problems. Reference Clinician diagnosis based on DSM-IV criteria	Hancock P, Larner A the Addenbrooke's 30. Study type	Cognitive Examinat Prospective cohort							
Sex 49.0% male Age Median age 67 years (range 29-94) Presentation Memory problems. Reference Clinician diagnosis based on DSM-IV criteria	Hancock P, Larner A the Addenbrooke's 30. Study type Country	Prospective cohort UK Memory clinics in a	ion-Revise	d (ACE-R) in a mer	mory clinic-bas	ed population. Intern	ational Ps	ychogeriatrics 2009	
Age Median age 67 years (range 29-94) Presentation Memory problems. Reference Clinician diagnosis based on DSM-IV criteria	Hancock P, Larner A the Addenbrooke's 30. Study type Country Setting	Prospective cohort UK Memory clinics in a centre	ion-Revise	d (ACE-R) in a mer	nory clinic-bas	ed population. Intern	ational Ps	ychogeriatrics 2009	
Presentation Memory problems. Reference Clinician diagnosis based on DSM-IV criteria	Hancock P, Larner A the Addenbrooke's 30. Study type Country Setting	Prospective cohort UK Memory clinics in a centre Patients attending i	psychiatric	d (ACE-R) in a mer hospital and cogniti	nory clinic-bas	ed population. Intern	ational Ps	ychogeriatrics 2009	
Reference Clinician diagnosis based on DSM-IV criteria	Hancock P, Larner A the Addenbrooke's 30. Study type Country Setting Inclusion criteria Exclusion criteria	Prospective cohort UK Memory clinics in a centre Patients attending in Patients lacking an	psychiatric	d (ACE-R) in a mer hospital and cogniti	nory clinic-bas	ed population. Intern	ational Ps	ychogeriatrics 2009	
	Hancock P, Larner A the Addenbrooke's 30. Study type Country Setting Inclusion criteria Exclusion criteria Sex	Prospective cohort UK Memory clinics in a centre Patients attending in Patients lacking an 49.0% male	psychiatric memory/cog informant to	hospital and cognition clinic complete the IQCO	nory clinic-bas	ed population. Intern	ational Ps	ychogeriatrics 2009	
	Hancock P, Larner A the Addenbrooke's 30. Study type Country Setting Inclusion criteria Exclusion criteria Sex Age	Prospective cohort UK Memory clinics in a centre Patients attending in Patients lacking an 49.0% male Median age 67 year	psychiatric memory/cog informant to	hospital and cognition clinic complete the IQCO	nory clinic-bas	ed population. Intern	ational Ps	ychogeriatrics 2009	

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QCODE (26 item) or	timised 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	ier L. Test your mer	mory test: d	liagnostic utility in	a memory clini	c population. Int. Jou	urnal Geriat	r Psych 2011; 25: 9	976-980.			
Study type	Prospective cohort										
Country	UK										
Setting	A memory clinic in	A memory clinic in a psychiatric hospital and a cognitive functional clinic in a regional neuroscience centre.									
Inclusion criteria	People referred to	eople referred to the memory clinics over a 23- month period (February 2008- December 2009).									
Exclusion criteria	Not stated										
Sex	58.0% male										
Age	Mean age 63.3 yea	ars (SD 12.6)								
Presentation	Suspected dement	Suspected dementia									
Reference standard	_	_	IV for dementia and ary, 1998 and Peter		eria for dementia subt	ypes (McKha	ann, 1984, 2001; Ro	man,			
Dementia versus no	t dementia (includii	ng MCI)									
Index Test: Test You	ur Memory, TYM (≤4	l2)									
Test your memory (T	YM), 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			

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Hancock P and Larn	er L. Test your mer	mory test: c	liagnostic utility in	a memory clin	ic population. Int. Jo	urnal Geriat	r Psych 2011; 25: 9	76-980.
	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	• •	30)						
Test your memory (T)	, , , , , , , , , , , , , , , , , , ,							
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	test thresh	old.)					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (<	<24)							
MMSE, ≤ 23/30 (Folst	tein 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	test thresh	old.)					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		

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Hancock P and Larn	er L. Test your mer	nory test: c	liagnostic utility in	a memory clin	ic population. Int. Jo	urnal Geriat	r Psych 2011; 25: 9	976-980.
Overall indirectness	Not serious							
Index Test: Addenbe Addenbrooke's Cogni			•	<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 thresh	old.)					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

Hanyu H, Shimizu S	6, 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.	

30 4 .	
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.

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Hanyu H, Shimizu S, Hirao K, Sakurai H, Iwamoto T, Chikamori T, Hida S et al. The role of 123-I Metaiodobenzylguanidine myocardial scintigraphy in the diagnosis of Lew Body Disease in patients with dementia in a memory clinic. Dementia Geriatr Cogn Disord 2006; 22: 379-384.

Reference standard

Clinician diagnosis based on NINCDS-ADRDA for AD, the consortium for DLB international criteria (McKeith, 1996) for DLB, NINDS-AIREN for VaD and PDD according to the UK Brain Bank (Hughes, 1992) and McKeith (1996). Other diagnoses made using the DSM-IV.

PDD and DLB versus other dementias

Index Test: 123I-MIBG cardiac scintigraphy

MIBG scintigraphy, heart-to-mediastinum (H/M) ratio. Early and delayed SPECT was performed 20 min and 4 hr after injection, respectively. Planar scan and SPECT were performed with a double-headed camera equipped with a low -energy, high resolution parallel hole collimator (PRISM 2000VP, Pickers). After scatter correction, relative organ uptake was determined by setting the region of interest (ROI) on the anterior view. The H/M ratio was calculated by dividing the count density of the left ventricle ROI by the mediastinal ROI according to standard methods. Values were compared to those from normal controls obtained at the Institute.

Results	True positives:	39	False negatives:	2	False positives:	7	True negatives:	48
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Unclear	Flow and timing:	Low
Overall risk of bias					ted without knowledge at knowledge of the re			standard
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

	hompson JC, Richardson AMT, Neary D et al. Sensitivity and specificity of FTDC criteria for behavioural frontotemporal y 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.

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Sex	58.2% male										
Age	Mean age 60.7 yea	Mean age 60.7 years (SD not calculable)									
Presentation	Early onset demen	Early onset dementia									
Reference standard	Neuropathology - o	Neuropathology - criteria not stated									
Probable by FTD v	versus not bv FTD (in	cluding pos	ssible)								
	criteria for bv FTD FTD (Rascovsky, 201	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 o	of sample at initial so	creening)							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										
Possible by FTD v	ersus not bv FTD										
Index Test: FTDC of FTDC criteria for by	criteria for bv FTD FTD (Rascovsky, 201	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										

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Study type	Retrospective coho	ort							
Country	UK								
Setting	National CJD Surveillance Unit								
Inclusion criteria	Cases of suspected CJD referred to the surveillance unit between 1995 and 2004 with subsequent autopsy/ biopsy confirmation of vCJD or an alternative diagnosis (non-CJD).								
Exclusion criteria	None stated								
Sex	58.9% male								
Age	Mean age at onset	32.0. years	(SD not stated)						
Presentation	Suspected CJD								
Reference standard	Autopsy/cerebral 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					out knowledge of the roriate exclusions were		e reference test; whe	ther a	
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low			
Overall indirectness	Serious (Mean age	at onset< 4	0 years old)						
CJD (probable) vers	us not CJD (includi	ing possible	e CJD)						
Index Test: WHO CJ	D criteria								
Diagnostic criteria for	CJD (WHO, 2002)								

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			negatives:								
Risk of bias	Patient selection:	Unclear	Index test:	Unclear	Reference standard:	Low	Flow and timing:	Low			
Overall risk of bias	`			•	hout knowledge of the ropriate exclusions were		e reference test; whe	ther a			
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 diagnosis of demen					ral neuroimaging with 45-50.	MRI for di	agnosis and differer	ntial			
Study type	Prospective cohort										
Country	Germany										
Setting	Memory clinic of the	e Central Ins	stitute for Mental He	alth, University	of Heidelberg						
Inclusion criteria	People referred to	he memory	clinic with cognitive	disturbances							
Exclusion criteria	Not stated										
Sex	Not stated										
	Mean age 68.6 years (SD8.6)										
Age	Mean age 68.6 yea	15 (300.0)									
	Suspected dement	` ,									
Presentation Reference	Suspected dement AD diagnosed acco	a ording to the entia group ir	ncluded people with		ording to NINDS-AIREN ognitive disturbances. T						
Presentation Reference standard	Suspected dement AD diagnosed acco specified. No deme available to clinicia	a ording to the entia group ir	ncluded people with								
Presentation Reference standard Dementia versus no	Suspected dement AD diagnosed accompecified. No dementia	a ording to the entia group ir ns during dia	ncluded people with								
Age Presentation Reference standard Dementia versus no Index Test: MRI MRI using T1, double Results	Suspected dement AD diagnosed accompecified. No dementia	ra ording to the entia group in ns during dia quence.	ncluded people with	MCI and no co							

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	selection:				standard:		timing:	
Overall risk of bias					ne primary care diagno vailable data including			-specified
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: CERAD I	battery							
MMSE; Word List Tes them after a delay).	st (10 words – immed	liate and de	layed recall and rec	ognition); Const	ing); Modified Boston ructional praxis (copyir	ng drawn fig	ures and then reprod	ducing
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					ne primary care diagno vailable data including			-specified
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Hoffman JM, Welsh- Nucl Med. 2000; 41:		n M, Krain	B, Hulette C, Earl N	N etal. FDG PE1	imaging in patients	with patho	logically verified de	ementia.
Study type	Prospective cohort							
Country	USA							
Setting	Memory Disorder C	linic of the	Joseph and Kathlee	n Bryan Alzheim	ner's Disease Researc	h Centre at	Duke University.	
Inclusion criteria	Patients at the Mer	nory Disord	ar Clinic with diagno	etically challeng	ing or difficult to identif	fy domontia	(using clinical criteri	٥١

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Country

Exclusion criteria	Not stated								
Sex	63.6% male	63.6% male							
Age	Mean age 67.5 years (SD 9.6)								
Presentation	Diagnostically chall	Diagnostically challenging dementia							
Reference standard	Pathologic confirma criteria.	ation of diag	nosis was obtained	(biopsy, n =2; a	utopsy, n= 19; biopsy	and autops	y, n= 1) using the CE	RAD	
AD versus non-AD	dementias								
							bilateral temporo-pa		
hypometabolism; 3 =	classic bilateral temp	oro-parietal	hypometabolism; ar	nd 4 = abnormal	but not AD pattern (in	cluding fror	ntal, focal, or only uni	lateral	
hypometabolism; 3 =	classic bilateral temp	oro-parietal	hypometabolism; alsis, grades 2 and 3	nd 4 = abnormal FDG PET interp		cluding fror	ntal, focal, or only uni	lateral	
hypometabolism; 3 = hypometabolism). Fo diagnostic of AD. Results	classic bilateral temp or the purposes of state True positives:	oro-parietal tistical analy	hypometabolism; ar sis, grades 2 and 3 False negatives:	nd 4 = abnormal FDG PET interp	but not AD pattern (in pretations were groupe False positives:	cluding from d together	ntal, focal, or only uni as being metabolical True negatives:	lateral ly	
hypometabolism; 3 = hypometabolism). For	classic bilateral temp or the purposes of state True positives:	oro-parietal tistical analy 13 cted to exan	hypometabolism; and issis, grades 2 and 3 False negatives:	nd 4 = abnormal FDG PET interp 1 test accuracy of	but not AD pattern (in pretations were groupe False positives: the NINCDS-ADRDA	cluding from d together	ntal, focal, or only uni as being metabolical True negatives:	lateral ly	
hypometabolism; 3 = hypometabolism). For diagnostic of AD. Results Additional comme	classic bilateral temp or the purposes of state True positives: Data was not extra	oro-parietal tistical analy 13 cted to exan a newer ver	hypometabolism; and issis, grades 2 and 3 False negatives:	nd 4 = abnormal FDG PET interp 1 test accuracy of DRDA is now in u	but not AD pattern (in pretations were groupe False positives: the NINCDS-ADRDA	cluding from d together	ntal, focal, or only uni as being metabolical True negatives:	lateral ly	
hypometabolism; 3 = hypometabolism). For diagnostic of AD. Results Additional comments	classic bilateral temp or the purposes of state True positives: Data was not extra neuropathology as Patient	oro-parietal tistical analy 13 cted to exan a newer ver	hypometabolism; and sis, grades 2 and 3 False negatives: nine the diagnostic fision of NINCDS-AD	nd 4 = abnormal FDG PET interp 1 test accuracy of DRDA is now in u	False positives: the NINCDS-ADRDA use (2011). Reference	cluding from ed together 3 clinical crite	True negatives: eria compared to Flow and	lateral ly 5	
hypometabolism; 3 = hypometabolism). For diagnostic of AD. Results Additional comments Risk of bias	classic bilateral tempor the purposes of state. True positives: Data was not extraneuropathology as Patient selection:	oro-parietal tistical analy 13 cted to exan a newer ver Low	hypometabolism; and sis, grades 2 and 3 False negatives: nine the diagnostic fision of NINCDS-AD	nd 4 = abnormal FDG PET interp 1 test accuracy of DRDA is now in u	False positives: the NINCDS-ADRDA use (2011). Reference	cluding from ed together 3 clinical crite	True negatives: eria compared to Flow and	lateral ly 5	

USA

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Holman BL, Johnson technetium-99m-HM				graphic appear	ance of Alzheimer's	disease: a	prospective study ι	using		
Setting	Nuclear medicine of	linic								
Inclusion criteria	Referral to the nuclear medicine clinic with a complaint of memory or cognitive impairment.									
Exclusion criteria	Not stated	Not stated								
Sex	Not stated	Not stated								
Age	Not stated									
Presentation	Memory loss or cog	gnitive abno	rmalities							
Reference standard	Diagnosis was carr criteria and CT and	-		perience of diag	nosing dementia using	NINDS-AD	RDA for AD, other d	iagnostic		
AD versus non-AD										
using a colour scale a	and classified into diff	erent perfus	sion pattern groups (A to F). A was o			-			
Results	True positives:	48	False negatives:	4	False positives:	44	True negatives:	17		
Additional comme nts		ormal). The	non-AD group cons		agnostic for AD we onl diagnosed with other					
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									

P.1.9

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.

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Ibach B, Binder H, D controls and an age					uid tau and beta-amy	yloid in Alz	heimer patients, dis	sease	
Study type	Prospective cohort								
Country	Germany								
Setting	In-patient service and/or memory disorders outpatient clinic at State Hospital for Psychiatry and Psychotherapy, Bezirksklinikum Regensburg, Germany.								
Inclusion criteria	Participants undergoing diagnostic procedure for suspected dementia or cognitive decline in a memory clinic or in-patient clinic at the Stste Hospital.								
Exclusion criteria	Not stated								
Sex	43.0% male								
Age	Mean age 65.5 yea	ars (SD 10.2)						
Presentation	Suspected cognitiv	e decline or	dementia.						
Reference standard			dementia with all oth Newcastle criteria		t information apart fror B.	n CSF index	test results. AD dia	gnosed	
AD versus other der	nentias								
Index Test: Amyloid Beta Amyloid 1–42 in		_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	were avoided; the t	est threshol	ds were not pre-spe	cified and it is u	e of patients was enro nclear whether the ind 10% study population	ex test was	interpreted without k		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								
Index Test: Total Ta	u								
Tau in CSF, INNOTE	ST hTAu-Ag ELISA,	cut off 400p	g/ml						
Results	True positives:	55	False	21	False positives:	14	True negatives:	34	

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bach 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	were avoided; the t	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 18 p-tau 181 in CSF, INN		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	were avoided; the t	est threshol	lds were not pre-spe	cified and it is u	e of patients was enro nclear whether the ind 10% study population	ex test was	interpreted without k				
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										
Index Test: Total Ta Tau/Beta Amyloid 1-4		2									
Results	True positives:	57	False	19	False positives:	12	True negatives:	36			

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			negatives:								
Additional comme nts											
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High			
Overall risk of bias	were avoided; the t	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/An p-tau 181/Beta Amylo											
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	were avoided; the t	est threshol	ds were not pre-spe	cified and it is u	e of patients was enrol nclear whether the ind 10% study population	ex test was	interpreted without k				
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										

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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							

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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.

Jahn H. Wittke S. Zurbig P. Raedler TJ. Arlt S. Kellmn M. Mullen W. Eichenlaub M. Mischak H. Wiedmann K. Peptide Fingerprinting of

indirectness

Overall

Study type	Prospective cohort										
Country	Germany										
Setting	University Hospital	Hamburg- E	Eppendorf memory	clinic							
Inclusion criteria	People referred to	People referred to the memory clinic of the University Hospital Hamburg- Eppendorf.									
Exclusion criteria	Not stated	Not stated									
Sex	49.0% male										
Age	Mean age 65.3 yea	rs (12.3)									
Presentation	Memory problems										
Reference standard	Disorders Associat	on criteria (NINCDS-ADRDA) to	o identify patient	ve Disorders and the s with vascular demer e Lund–Manchester cr	ntia. MCI dia					
AD versus non-AD (excluding MCI)										
	oxordanig iii o i										
CE-MS analysis was	ec(trometry)	ed using a	P/ACEMDQ (Beckn	nan Coulter, Fullo	erton, USA) system or	n-line couple	ed to a Micro- TOF M	1S (Brul			
CE-MS analysis was Daltonic).	ec(trometry)	ed using a	P/ACEMDQ (Beckn False negatives:		erton, USA) system or False positives:		ed to a Micro- TOF M	1S (Brul 19			
CE-MS analysis was Daltonic). Results	pec(trometry) performed as describ		False	8				·			
Index Test: Mass sp CE-MS analysis was Daltonic). Results Risk of bias Overall risk of bias	pec(trometry) performed as describ True positives: Patient selection: Serious (>10% pop	55 Unclear ulation excl	False negatives: Index test: uded from analysis;	8 Low unclear whether	False positives:	4 Unclear	True negatives: Flow and timing: onsecutive sample or	19 High			

Not serious

selection:

standard:

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Jahn H, Wittke S, Zurbig P, Raedler TJ, Arlt S, Kellmn M, Mullen W, Eichenlaub M, Mischak H, Wiedmann K. Peptide Fingerprinting of Alzheimer's Disease in Cerebrospinal Fluid: Identification and Prospective Evaluation of New Synaptic Biomarkers. PLoS ONE 2011; 6: e26540.										
indirectness										
Index Test: Amyloid Beta 1-42, Total Tau and p-tau abnormal The CSF levels of Aß42, total tau, and phospho181-tau were measured using commercial ELISAs (Innogenetics). Cut-off values for AD suspicious biomarker concentrations were >540 pg/ml for total-tau, >61 pg/ml for phospho181-tau and beta-amyloid 1–42 values, <240+1.186 total-tau pg/ml.										
Results	True positives:	50	False negatives:	7	False positives:	7	True negatives:	14		
Additional comme nts										
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Unclear	Flow and timing:	High		
Overall risk of bias					r the patients were a rance standard was inte		•			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									

Jubb MT, Evand JJ. An Investigation of the Utility of the Addenbrooke's Cognitive Examination III in the Early Detection of Dementia in Memory
Clinic Patients Aged over 75 Years. Dement Geriatr Cogn Disord 2015; 40:222–232.

Cliffic Patients Aged over 75 Tears. Definent Genati Cogni Disord 2015, 40.222-252.								
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.							

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Sex	61.0% male			5; 40:222–23						
		(0.7)								
Age	Mean age 80.0 yea	` '								
Presentation	•	Memory or other cognitive problems								
Reference standard	Dementia was diag	Dementia was diagnosed based on DSM-IV; AD according to NINCDS-ADRDA; NINCDS-AIREN for VaD; Peterson criteria for MCI.								
Dementia versus	no dementia									
	nbrooke's Cognitive E									
Addenbrooke's Co	gnitive ExaminationIII, /									
Results	True positives:	25	False negatives:	1	False positives:	17	True negatives:	17		
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	Low		
Overall risk of bia	S Not serious									
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low				
Overall indirectness	Serious (Study pop	oulation was	confined to >75 year	ars)						
Index Test: Adder	nbrooke's Cognitive E	xamination	-III, ACE- III (<84)							
Addenbrooke's Co	gnitive ExaminationIII, A	ACE- III (<84	1)							
Results	True positives:	24	False negatives:	2	False positives:	13	True negatives:	20		
Additional commonts	e									
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	Low		
Overall risk of bia	Serious (Optimised	I threshold u	sed for analysis.)							
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low				

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indirectness								
Index Test: Addenb	rooke's Cognitive E	xamination	-III, ACE- III (<81)					
	nitive ExaminationIII,		•					
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	Serious (Study pop	oulation was	confined to >75 year	ars)				
	prooke's Cognitive E							
	nitive ExaminationIII, /			_				
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	l threshold ι	used for analysis.)					
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low		
Overall indirectness		oulation was	confined to >75 year	ars)	33333			

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P.1.11 K

Kaneta T, Nakatsuka M, Nakamura K, Seki T, Yamaguchi S et al. Improved diagnostic accuracy of SPECT through statistical analysis and the detection of hot spots at the primary sensorimotor area for the diagnosis of Alzheimer disease in a community-based study. Clinical Nuclear Medicine 2016; 41: e1-6.

Study type	Prospective cohort
Country	Japan
Setting	Memory clinic at Osaki-Tajiri SKIP Centre
Inclusion criteria	Patients visiting the clinic with a previous diagnosis of dementia based on DSM-IV, a CDR of 1+ and who received a final diagnosis of dementia subtype; medical treatment for dementia for > 3 months and additional evidence of dementia on the Cognitive Abilities Screening instrument and Wechsler Memory Scale-Revised Neuropsychological Tests.
Exclusion criteria	Patients with depression according to the Geriatric Depression Scale.
Sex	23.6% male
Age	Mean age 81.6 years (SD 5.0)
Presentation	Dementia with subtype to be determined
Reference standard	Clinician diagnosis using the following criteria and additional tests: NINCDS-ADRDA for probable AD and AD with cerebrovascular disease; VaD according to NINDS-AIREN; DLB/PDD and FTLD using McKeith (1996, 2006).
	IAD IV D

AD (including mixed AD and VaD) versus not AD

Index Test: 99mTc-ECD SPECT, visual assessment method

99mTc-ECD SPECT was carried out using a triple-headed gamma camera (Prism Irix) with high-resolution fan beam collimators. Visual assessment of images by specialist.

Results	True positives:	16	False negatives:	32	False positives:	11	True negatives:	30
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Unclear	Flow and timing:	Low
Overall risk of bias	Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

Index Test: 99mTc-ECD SPECT, automated method

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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%.

	0 0 7			•	•		•	
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-ECD SPECT, automated and visual method

99mTc-ECD SPECT was carried out using a triple-headed gamma camera (Prism Irix) with high-resolution fan beam collimators. Automated diagnosis based on visual assess ment and Easy Z- score imaging system with a cut-off value for discriminating between healthy controls and patients with early AD of 14.2%.

Results	True positives:	20	False negatives:	28	False positives:	6	True negatives:	35
Additional 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-ECD SPECT, positive SMG sign

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detection of hot spo	ts at the primary se				ic accuracy of SPEC ner disease in a com					
Medicine 2016; 41: e 99mTc-ECD SPECT sensorimotor hotspot	was carried out using	ງ a triple-hea	aded gamma camer	a (Prism Irix) wit	h high-resolution fan t	peam collima	ators. Diagnosis usin	g positive		
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 sensorimotor hotspot	was carried out using	a triple-hea			h high-resolution fan t	peam collima	ators. Diagnosis usin	g positiv		
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		esults of the			ear whether the index treference standard res					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall	Not serious									

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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		esults of the			ear whether the index teference standard res			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

Kemp PM, Clyde K, Holmes C. Impact of 123I-FP-CIT (DaTSCAN) SPECT on the diagnosis and management of patients with dementia with Lewy bodies: a retrospective study. Nucl Med Commun 2011;32: 298-302.

Study type	Retrospective cohort
Country	UK
Setting	Department of Nuclear Medicine, Southampton University Hospitals Trust
Inclusion criteria	Referred to the unit for imaging with suspected DLB by a specialist in old age psychiatry working at a memory clinic
Exclusion criteria	None stated
Sex	51.0% male
Age	Mean age 79.0 years (SD7.3)

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Presentation	Clinical suspicion of DLB								
Reference standard	Clinician diagnosis - not supported by any specific set of diagnostic criteria, but using the results of the imaging								
DLB vs no-DLB									
Index Test: 123I-FP-MEDISO Nucline X-F photopeak window at	Ring/4R SPECT came			with low-energy	high-resolution collima	itors. 128 pr	rojections 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 pa	rt of the reference s	tandard)					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall	Not serious								

Kenney K, Brechtel C, Takahashi H, Kurohara K, Anderson P, Gibbs CJ Jr. An enzyme-linked immunosorbent assay to quantify 14-3-3 proteins
in the cerebrospinal fluid of suspected Creutzfeldt-Jakob disease patients. Ann Neurol 2000; 48: 395–398.

Study type	Prospective cohort
Country	USA
Setting	Not stated
Inclusion criteria	People referred for diagnosis with suspected CJD
Exclusion criteria	Not stated
Sex	Not stated
Age	Not stated
Presentation	Rapidly progressive dementia leading to suspected CJD
Reference standard	Criteria for CJD based on Kretzschmar (1996)

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CJD (definite and pr	obable) versus not	CJD						
Index Test: CSF 14-3 CSF 14-3-3 protein de		:h 8.3ng/ml	cut off					
Results	True positives:	56	False negatives:	7	False positives:	2	True negatives:	82
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Unclear	Flow and timing:	Low
Overall risk of bias	enrolled or inappro	priate exclu	sions avoided; the in	ndex test results	ar whether: a consecu were interpreted witho ted without knowledge	out knowled	ge of the results of th	
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		h 8.3ng/ml	cut off					
Results	True positives:	38	False negatives:	3	False positives:	2	True negatives:	82
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Unclear	Flow and timing:	High
Overall risk of bias	whether: a consecu	utive or rand knowledge	lom sample of patier of the results of the	nts was enrolled	he test threshold was or inappropriate exclu ard or the reference st	sions avoid	ed; the index test res	ults wer
	Dations	Low	Index test:	Low	Reference	Low		
Indirectness	Patient selection:	LOW			standard:			

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					me-linked immunoso ırol 2000; 48: 395–39		y to quantify 14-3-3	proteins
Index Test: CSF 14-3	3-3 immunoblotting							
CSF 14-3-3 protein de	etected by immunobl	otting						
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	index test results w	ere interpre		ge of the results	of patients was enrolle s of the reference stand)			
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	_							
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	patients was enroll	ed or inappr	opriate exclusions a	voided; the inde	was unclear whether: a ex test results were inte terpreted without know	erpreted with	hout knowledge of th	e results
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

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

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Study type	Retrospective coho	Retrospective cohort								
Country	The Netherlands									
Setting	VU Medical centre	Alzheimer's	Centre							
Inclusion criteria	Clinical suspicion of the scan.	Clinical suspicion of bvFTD; no MRI abnormalities characteristic of a neurodegenerative disorder; 2 years of clinical follow up after the scan.								
Exclusion criteria	None	None								
Sex	81.0% male	81.0% male								
Age	Mean age 65.0 (SE	Mean age 65.0 (SD 8.1)								
Presentation	Suspected bvFTD	Suspected bvFTD								
Reference standard	FTD diagnosed acc	cording to N	eary (1998) plus fur	ectional decline a	at 2 years.					
bvFTD/fd+ versus n	ot bvFTD/fd+									
Index Test: FDG-PE 18f-FDG -PET. EC80	· -	er. Imaging v	was interpreted as p	ositive (FTD pat	ttern), normal or devia	nt otherwise	(non-FTD pattern).			
Results	True positives:		False negatives:		False positives:		True negatives:	34		
	bvFTD/fd+ refers to	bvFTD with	h cognitive decline							
nts	bvFTD/fd+ refers to Patient selection:	bvFTD with	n cognitive decline	Low	Reference standard:	Low	Flow and timing:	Low		
nts Risk of bias	Patient			Low		Low		Low		
Additional comme nts Risk of bias Overall risk of bias Indirectness	Patient selection:			Low		Low		Low		

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

Study type Prospective cohort

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					The Movement disor s. J. Neurol 2013; 260			ignosis		
Country	France			court, patient						
Setting	Strasbourg geriatri	Strasbourg geriatric centre								
Inclusion criteria	≥ 65 years old; PD	≥ 65 years old; PD diagnosed with the UK PDS Brain bank criteria; stable motor function; CDR. 0.5 and MMSE> 16.								
Exclusion criteria		Dementia due to a cause other than PD; delirium < 3 months before study inclusion; severe depressive syndrome; previous major stroke, anticholinergic treatment and unable to consent.								
Sex	40.0% male									
Age	Mean age 80.5 yea	Mean age 80.5 years (SD 4.9)								
Presentation	Suspected PDD									
Reference standard	Clinician diagnosis									
PDD versus not PDI										
Index Test: Moveme	ent disorders criteri	a for PDD (:	≤120)							
Movement disorders	criteria for PDD, cut-	off ≤ 120								
Results	True positives:	25	False negatives:	6	False positives:	0	True negatives:	9		
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low		
Overall risk of bias	Serious (Test thres	shold was no	ot pre-specified.)							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									
Index Test: Moveme Movement disorders		•	≤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		

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	selection:				standard:		timing:	
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							
Index Test: Moveme	ent disorders criteri	a for PDD (≦132)					
Movement disorders	criteria for PDD, Cut-	off ≤ 132						
Results	True positives:	31	False negatives:	0	False positives:	5	True negatives:	4
Additional 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	chke's 3 and cued se	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	shold was no	ot pre-specified.)					
Indirectness	Patient	Low	Index test:	Low	Reference	Low		

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	selection:				standard:			
Overall indirectness	Not serious							
Index Test: Rey-Ost	errieth complex figu	ure test, R0	OCF (≤21)					
The Rey-Osterrieth co	omplex figure test, cu	ıt-off ≤ 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	ot pre-specified.)					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

	ce D, Harrigan S, Cook R, Flicker L, Mackinnon A, et al. The combination of cognitive testing and an informant eening 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

Dementia versus no	dementia							
Index Test: Informar IQCODE (16 item) 3.6		Cognitive	Decline ,IQCODE (16 item, >3.5)				
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	•	atients were include	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		test, cut-off	f< 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		atients were include	d in the analysis	; unclear interval betw	een index a	and reference tests; la	ack of a
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

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

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Study type	Retrospective coho	ort									
Country	Norway										
Setting	Oslo University Ho	spital									
Inclusion criteria	Patients undergoin	atients undergoing lumbar puncture for the study of amyloid beta and tau.									
Exclusion criteria	None	lone									
Sex	53.7% male										
Age	Mean age 61 (SD 6	6.4)									
Presentation	Suspected dement	ia									
Reference standard	ICD-10 for dement	ia									
AD versus not AD											
Index Test: Amylo Amyloid Beta 1-42 I	id Beta 1-42 NNOTEST ELISA, cut	-off < 550 p	_								
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 T	au										
	ST ELISA with cut-offs	> 300 pg/m	l for people under 50), > 450 pg/ml fc	or people 50-69, > 500	pg/ml for 7	70 or older				
Total-tau, INNOTES				48	False positives:		True negatives:	52			

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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 p-tau, INNOTEST EL		ml						
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							

Study type	Prospective cohort
Country	The Netherlands
Setting	Alzheimer Centre of the VU University Medical Centre.
Inclusion criteria	Patients referred to the centre for analysis of their cognitive complaints (and subsequently enrolled in the Amsterdam Dementia Cohort). Patients were included if MRI and MMSE results were available

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Exclusion criteria	Not stated
Sex	66.0% male
Age	Mean age 64.0 years (8.0)
Presentation	Cognitive complaints
Reference standard	Patients were diagnosed with probable AD using the criteria of the National Institute for Neurological and Communicative Diseases Alzheimer's Disease and Related Disorders Association; all patients also met the core clinical criteria of the National Institute on Aging-Alzheimer's Association guidelines for AD (McKhann et al., 1984; McKhann et al., 2011). FTD was diagnosed using the Neary criteria; patients also met the core criteria from Rasckovsky (Neary et al., 1998; Rascovsky et al., 2011). VaD was diagnosed using the National Institute of Neurological Disorders and Stroke and Association Internationale pour la Recherché et l'Enseignement en Neurosciences criteria (Román et al., 1993), and DLB using the McKeith criteria (McKeith et al., 1996; McKeith et al., 2005)

AD versus non-AD

Index Test: MRI

MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes.

Results	True positives:	65	False negatives:	158	False positives:	45	True negatives:	236
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Unclear	Flow and timing:	Low

Results	True positives:	65	False negatives:	Overall risk of bias	Not serious	37	True negatives:	126
Risk of bias	Patient selection:	Unclear	Index test:	Indirectness	Patient selection:	Low	Index test:	Low

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Overall risk of bias	patients was enroll	ed and inap	propriate exclusions	were avoided;	unclear whether: a co the index test was inte ently of the index test.)	rpreted with		
Indirectness	Patient selection:	Low	Index test:	AD versus non-AD dementias	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MRI MRI imaging using 1 Imaging data were as				3-dimensional T	1-weighted gradient ed	cho sequend	ce and a fast FLAIR s	sequer
Index Test: MRI MRI imaging using 1 Imaging data were as changes.		trophy and		3-dimensional T 158		cho sequend	ce and a fast FLAIR s	sequer 71
Index Test: MRI MRI imaging using 1. Imaging data were as changes. Results	ssessed visually for a	trophy and v	vascular False					·
Index Test: MRI MRI imaging using 1. Imaging data were as changes. Results Risk of bias	True positives: Patient selection: Serious (Subgroup patients was enroll	65 Unclear analysis whed and inap	False negatives: Index test: nere >10% populatio propriate exclusions	158 Low on excluded and a were avoided;	False positives:	21 Unclear nsecutive or	True negatives: Flow and timing:	71 High
AD versus FTD Index Test: MRI MRI imaging using 1 Imaging data were as changes. Results Risk of bias Overall risk of bias Indirectness	True positives: Patient selection: Serious (Subgroup patients was enroll	65 Unclear analysis whed and inaple or the refer	False negatives: Index test: nere >10% populatio propriate exclusions	Low on excluded and were avoided; to preted independent	False positives: Reference standard: unclear whether: a co	21 Unclear nsecutive or	True negatives: Flow and timing:	71 High

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Index Test: MRI

MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes.

Results	True positives:	65	False negatives:	158	False positives:	13	True negatives:	34	
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Unclear	Flow and timing:	High	
Overall risk of bias	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)								
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								

AD versus VaD

Index Test: MRI

MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes

oriarigoo.								
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	patients was enroll	ed and inap	propriate exclusions	were avoided; t	unclear whether: a co he index test was inte ently of the index test.)	rpreted with		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		

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Overall indirectness

Not serious

FTD versus non-FTD

Index Test: MRI

MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes.

Results	True positives:	46	False negatives:	46	False positives:	66	True negatives:	346
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Unclear	Flow and timing:	Low
Overall risk of bias	Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

FTD versus non-FTD dementias

Index Test: MRI

MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes.

Results	True positives:	46	False negatives:	46	False positives:	66	True negatives:	228
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Unclear	Flow and timing:	High
Overall risk of bias								
Indirectness	Patient	Low	Index test:	Low	Reference	Low		

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	selection:			standard:		
Overall	Not serious					
indirectness						
FTD versus AD						
Index Test: MRI						
MRI imaging using 1.	0 T, 1.5 T or 3.0 T MRI device	s. All scans include a	3-dimensional T1	-weighted gradient ech	sequence and a fast	FLAIR sequence.
Imaging data were as	ssessed visually for atrophy ar	d 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	patients was enrolle	erious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible atients 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									

FTD versus DLB

Index Test: MRI

MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes.

Results	True positives:	46	False negatives:	46	False positives:	3	True negatives:	44
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Unclear	Flow and timing:	High
Overall risk of bias	Serious (Subgroup	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible						

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	•	•	·		he index test was inteently of the index test.)	•	out knowledge of the	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
FTD versus VaD								
lmaging data were as changes. Results	True positives:	trophy and v	vascular False	46	False positives:	1	True negatives:	23
results	True positives.	40	negatives:	40	i dise positives.	'	True negatives.	20
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Unclear	Flow and timing:	High
Overall risk of bias	Serious (Subaroup				unclear whether: a co			
	patients was enroll				ently of the index test.)		out knowledge of the)
	patients was enroll	or the refer		reted independe			out knowledge of the	•
Indirectness Overall	patients was enroll reference standard Patient	or the refer	ence test was interp	reted independe	ently of the index test.) Reference		out knowledge of the)
Indirectness Overall Indirectness	patients was enroll reference standard Patient selection: Not serious	or the refer	ence test was interp	reted independe	ently of the index test.) Reference		out knowledge of the	•
Indirectness Overall Indirectness DLB versus non-DL	patients was enroll reference standard Patient selection: Not serious	or the refer	ence test was interp	reted independe	ently of the index test.) Reference		out knowledge of the	
Indirectness Overall indirectness DLB versus non-DL Index Test: MRI MRI imaging using 1. Imaging data were as	patients was enroll reference standard Patient selection: Not serious B O T, 1.5 T or 3.0 T M	or the refer Low	ence test was interp Index test: All scans include a	preted independe Low	ently of the index test.) Reference	Low		
Indirectness Overall indirectness DLB versus non-DL Index Test: MRI	patients was enroll reference standard Patient selection: Not serious B O T, 1.5 T or 3.0 T M	or the refer Low	ence test was interp Index test: All scans include a	oreted independent Low 3-dimensional T	ently of the index test.) Reference standard:	Low		

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Risk of bias Patient selection: Overall risk of bias Serious (Subgroup analysis where >10% population excluded and unclear patients was enrolled and inappropriate exclusions were avoided; the indereference standard or the reference test was interpreted independently of the selection: Not serious	standard:	Unclear	Flow and timing:	Low
Selection: Not serious Not serious DLB versus non-DLB dementias Index Test: MRI MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weigh Imaging data were assessed visually for atrophy and vascular changes. Results True positives: Patient selection: Overall risk of bias Serious (Subgroup analysis where >10% population excluded and unclear patients was enrolled and inappropriate exclusions were avoided; the inde reference standard or the reference test was interpreted independently of the inderectness Patient selection: Not serious Not serious Not serious Not serious Not serious MRI maging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weigh				
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-weigh Imaging data were assessed visually for atrophy and vascular changes. Results True positives: 20 False negatives: Not selection: Serious (Subgroup analysis where >10% population excluded and unclear patients was enrolled and inappropriate exclusions were avoided; the indereference standard or the reference test was interpreted independently of indirectness 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-weigh 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-weigh	Reference standard:	Low		
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-weigh Imaging data were assessed visually for atrophy and vascular changes. Results True positives: Patient selection: Overall risk of bias Serious (Subgroup analysis where >10% population excluded and unclear patients was enrolled and inappropriate exclusions were avoided; the inde reference standard or the reference test was interpreted independently of indirectness Patient selection: Not serious Not serious Not serious Not serious MRI devices. All scans include a 3-dimensional T1-weigh				
MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weigh Imaging data were assessed visually for atrophy and vascular changes. Results True positives: Patient selection: Overall risk of bias Serious (Subgroup analysis where >10% population excluded and unclear patients was enrolled and inappropriate exclusions were avoided; the index reference standard or the reference test was interpreted independently of the selection: Not serious Not				
Risk of bias Patient selection: Overall risk of bias Serious (Subgroup analysis where >10% population excluded and unclear patients was enrolled and inappropriate exclusions were avoided; the indereference standard or the reference test was interpreted independently of the selection: Not serious				
Serious (Subgroup analysis where >10% population excluded and unclear patients was enrolled and inappropriate exclusions were avoided; the index reference standard or the reference test was interpreted independently of the selection: Description	lse positives:	80	True negatives:	259
patients was enrolled and inappropriate exclusions were avoided; the indereference standard or the reference test was interpreted independently of the reference test was inte	Reference standard:	Unclear	Flow and timing:	High
Selection: Overall Not serious Indirectness 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-weigh	ex test was inter	rpreted withou		
indirectness 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-weigh	Reference standard:	Low		
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-weigh				
MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weigh				
maging data were assessed visually for atrophy and vascular	hted gradient ec	cho sequenc	e and a fast FLAIR s	sequenc
changes. Results True positives: 20 False 27 False			True negatives:	159

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			negatives:							
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Unclear	Flow and timing:	High		
Overall risk of bias										
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	patients was enroll	ed and inap	propriate exclusions	were avoided; t	unclear whether: a co the index test was inte ently of the index test.)	rpreted with		
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.

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Imaging data were assessed visually for atrophy and vascular changes.

Results	True positives:	20	False negatives:	27	False positives:	3	True negatives:	21		
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Unclear	Flow and timing:	High		
Overall risk of bias	patients was enroll	Serious (Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.)								
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									

VaD versus non-VaD dementias

Index Test: MRI

MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes.

Results	True positives:	17	False negatives:	7	False positives:	18	True negatives:	462
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Unclear	Flow and timing:	Low
Overall risk of bias	Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall	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.

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Imaging data were as	sessed visually for a	trophy and v	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	patients was enroll	ed and inap	propriate exclusions	were avoided; t	unclear whether: a co the index test was inte ently of the index test.)	rpreted with		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall	Not serious							
indirectness	Not schous							
indirectness VaD versus AD	Not serious							
VaD versus AD Index Test: MRI	0 T, 1.5 T or 3.0 T M			3-dimensional T	1-weighted gradient ed	cho sequend	ce and a fast FLAIR s	sequen
VaD versus AD Index Test: MRI MRI imaging using 1. Imaging data were as changes.	0 T, 1.5 T or 3.0 T M		/ascular	3-dimensional T	1-weighted gradient ed False positives:	·	ce and a fast FLAIR s	sequen 216
VaD versus AD Index Test: MRI MRI imaging using 1. Imaging data were as changes. Results	0 T, 1.5 T or 3.0 T M sessed visually for a	trophy and v	/ascular False			·		·
VaD versus AD Index Test: MRI MRI imaging using 1. Imaging data were as	O T, 1.5 T or 3.0 T M seessed visually for a True positives: Patient selection: Serious (Subgroup patients was enrolled)	17 Unclear analysis whed and inap	False negatives: Index test: ere >10% population propriate exclusions	7 Low In excluded and were avoided; t	False positives:	7 Unclear nsecutive or	True negatives: Flow and timing:	216 High

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Overall indirectness

Not serious

VaD versus FTD

Index Test: MRI

MRI imaging using 1.0 T, 1.5 T or 3.0 T MRI devices. All scans include a 3-dimensional T1-weighted gradient echo sequence and a fast FLAIR sequence. Imaging data were assessed visually for atrophy and vascular changes.

Results	True positives:	17	False negatives:	7	False positives:	4	True negatives:	88
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Unclear	Flow and timing:	High
Overall risk of bias	patients was enrolle	ed and inap	propriate exclusions	were avoided; t	unclear whether: a co the index test was inte ently of the index test.)	rpreted with		
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	7	False positives:	2	True negatives:	45
			negatives:					
Risk of bias	Patient	Unclear	Index test:	Low	Reference	Unclear	Flow and	High
	selection:				standard:		timing:	
Overall risk of bias	` •	•	• •		unclear whether: a co		· ·	_

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	reference standard	or the refer	ence test was interp	oreted independe	ently of the index test.)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus non-AD								
Imaging data were a	assessed using an aut	omatic imag	e quantification met	thod.	1-weighted gradient ed			·
Results	True positives:	164	False negatives:	59	False positives:	47	True negatives:	234
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Unclear	Flow and timing:	Low
Overall risk of bias	Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus non-AD	dementias							
Index Test: MRI	1.0 T, 1.5 T or 3.0 T M assessed using an aut				1-weighted gradient ed	cho sequend	ce and a fast FLAIR	sequenc
		164	False	59	False positives:	37	True negatives:	126
	True positives:		negatives:					

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Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus FTD								
Imaging data were a	ssessed using an auto	omatic imag	e quantification met	hod.	1-weighted gradient ed			·
Results	True positives:	164	False negatives:	59	False positives:	19	True negatives:	73
Diale of bios	Patient	Unclear	Index test:	Low	Reference	Unclear	Flow and	High
RISK OF DIAS	selection:	Onoicai			standard:		timing:	
	selection: Serious (Subgroup patients was enrolled)	analysis wh ed and inap	ere >10% populatio	were avoided;	standard: unclear whether: a co the index test was inte ently of the index test.)	rpreted with	random sample of e	
Overall risk of bias	selection: Serious (Subgroup patients was enrolled)	analysis whed and inap	ere >10% populatio	were avoided; to were a	unclear whether: a co	rpreted with	random sample of e	
Overall risk of bias Indirectness Overall	selection: Serious (Subgroup patients was enrolle reference standard Patient	analysis whed and inap	ere >10% populatio propriate exclusions ence test was interp	were avoided; to were a	unclear whether: a co the index test was inte ently of the index test.) Reference	rpreted with	random sample of e	
Risk of bias Overall risk of bias Indirectness Overall indirectness AD versus DLB	selection: Serious (Subgroup patients was enrolle reference standard Patient selection:	analysis whed and inap	ere >10% populatio propriate exclusions ence test was interp	were avoided; to were a	unclear whether: a co the index test was inte ently of the index test.) Reference	rpreted with	random sample of e	
Overall risk of bias Indirectness Overall indirectness AD versus DLB Index Test: MRI MRI imaging using 1	selection: Serious (Subgroup patients was enrolle reference standard Patient selection: Not serious	analysis whed and inapported for the reference Low	nere >10% population propriate exclusions ence test was interp Index test: All scans include a 3	s were avoided; to reted independent Low 3-dimensional T	unclear whether: a co the index test was inte ently of the index test.) Reference	rpreted with	random sample of eout knowledge of the	
Overall risk of bias Indirectness Overall indirectness AD versus DLB Index Test: MRI MRI imaging using 1	selection: Serious (Subgroup patients was enrolle reference standard Patient selection: Not serious	analysis whed and inapported for the reference Low	nere >10% population propriate exclusions ence test was interp Index test: All scans include a 3	were avoided; breted independent Low 3-dimensional Thod.	unclear whether: a co the index test was inte ently of the index test.) Reference standard:	rpreted with Low cho sequence	random sample of eout knowledge of the	

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	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								
Imaging data were a	ssessed using an aut	omatic imag	e quantification met	hod.	1-weighted gradient ed	·		
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	patients was enroll	ed and inap	propriate exclusions	were avoided; t	unclear whether: a co the index test was inte ently of the index test.)	rpreted with		
	Totororioo otariaara							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Indirectness Overall indirectness	Patient	Low	Index test:	Low		Low		
Overall	Patient selection: Not serious	Low	Index test:	Low		Low		
Overall indirectness FTD versus non-F1 Index Test: MRI MRI imaging using 1	Patient selection: Not serious	RI devices.	All scans include a 3	3-dimensional T			ce and a fast FLAIR s	sequenc
Overall indirectness FTD versus non-F1 Index Test: MRI MRI imaging using 1	Patient selection: Not serious O T, 1.5 T or 3.0 T M	RI devices.	All scans include a 3	3-dimensional T	standard:	cho sequend	ce and a fast FLAIR s	sequenc 392

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Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
FTD versus non-FT	D dementias							
Imaging data were a	ssessed using an aut	omatic imag	e quantification met	hod.	1-weighted gradient ed			
Results	True positives:	57	False negatives:	35	False positives:	18	True negatives:	276
	D (1)	Unclear	Index test:	Low	Reference	Unclear	Flow and	High
Risk of bias	Patient selection:	Unclear	mack test.	20	standard:		timing:	J
	selection: Serious (Subgroup patients was enroll	analysis wh ed and inap	ere >10% populatio propriate exclusions	n excluded and were avoided;		nsecutive o	timing: r random sample of e	eligible
Overall risk of bias	selection: Serious (Subgroup patients was enroll	analysis whed and inapport or the reference	ere >10% populatio propriate exclusions	n excluded and were avoided; reted independe	standard: unclear whether: a co the index test was inte	nsecutive o	timing: r random sample of e	eligible
Overall risk of bias Indirectness Overall	selection: Serious (Subgroup patients was enroll reference standard	analysis whed and inapport or the reference	ere >10% populatio propriate exclusions ence test was interp	n excluded and were avoided; reted independe	standard: unclear whether: a co the index test was inte ently of the index test.) Reference	nsecutive o rpreted with	timing: r random sample of e	eligible
Risk of bias Overall risk of bias Indirectness Overall indirectness FTD versus AD	selection: Serious (Subgroup patients was enroll reference standard Patient selection:	analysis whed and inapport or the reference	ere >10% populatio propriate exclusions ence test was interp	n excluded and were avoided; reted independe	standard: unclear whether: a co the index test was inte ently of the index test.) Reference	nsecutive o rpreted with	timing: r random sample of e	eligible
Overall risk of bias Indirectness Overall indirectness FTD versus AD Index Test: MRI MRI imaging using 1	selection: Serious (Subgroup patients was enroll reference standard Patient selection: Not serious	analysis whed and inapported for the reference Low	ere >10% populatio propriate exclusions ence test was interp Index test:	on excluded and were avoided; creted independent Low	standard: unclear whether: a co the index test was inte ently of the index test.) Reference	nsecutive o rpreted with Low	timing: r random sample of electric transfer sample of the	eligible e
Overall risk of bias Indirectness Overall Indirectness FTD versus AD Index Test: MRI MRI imaging using 1	selection: Serious (Subgroup patients was enroll reference standard Patient selection: Not serious O T, 1.5 T or 3.0 T M	analysis whed and inapported for the reference Low RI devices. A comatic image	ere >10% populatio propriate exclusions ence test was interp Index test:	on excluded and were avoided; breted independent Low 3-dimensional T hod.	standard: unclear whether: a co the index test was inte ently of the index test.) Reference standard:	nsecutive o rpreted with Low	timing: r random sample of electric transfer sample of the	eligible e

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	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							
FTD versus DLB								
Imaging data were a	ssessed using an aut	omatic imag	e quantification met	hod.	1-weighted gradient ed			
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	patients was enroll	ed and inap	propriate exclusions	were avoided; t	unclear whether: a co the index test was inte ently of the index test.)	rpreted with		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
FTD versus VaD								
Index Test: MRI	0 T 4 T 0 0 T 14	RI devices.			1-weighted gradient ed	cho sequend	ce and a fast FLAIR s	sequenc
MRI imaging using 1	.0 T, 1.5 T or 3.0 T M ssessed using an aut		e quantification met	noa.				
MRI imaging using 1		omatic imag	e quantification met False negatives:		False positives:	0	True negatives:	24

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					the index test was inte ently of the index test.)		out knowledge of the)
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
DLB versus non-Di	_B							
Imaging data were a	ssessed using an aut	omatic imag	e quantification met	hod.	1-weighted gradient ed			·
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	Not serious							
indirectness	Dalamantias							
indirectness DLB versus non-Dl	-B dementias							
DLB versus non-Di Index Test: MRI MRI imaging using 1					1-weighted gradient ed	cho sequend	ce and a fast FLAIR s	sequend
DLB versus non-Di Index Test: MRI MRI imaging using 1	.0 T, 1.5 T or 3.0 T M	omatic imag		hod.	1-weighted gradient ed	cho sequend	ce and a fast FLAIR s	sequend 321

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	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							
DLB versus AD								
	.0 T, 1.5 T or 3.0 T M ssessed using an aut				1-weighted gradient ed	cho sequend	ce and a fast FLAIR	sequenc
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	patients was enroll	ed and inap	propriate exclusions	were avoided; t	unclear whether: a co he index test was inte ently of the index test.)	rpreted with		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
	Not serious							
Overall indirectness								
								<u> </u>
indirectness DLB versus FTD Index Test: MRI MRI imaging using 1	.0 T, 1.5 T or 3.0 T M ssessed using an aut				1-weighted gradient ed	cho sequend	ce and a fast FLAIR	sequenc
indirectness DLB versus FTD Index Test: MRI MRI imaging using 1		omatic imag		thod.	1-weighted gradient ed False positives:		ce and a fast FLAIR s	·

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					the index test was inte ently of the index test.)		out knowledge of the)
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
DLB versus VaD								
Imaging data were as	sessed using an aut	omatic imag	e quantification met	hod.	1-weighted gradient ed			·
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	patients was enroll	ed and inap	propriate exclusions	were avoided; t	unclear whether: a co the index test was inte ently of the index test.)	rpreted with		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
V-D V-F)							
VaD versus non-Va[All agenc include a f	3-dimensional T	1-weighted gradient ed	cho sequenc	ce and a fast FLAIR :	sequenc
Index Test: MRI MRI imaging using 1.								
VaD Versus non-val Index Test: MRI MRI imaging using 1. Imaging data were as Results		omatic imag			False positives:	26	True negatives:	454

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Overall risk of bias	Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall Indirectness	Not serious							
VaD versus non-Val) dementias							
Imaging data were as	ssessed using an auto	omatic imag	e quantification met	thod.	1-weighted gradient ed	·		·
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	patients was enrolle	ed and inap	propriate exclusions	were avoided; t	unclear whether: a co he index test was inte ently of the index test.)	rpreted with		
		Laur	Index test:	Low	Reference	Low		
Indirectness	Patient selection:	LOW	mack tooti		standard:			
Indirectness Overall indirectness		LOW			standard:			
Overall	selection:	Low			standard:			
Overall indirectness VaD versus AD Index Test: MRI MRI imaging using 1.	selection: Not serious 0 T, 1.5 T or 3.0 T M	RI devices.	All scans include a 3		standard: 1-weighted gradient ed	cho sequend	ce and a fast FLAIR s	sequenc
Overall indirectness VaD versus AD Index Test: MRI	selection: Not serious 0 T, 1.5 T or 3.0 T M	RI devices. omatic imag	All scans include a 3	thod.			ce and a fast FLAIR s	·

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					he index test was inteently of the index test.)		out knowledge of the)
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall Indirectness	Not serious							
VaD versus FTD								
maging data were as	ssessed using an auto	omatic imag	e quantification met	hod.	1-weighted gradient ed			·
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	patients was enrolle	ed and inap	propriate exclusions	were avoided; t	unclear whether: a co he index test was inte ently of the index test.)	rpreted with		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
	Not serious							
indirectness	Not serious							
Indirectness VaD versus DLB Index Test: MRI MRI imaging using 1.	0 T, 1.5 T or 3.0 T MI				1-weighted gradient ed	cho sequenc	ee and a fast FLAIR s	sequenc
Overall indirectness VaD versus DLB Index Test: MRI MRI imaging using 1. Imaging data were as Results	0 T, 1.5 T or 3.0 T MI	omatic imag		hod.	1-weighted gradient ed False positives:		ee and a fast FLAIR s	sequenc 45

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Overall risk of bias	patients was enroll	ed and inap	propriate exclusions	were avoided; t	unclear whether: a conthe index test was interest.)	rpreted with		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Kukull WA, Larson I dementia. J Clin Epi			k W, Pfanschmidt	ML. The mini m	ental state examinat	ion score a	nd the clinical diag	nosis of
Study type	Prospective Cohor	ŧ						
Country	USA							
Setting	Not stated							
Inclusion criteria			ia who had medical her speciality clinics		with a particular healt	h maintenar	nce organisation. Ide	ntified by
Exclusion criteria	Previous diagnosis	of dementia	a					
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 d	diagnose dementia.					
Dementia versus no	dementia							
Index Test: MMSE (<25)							
MMSE, 25			False	24	False positives:	7	True negatives:	46
,	True positives:	56	negatives:	21				
MMSE, 25 Results Additional comme nts	·		negatives:		re not commonly used			

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	selection:				standard:		timing:	
Overall risk of bias		ed cut-offs v			d without knowledge o cut-off; the index test r			
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		ed cut offs v			d without knowledge o cut off; the index test re			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (4 MMSE, 23	<23)							
Results	True positives:	45	False negatives:	35	False positives:	0	True negatives:	53

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Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias		ed cut offs v			d without knowledge o cut off; the index test re			
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 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		ed cut offs v			d without knowledge o cut off; the index test re			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		

P.1.12 L

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

Study type Prospective cohort

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	109 : 491–494							
Country	UK							
Setting	Cognitive function of							
Inclusion criteria	Consecutive new re		e 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	DSM-IV criteria.					
Dementia versus no	dementia							
Index Test: Addenbr Addenbrooke's Cogni								
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		to differentiate bety	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							
Overall risk of bias Indirectness	Not serious Patient selection:	Low	Index test:	Low	Reference standard:	Low		
	Patient	Low	Index test:	Low		Low		
Indirectness Overall	Patient selection: Not serious			Low		Low		
Indirectness Overall indirectness	Patient selection: Not serious rooke's Cognitive E	xamination	, ACE (<83)	Low		Low		

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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	_							
Results	True positives:	119	False negatives:	21	False positives:	25	True negatives:	120
Additional comme nts	The data on using in practice for this		s to differentiate bety	ween dementia	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							

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

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Larner AJ. AD8 Infor	mant questionnair	e: pragmati	ce diagnostic test	accuracy study	y. Journal of Geriatr.	Psychiatry,	2015; 28: 198-202.	
Age	Median age 64.4 ye	ears (range	16-92)					
Presentation	Cognitive complain	its						
Reference standard	Dementia diagnose	ed according	to DSM-IV criteria.					
Dementia versus no	t dementia							
Index Test: AD8 (≥2)								
AD8, ≥ 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 cognit	ive impairment (demei	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 (<	:25)							
MMSE, ≤24/30								
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 cognit	ive impairment (demei	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	Low		
	Selection.				standard:			

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

Study type	Prospective cohort							
Country	UK							
Setting	Cognitive functions	al clinic at a	regional neuroscien	ce centre				
Inclusion criteria	New patient referra	als from a co	gnitive function clini	C.				
Exclusion criteria	Pre-existing diagno	osis of deme	entia					
Sex	65.0% male							
Age	Median 69 years (r	ange 31-89	years)					
Presentation	Not specified.							
Reference standard	DSM-IV diagnosis	of dementia						
Dementia versus no	dementia (includin	ng MCI and	SMC)					
Index Test: Mini-AC Mini-ACE, ≤ 25/30	<u> </u>							
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	Not serious							
indirectness								
	dementia MCI and	SMC						
	o dementia MCI and al Cognitive Assess		A (<26)					

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Larner AJ. MACE ve	rsus MoCA: equiva	lence or su	periority? Pragma	tic diagnostic t	est accuracy study. I	nt. Psych. (Geriatr. 2017; 29: 9:	31-7.
			negatives:					
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

Lattanzio F, Abu-Rumelleh S, Franceschini A, Kal H, Amore G et al. Prion-specific and surrogate CSF biomarkers in Creutzfeldt-Jakob disease: diagnostic accuracy in relation to molecular subtypes and analysis of neuropathological correlates of p-tau and Aβ42 levels. Acta Neuropathol 2017; 133: 559–578.

•	
Study type	Retrospective cohort
Country	Italy
Setting	Laboratory of Neuropathology (NP-Lab) of the Institute of Neurological Sciences of Bologna (ISNB) (major reference laboratory for prion disease in Italy).
Inclusion criteria	Samples from suspected CJD cases submitted for diagnostic purposes between January 2003 and June 2016, to the Laboratory of Neuropathology.
Exclusion criteria	None stated
Sex	Not stated
Age	Not stated
Presentation	Suspected CJD
Reference standard	Diagnosis of CJD was carried out using the updated WHO criteria (Zerr, 2009), with the exclusion of CSF biomarker data for the classification of "possible" and "probable" CJD. Definite CJD cases were classified based on post-mortem examination, but also included genetic cases lacking neuropathology data.

CJD (definite, probable, possible and genetic) versus not CJD

Index Test: Real-time quaking-induced prion conversion, RT-QuIC.

Real-time quaking-induced prion conversion (RT-QuIC). The fluorescence intensity of ThT-PrPSc aggregates, expressed as relative fluorescence units (rfu), was taken every 45 min using 450 ± 10 nm (excitation) and 480 ± 10 nm (emission) wavelengths, with a bottom read. A CSF sample was considered prion positive if the mean of at least two out four sample replicates gave a fluorescence signal higher than the threshold cut-off value of 7000 rfu. This

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Lattanzio F, Abu-Rumelleh S, Franceschini A, Kal H, Amore G et al. Prion-specific and surrogate CSF biomarkers in Creutzfeldt-Jakob disease: diagnostic accuracy in relation to molecular subtypes and analysis of neuropathological correlates of p-tau and Aβ42 levels. Acta Neuropathol 2017; 133: 559–578.

threshold represents the mean rfu values of negative samples plus at least five standard deviations. Samples were considered negative if none of the replicates surpassed the chosen cut-off. In case only one replicate went over the threshold, the test was considered ambiguous/ unclear and repeated.

Results	True positives:	289	False negatives:	63	False positives:	2	True negatives:	346
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

CJD (definite) versus not CJD (definite)

Index Test: Real-time quaking-induced prion conversion, RT-QuIC.

Real-time quaking-induced prion conversion (RT-QuIC). The fluorescence intensity of ThT-PrPSc aggregates, expressed as relative fluorescence units (rfu), was taken every 45 min using 450 ± 10 nm (excitation) and 480 ± 10 nm (emission) wavelengths, with a bottom read. A CSF sample was considered prion positive if the mean of at least two out four sample replicates gave a fluorescence signal higher than the threshold cut-off value of 7000 rfu. This threshold represents the mean rfu values of negative samples plus at least five standard deviations. Samples were considered negative if none of the replicates surpassed the chosen cut-off. In case only one replicate went over the threshold, the test was considered ambiguous/ unclear and repeated.

Results	True positives:	190	False negatives:	35	False positives:	1	True negatives:	162
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

CJD (definite, probable, possible and genetic) versus not CJD

Index Test: CSF 14-3-3 immunoblotting

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Lattanzio F, Abu-Rumelleh S, Franceschini A, Kal H, Amore G et al. Prion-specific and surrogate CSF biomarkers in Creutzfeldt-Jakob disease: diagnostic accuracy in relation to molecular subtypes and analysis of neuropathological correlates of p-tau and Aβ42 levels. Acta Neuropathol 2017; 133: 559–578.

14-3-4 detected by immunoblotting. The immunoreactivity signals were rated as negative, ambiguous or positive, on the basis of the optical densitometric (OD) comparison with the weakly positive control.

Results	True positives:	298	False negatives:	61	False positives:	118	True negatives:	585
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

CJD (definite) versus not CJD (definite)

Index Test: CSF 14-3-3 immunoblotting

14-3-4 detected by immunoblotting. The immunoreactivity signals were rated as negative, ambiguous or positive, on the basis of the optical densitometric (OD) comparison with the weakly positive control.

Results	True positives:	194	False negatives:	39	False positives:	79	True negatives:	133
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

CJD (definite, probable, possible and genetic) versus not CJD

Index Test: Total Tau

Total-tau, > 1250pm/ml. INNOTEST ELISA.

Results True positives: 321 False 38 False positives: 84 True negatives: 619
--

				•	and surrogate CSF bi			
diagnostic accuracy 2017; 133: 559–578.	in relation to mole	cular subty	pes and analysis o	of neuropatholo	ogical correlates of p	-tau and A∫	342 levels. Acta Ne	ıropath
,			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 Tar Total-tau, > 1250pm/r		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 Communications 19		kinen P, Lin	droth L, Liewenda	hl K, et al. 99To	m-HMPAO SPECT in	suspected	l dementia. Nuclear	Medici
Study type	Prospective cohort							
Country	Finland							
Setting	University hospital	out-patient r	nemory disorder cli	nic				
Inclusion criteria	Patients with suspe	ected demer	ntia admitted to the	outpatient memo	ory disorder clinic			

Not stated

Exclusion criteria

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Launes J, Sulkava R, Erkinjuntti T, Nikkinen P, Lindroth L, Liewendahl K, et al. 99Tcm-HMPAO SPECT in suspected dementia. Nuclear Medicine Communications 1991;12: 757–65.							
Sex	38.8% male						
Age	mean age 64.2 years (SD 8.7)						
Presentation	Suspected dementia						
Reference standard	Neary 1998 criteria (FTD), NINCDS-ADRDA (AD), DSM-III-R (VaD)						

AD versus non-AD

Index Test: 99mTc-HMPAO SPECT

99mTc-HMPAO SPECT; threshold: not pre-specified; visual interpretation, using magenta scale: bilateral anterior CBF abnormality or bilateral anterior plus unilateral posterior CBF abnormality (SPECT indicative of FTLD). Visual interpretation with image analysis; single- headed camera used to take images. SPECT FTD pattern indicative of FTD: bilateral anterior brain hypoperfusion.

Results	True positives:	23	False negatives:	13	False positives:	17	True negatives:	107
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall	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	Unclear	Index test:	Low	Reference	Low	Flow and	High
	selection: standard: timing:							
Overall risk of bias	Serious (Subgroup analysis used with >10% study population excluded.)							

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Launes J, Sulkava I Communications 19		kinen P, Lin	droth L, Liewenda	hl K, et al. 99Tc	m-HMPAO SPECT in	suspected	dementia. Nuclear	Medicin
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus FTD								
	CT; threshold pre-sp	s. BUT singl	e head camera used		atterns on the SPECT and not in clinical use			and
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 excl	uded.)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
VaD versus non-Va	D							
Index Test: 99mTc-HMPAO SPECT 99mTc-HMPAO SPECT; threshold pre-specified at 25% for lower threshold value; rCBF patterns on the SPECT scans were interpreted visually and without knowledge of the clinical diagnosis. BUT single head camera used - less accurate and not in clinical use today. Image analysis was not performed. VaD pattern used to determine positive results.								
Results	True positives:	25	False negatives:	8	False positives:	60	True negatives:	67
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Not serious							
Indirectness	Patient	Low	Index test:	Low	Reference	Low		

selection:

standard:

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•	R, Erkinjuntti T, Nikkinen P, Lindroth L, Liewendahl K, et al. 99Tcm-HMPAO SPECT in suspected dementia. Nuclear Medicine
Communications 19	91;12: 757 – 65.
Overall	Not serious

indirectness

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

VaD versus FTD

Index Test: 99mTc-HMPAO SPECT

99mTc-HMPAO SPECT; threshold pre-specified at 25% for lower threshold value; rCBF patterns on the SPECT scans were interpreted visually and without knowledge of the clinical diagnosis. BUT single head camera used - less accurate and not in clinical use today. Image analysis was not performed. VaD pattern used to determine positive results.

Results	True positives:	25	False negatives:	8	False positives:	2	True negatives:	3
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Serious (Subgroup	analysis us	ed with >10% study	population excl	uded.)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

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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.

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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	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-HMPAO SPECT

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Results

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 excl	uded.)			
Indirectness	Patient selection:		Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

Leitao MJ, Baldeiras I, Almeida MR, Ribeiro MH, Santos AC, Ribeiro M, Tomas J et al. Sporadic Creutzfeldt-Jakob disease diagnostic accuracy is improved by a new CSF ELISA 14-3-3y assay. Neuroscience 2016; 322: 398-407.

Study type	Retrospective cohort
Country	Portugal
Setting	Neurochemistry laboratory at University Hospital, Coimbra
Inclusion criteria	Clinical suspicion of sporadic CJD
Exclusion criteria	None stated
Sex	88.3% male
Age	Mean age 64.6 (SD 12.1)
Presentation	Suspected CJD
Reference standard	Neuropathology
CJD versus not CJD	
Index Test: CSF 14-	3-3 ELISA
14-33, Circulex 14-3	3-3γ ELISA. Cut-off >14552 arbitrary units/ml

True positives: 70

False positives: 4

True negatives: 69

False 2

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			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 three			random sample	of patients was enrolle	d; the study	avoided inappropria	te
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Total Ta Total tau, INNOTEST		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 three			random sample	of patients was enrolle	d; the study	avoided inappropria	te
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: p-tau/tot ratio of p-tau/t-tau, IN		-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

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	selection:				standard:		timing:	
Overall risk of bias	Serious (It was und exclusions; test thr			random sample o	of patients was enrolle	d; the study	avoided inappropria	ite
ndirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall Indirectness	Not serious							
	eegen MT, Vreyling rospective study in				, van Gool WA. 14-3-	3 testing in	ı diagnosing Creutz	feldt-
Study type	Prospective cohort							
Country	Netherlands							
Setting	The only specialist	laboratory fa	acility used to test for	or 14-3-3 in CSF	in Netherlands.			
nclusion criteria	Samples from patie	ents with sus	spected CJD that we	ere sent to the la	boratory for testing.			
Exclusion criteria	Not stated							
Sex	Not stated							
Age	Not stated							
Presentation	Rapidly progressiv	e dementia l	eading to suspected	d CJD				
Reference standard	Diagnosis based o cases. The criteria			referring physici	ans, with pathology co	onfirmation of	of CJD in 25/33 CJD	positive
CJD versus not CJI)							
ndex Test: CSF 14-	3-3 immunoblotting							
Detection of presence	e of 14-3-3 protein in	CSF by imm	nunoblotting, thresh	old of detection i	not stated.			
Results	True positives:	32	False negatives:	1	False positives:	10	True negatives:	67
Risk of bias	Patient	Low	Index test:	High	Reference	Unclear	Flow and	Low

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Lemstra AW, van Mo Jakob disease: A pr					, van Gool WA. 14-3-	3 testing in diagnosing Creutzfeldt-
Indirectness	Patient selection:	_	Index test:	Low	Reference standard:	Low
Overall indirectness	Not serious					

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fluid ratio of phosph Study type	norylated tau protein Prospective cohort		myloid peptide(42).	Arch Neurol 20	003; 60: 1202–6.			
Country	Switzerland							
Setting	Memory disorders	unit						
Inclusion criteria	•		ders unit who were i	referred for diagr	nostic workun			
Exclusion criteria	Not stated	Siliory disort	ders drift who were i	cicirca ioi diagi	lostic workup.			
Sex	54.0% male							
Age	Mean age 68.4 yea	rc (SD0 4)						
	• •	, ,						
Presentation	Suspected dementia Diagnosis according to NINCDS-ADRDA for AD; The Lund and Manchester groups criteria for FTD; McKeith criteria for DLB;							
Reference standard	NINDS-AIREN for '		S-ADRDA for AD; I	ne Lund and Ma	inchester groups critei	ria for FTD;	McKeith criteria for L)LB;
AD versus non-AD	dementia							
Index Test: Amyloid Amyloid Beta 1-42, IN		oid ELISA,	cut off 0.49mg/ml					
Results	True positives:	40	False negatives:	11	False positives:	9	True negatives:	21
Additional comme	We excluded healtl	hy controls a	as they did not have	suspected dem	entia at baseline.			
nts			ementia versus no don a 2x2 table of the o		authors used different et as a result.	cut offs with	nin the same test for	different
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low

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Overall risk of bias					made; an optimised t nd reference tests wer			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: p-tau 18 p-tau, INNOTEST p-t		f 35pg/ml						
Results	True positives:	37	False negatives:	14	False positives:	11	True negatives:	19
Additional comme nts	We were unable to	compare de	as they did not have ementia versus no d a 2x2 table of the c	ementia as the a	authors used different	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					made; an optimised t nd reference tests wer			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: p-tau/An p-tau/Amyloid Beta 1-								
Results	True positives:	41	False negatives:	10	False positives:	8	True negatives:	22
Additional comme nts	We excluded health We were unable to	•	as they did not have	•		cut offe with	in the same test for	different

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Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias					made; an optimised t nd reference tests wer			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus no deme	ntia							
Index Test: Amyloid Amyloid Beta 1-42, IN		oid ELISA,	cut off 0.58ng/ml					
Results	True positives:	43	False negatives:	8	False positives:	3	True negatives:	16
Additional comme nts	We were unable to	compare de	as they did not have ementia versus no d a a 2x2 table of the c	ementia as the a	authors used different	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					made; an optimised t nd reference tests wer			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: p-tau 18	1 au 181 ELISA, cut of	f 39na/ml						
u-lau, linino i Es i b-li	au ioi Elion, cat oi	1 00009/1111						

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Maddalena A, Papas fluid ratio of phosph					is of Alzheimer disea 003; 60: 1202–6.	se by meas	suring the cerebros	pinal
Additional comme nts	We were unable to	compare de	as they did not have ementia versus no d a 2x2 table of the c	ementia as the a	authors used different	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	`				nmade; an optimised t nd reference tests wer			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: p-tau/Amp-tau/Amyloid Beta 1-								
Results	True positives:	41	False negatives:	10	False positives:	2	True negatives:	17
Additional comme nts	We were unable to	compare de	as they did not have ementia versus no d a 2x2 table of the c	ementia as the a	authors used different	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					n made; an optimised t nd reference tests wer			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

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Singapore. Ann Aca			9-9.								
Study type	Prospective cohort										
Country	Singapore	, ,,					0 11 '' 1				
Setting			· ·	i Hospital, Chan	gi General Hospital ar	id Ian 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										
Reference standard	Clinician diagnosis	-criteria not	stated								
Dementia versus no	dementia (includin	g MCI)									
Index Test: Short Po	ortable Mental Statu	s Question	naire, SPMSQ (≥5)								
Short Portable Menta	l Status Questionnair	e (SPMSQ)	• • • • • • • • • • • • • • • • • • • •								
	I Status Questionnair True positives:	` ′	• • • • • • • • • • • • • • • • • • • •	ish or Chinese	False positives:	6	True negatives:	18			
Results		` ′	, cut-off ≥ 5, in Engl False	ish or Chinese 23	False positives: Reference standard:	6 Yes	True negatives: Flow and timing:	18 Low			
Results Risk of bias	True positives: Patient selection:	80 Unclear	, cut-off ≥ 5, in Engl False negatives: Index test:	ish or Chinese 23 High	Reference	Yes	Flow and timing:	Low			
Results Risk of bias Overall risk of bias	True positives: Patient selection: Serious (It was und	80 Unclear lear whethe	, cut-off ≥ 5, in Engl False negatives: Index test:	ish or Chinese 23 High inappropriate ex	Reference standard:	Yes	Flow and timing:	Low			
Results Risk of bias Overall risk of bias Indirectness Overall	Patient selection: Serious (It was und population groups.) Patient selection:	80 Unclear lear whethe High	, cut-off ≥ 5, in Engl False negatives: Index test: r the study avoided	ish or Chinese 23 High inappropriate ex	Reference standard: cclusions and optimise Reference	Yes d test cut-of	Flow and timing:	Low			
Results Risk of bias Overall risk of bias Indirectness Overall indirectness	Patient selection: Serious (It was und population groups.) Patient selection: Serious (60% partic	80 Unclear lear whethe High cipants had	r the study avoided Index test: Index test: Index test: Index test: Index test:	ish or Chinese 23 High inappropriate ex Low	Reference standard: cclusions and optimise Reference	Yes d test cut-of	Flow and timing:	Low			
Short Portable Menta Results Risk of bias Overall risk of bias Indirectness Overall indirectness Index Test: Short Po Short Portable Menta	Patient selection: Serious (It was und population groups.) Patient selection: Serious (60% particular portable Mental Statu	80 Unclear lear whethe High cipants had	r the study avoided Index test: Index test:	ish or Chinese 23 High inappropriate ex	Reference standard: cclusions and optimise Reference	Yes d test cut-of	Flow and timing:	Low			

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Additional comme nts								
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Yes	Flow and timing:	High
Overall risk of bias					te exclusions; optimised 40% study population		offs were used for dif	ferent
ndirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low		
Overall indirectness	Serious (Participan	ts had < 6 y	ears education)					
Index Test: Short Po Short Portable Menta								
Results	True positives:	81	False negatives:	22	False positives:	6	True negatives:	18
Additional comme								
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Yes	Flow and timing:	High
Overall risk of bias					te exclusions; optimised 60% study population		offs were used for dif	ferent
ndirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low		
		nanta had >	6 years education)				
	Not serious (Partici	pants nau ≥	o yeare education ,					
indirectness Manabe Y, Inui Y, To	yama H and Kosak	a K. 123I-m	etaiodobenzylgua		ial scintigraphy with		es alone is useful f	or the
	yama H and Kosak	a K. 123I-m Lewy bodie	etaiodobenzylgua		ial scintigraphy with aging, 2017; 261: 75-		es alone is useful f	or the

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	oyama H and Kosaka K. 123I-metaiodobenzylguanidine myocardial scintigraphy with early images alone is useful for the is 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					whether the reference without knowledge			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		

					dial scintigraphy with naging, 2017; 261: 75-		es alone is useful f	or the
Overall indirectness	Not serious							
Index Test: 123I-MIE	BG cardiac scintigra	phy						
equipped with an LMI followed by a 20-min neurologist. In additio	EGP collimator. They SPECT acquisition if n, semi-quantitative of for Automatic Regio	carried out uptake was evaluation on of Interes	a 4-min static acques observed. MIBG in of the H/M ratio was t (ROI) setting in MII	isition 15 min aft naging scans we performed. The	med using a Symbia T ter intravenous injection ere read and interprete H/M ratio and washou B) software. According	n of 111 MB d centrally b t ratio were	q MIBG in the right a y a radiologist and a calculated using the	arm, É
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					r whether the reference erpreted without knowle			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
					nd positive predictive eurol 1997; 10: 15–21		chnetium 99-HMPA	O SPECT
Study type	Prospective cohort				,			
Country	USA							
Setting	UCLA Geriatric Bel	navioural Ne	eurology Clinic					
Inclusion criteria		and at leas	t mild abnormalities		c by physicians. Of the ed cognitive and behav			

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	Index MF, Fairbanks LA, Cummings JL. Sensitivity, specificity, and positive predictive value of technetium 99-HMPAO SPECT Ellabeimer'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

Clinician diagnosis of probable, possible or AD unlikely based on NINCDS-ADRDA for AD and other diagnoses made using all Reference available information. standard

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	ere >10% study por	oulation 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

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Overall risk of bias	Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
possible AD versus	AD unlikely							
	CT scanning 2 hrs af	line. Transa	xial, saggital and co	oronal images di	minutes, acquiring in 3 splayed with a colour s			
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 po	oulation exclude	d)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Mathuranath PS, Ne frontotemporal dem	•		_	. A biref cognit	ive test battery to dif	ferentiate	Alzheimer's disease	and
Study type	Prospective cohort							
Country	UK							
Setting	Cambridge memor	y clinic						

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. I Geriatr Psychiatry Neurol 1997: 10: 15-21

injuries, alcoholism).

Exclusion criteria

12 months; able to complete the full assessment; and CDR and neuropsychological tests completed within 90 days of ACE.

Evidence of two or more pathologies, either of which could independently be the main cause of dementia; major depression by the DSM-IV or other psychiatric illness; causes of cognitive impairment other than vascular or degenerative pathology (eg. head

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	<u></u>						<u></u>	
Mathuranath PS, Nes frontotemporal demo				. A biref cognit	ive test battery to dif	ferentiate A	Alzheimer's disease	and
Sex	57.6% male							
Age	Mean age 66.1 yea	ars (SD 8.6)						
Presentation	Suspected dement	ia						
Reference standard	Dementia was diag	nosed acco	rding to the DSM-IV	' .				
Dementia versus no	dementia							
Index Test: Addenbr Addenbrooke's Cogni			, ACE (<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 results of the refere			unclear whether	the index test results	were interpr	reted without knowled	dge of the
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Addenbr Addenbrooke's Cogni			, 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 refere			unclear whether	the index test results	were interpr	reted without knowled	dge of the
Indirectness	Patient	Low	Index test:	Low	Reference	Low		

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	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			unclear whether	the index test results	were inter	rpreted without knowle	dge of t
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (MMSE, conventional								
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		

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Study type	Retrospective cohort							
Country	USA							
Setting	Twenty-six Alzheimer's disease centres across USA.							
Inclusion criteria	People referred to 26 Alzheimer's disease centres for the evaluation of dementia.							
Exclusion criteria	Not stated							
Sex	49.0% male							
Age	Mean age 72.0 yea	rs (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 diseas which are similar to the CERAD criteria. If neither were used, centre investigators specified how the post-mortem diagnosis was made							
	made.				J ,			olo mao
AD dementia versus					3 1			olo ilido
Index Test: Apo E (2	non-AD dementia 1 allele)	sing DNA fro	om tissue or blood s	amples; if this w	ras not available frozer			
Index Test: Apo E (a Apo E, ≥ 1 allele as d	non-AD dementia 1 allele)		om tissue or blood s False negatives:			n tissue was		285
Index Test: Apo E (a Apo E, ≥ 1 allele as d Results Additional comme	s non-AD dementia 21 allele) etermined by PCR us True positives: Data on the diagno	1142 stic test acc	False negatives:	628 linical diagnosis	ras not available frozei	n tissue was 133	s assayed. True negatives:	285
Index Test: Apo E (a Apo E, ≥ 1 allele as d Results Additional comme nts	s non-AD dementia 21 allele) etermined by PCR us True positives: Data on the diagno	1142 stic test acc was used a	False negatives:	628 linical diagnosis sites.	as not available frozer False positives:	n tissue was 133	s assayed. True negatives:	285
Index Test: Apo E (a Apo E, ≥ 1 allele as d Results Additional comme nts Risk of bias	etermined by PCR use True positives: Data on the diagnoone clinical criteria Patient	1142 stic test acc was used a	False negatives: suracy of the initial c cross the 26 study s	628 linical diagnosis sites.	ras not available frozer False positives: was not compared to Reference	n tissue was 133 the patholog	s assayed. True negatives: gical diagnosis as mo	285 ore than
AD dementia versus Index Test: Apo E (a Apo E, ≥ 1 allele as d Results Additional comme nts Risk of bias Overall risk of bias Indirectness	etermined by PCR use True positives: Data on the diagnoone clinical criteria Patient selection:	1142 stic test acc was used a	False negatives: curacy of the initial c cross the 26 study s	628 linical diagnosis sites.	ras not available frozer False positives: was not compared to Reference	n tissue was 133 the patholog	s assayed. True negatives: gical diagnosis as mo	285 ore than

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	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.

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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-Va	D							
Results	schemic pattern (Val True positives:	ı İ	False		False positives:	10	True negatives:	32
		ı İ				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								
collected using a 128	ECT imaging was carr	an elliptical	orbit off 360 degree	s. Images were i	h-resolution parallel-heconstructed and clas			
Results	True positives:	ı İ	False negatives:	_	False positives:	4	True negatives:	22

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McMurdo ME, Grant Alzheimer's disease					e of HMPAO SPECT : ; 15: 405-409.	scanning ir	n the diagnosis of e	arly		
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									
Mendez MF, Shapira 830-835.	a JS, McMurtray A, I	Licht E, Mill	er BL. Accuracy of	f the clinical ev	aluation of Frontoter	mporal dem	entia. Arch Neurol	2007; 64		
Study type	Retrospective coho	ort								
Country	USA									
Setting	Neurology clinic at	leurology clinic at UCLA.								
Inclusion criteria	People with suspec	cted FTD ref	erred to the clinic fo	r diagnosis.						
Exclusion criteria	Patients with langu	age-predom	inant variants (PA o	or semantic dem	entia) and frontotempo	oral lobar de	generation.			
Sex	43.3% male									
Age	Mean age 63.4 yea	ars (SD 7.5)								
Presentation	Suspected FTD									
Reference standard	Clinician diagnosis	after 2 year	s follow up.							
FTD versus not FTD										
Index Test: FTD cor	sensus criteria									
FTD consensus criter	ria (Neary, 1998)									
Results	True positives:	23	False negatives:	40	False positives:	0	True negatives:	71		
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	Low		
Overall risk of bias	Not serious									

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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	sed by the rese	earchers.			
Results	True positives:	40	False negatives:	23	False positives:	21	True negatives:	50
Additional comme								
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/I	PET							
				ECT and others	PET results which we	re re-analy	sed by the researcher	s. Resu
rated for atrophy, hyp Results	True positives:		ri a 4 point scale.	6	False positives:	10	True negatives:	53
Results	True positives.	57	negatives:	O	raise positives.	10	True negatives.	55
			nogunivos.					
			nogunvoo.					
nts	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
nts Risk of bias		Low		Low		Low		Low
Additional comme nts Risk of bias Overall risk of bias	selection:			Low		Low		Low

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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

Study type	Retrospective Coh	ort									
Country	Germany										
Setting	Memory clinic of th	e Departme	nt of Psychiatry and	Psychotherapy	at the University Hosp	ital of Tubir	ngen.				
Inclusion criteria	People admitted to	eople admitted to the memory clinic between 2004 and 2009.									
Exclusion criteria	Not stated	ot stated									
Sex	38.6% male	8.6% male									
Age	Mean age 74.8 yea	ean age 74.8 years (SD 8.1)									
Presentation	Suspected dement	ia									
Reference standard	Diagnosis of deme	ntia based o	n the DSM-IV criteri	a and the NINC	DS-ADRDA criteria for	r AD.					
Dementia versus no	dementia										
Index Test: Mini-Cog	g (Scanlan and Bors	son algorith	nm)								
Mini-Cog, Scanlan an	d Borson algorithm										
Results	True positives:	380	False negatives:	58	False positives:	0	True negatives:	64			
Additional comme nts			vas not extracted for sis and no raw data		r non-AD dementia be	ecause it is u	unclear which compa	rator			
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Unclear	Flow and timing:	Low			
Overall risk of bias					whether the patients w wledge of the results o			mple and			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall	Not serious										

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Clock Drawing Test, (CDT, cut-off >2, mod	ified versior	of Shulman and Go	old (1 perfect, 6	no reasonable represe	ntation of a	clock)	
Results	True positives:	342	False negatives:	96	False positives:	2	True negatives:	62
Additional comme nts			was not extracted fo sis and no raw data		r non-AD dementia be	cause it is ι	ınclear which compa	rator
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Unclear	Flow and timing:	Low
Overall risk of bias					vhether the patients w vledge of the results o			nple 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	•	•	was not extracted fo ysis and no raw data		r non-AD dementia be	cause it is ι	ınclear which compa	rator
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Unclear	Flow and timing:	Low
Overall risk of bias					whether the patients w wledge of the results o			nple and
ndirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall	Not serious							

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	Milian M, Leiherr AM, Straten G, Muller S, Leyhe T, Eschweiler GW. The Mini-Cog versus the Mini-Mental State Examination and the Clock Drawing Test in daily clinical practice: screening value in a German Memory Clinic. International Psychogeriatrics 2012; 24: 766-74												
Results	True positives:	347	False negatives:	91	False positives:	0	True negatives:	64					
Additional comme nts	Diagnostic test accuracy data was not extracted for detecting AD or non-AD dementia because it is unclear which comparator groups were used for the analysis and no raw data is presented.												
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Unclear	Flow and timing:	Low					
Overall risk of bias					whether the patients w wledge of the results o			mple and					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low							
Overall indirectness	Not serious												

Inclusion criteria Fren Exclusion criteria MMS	nory clinic speaking participants at their first visit to the memory clinic. SE < 16, inadequate ability to understand and speak French, severe visual disturbance making reading impossible, refusal to
Inclusion criteria Fren Exclusion criteria MMS	ich speaking participants at their first visit to the memory clinic. SE < 16, inadequate ability to understand and speak French, severe visual disturbance making reading impossible, refusal to
Exclusion criteria MMS	SE < 16, inadequate ability to understand and speak French, severe visual disturbance making reading impossible, refusal to
	plete neuropsychological examination.
Sex 41.5°	% male
Age Mean	n age 70.0 (SD 9.4)
Presentation Susp	pected dementia
Reference Clinic standard	cian diagnosis of dementia according to DSM-IV.
Dementia versus SMC (MC	CI excluded)

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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 rec	all score of 5- word	test, ≤ 6 fo	r all dementia					
Free recall score of 5	- word test, ≤ 6 for al	I 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 red	call 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								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	High

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Mormont E, Jamart	J, Robaye L. Validit	y of the Fiv	e -word testfor the	evaluation of v	verbal episodic memo	ory and der	mentia in a memory	clinic
	Geriatr Psych and N						· ·	
Overall risk of bias	Very serious (Exclu	ısion 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		ord test, ≤	15					
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	ısion 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	CI 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	ısion of >35	% population at ana	lysis and use of	optimised test thresho	olds.)		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall	Not serious							

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indirectness Index Test: Free rec	all score of 5, word	tost < E fo	AD					
Free recall score of 5		•	I AD					
Results	True positives:		False negatives:	11	False positives:	0	True negatives:	49
Additional comme								
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							
Index Test: Total red Total recall score of 5		test, ≤ 9						
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	lds.)		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall	Not serious							

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	Mormont E, Jamart J, Robaye L. Validity of the Five -word testfor the evaluation of verbal episodic memory and dementia in a memory clinic setting. Journal of Geriatr Psych and Neurol 2012; 25: 78-84.											
Results	True positives:	55	False negatives:	6	False positives:	2	True negatives:	47				
Additional 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											

deoxy-D-glucose po	T, Russell G, Jamieson S, Ahmed S, Brindle N, Pillai A et al. Clinical impact and diagnostic accuracy of 2-[18F]- fluoro-2- positron-emission tomography/computed tomography (PET/CT) tients 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

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Motara H, Olusoga T, Russell G, Jamieson S, Ahmed S, Brindle N, Pillai A et al. Clinical impact and diagnostic accuracy of 2-[18F]- fluoro-2-deoxy-D-glucose positron-emission tomography/computed tomography (PET/CT)

brain imaging in patients with cognitive impairment: a tertiary centre experience in the UK. Clinical Radiology, 2017; 72: 63-73.

AD versus not AD

Index Test: FDG-PET/CT

18F FDG-PET examinations were performed on a GE Discovery 690 PET/CT system. Image reconstruction parameters were as follows: time-of-flight algorithm (Vue Point FX, GE Healthcare), with iterative reconstruction involving 24 subsets, two iterations, and a 3.2 mm spatial filter. The CT component of the study was carried out using the following parameters: 125 kV, 250 mAs, and 3.75 mm section thickness. The clinical reportwas generated following visual PET data review in transaxial, sagittal, and coronal planes with and without PET/CT image fusion on a GE Advantage Workstation. Standard and accepted reporting criteria were applied in terms of well- ecognised patterns of regional hypometabolism to distinguish between the various causes of cognitive impairment.

Results	True positives:	40	False negatives:	6	False positives:	2	True negatives:	50				
Additional 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 wer	e 22 unstate	ed reasons for exclu	ision)								

Phosphorylated Tau	A, van der Flier WM, Bouwman FH, Kok A, van Elk EJ, Scheltens P, Blankenstein MA. Amyloid- (1– 42), Total Tau, and I as 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

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Phosphorylated Tau Cerebrospinal Fluid		Diagnosis	of Alzheimer Dise	ase Clinical Ch	emistry 2010; 56: 24	8-253		
Exclusion criteria	Not stated	Diagnosis	Of Alzheimer Disco		2010, 00. 24	0-200.		
Sex	50.4% male							
Age	Mean age 64.9 yea	rs (SD 9.5)						
Presentation	Suspected dement	` '						
Reference standard			ccording to NINCDS and used as control		a; patients with all norn	nal test resu	Its were considered	to have
Probable AD versus	not AD							
Index Test: Amyloid CSF Beta Amyloid 42								
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	selected to obtain 8	35% sensitiv		een the referenc	ndomly recruited; the eand index tests is ur			
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								
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	Low

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Mulder C, Verway NA Phosphorylated Tau Cerebrospinal Fluid	as				s P, Blankenstein MA emistry 2010; 56: 24		(1– 42), Total Tau, a	and
Overall risk of bias	Very Serious (It is ubut selected to obtain	unclear whe ain 85% ser	ther participants we	re consecutively etween the refer	or randomly recruited ence and index tests is	; the test cu		
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	but selected to obta	ain 85% ser		etween the refer	or randomly recruited ence and index tests is lts)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

P.1.14 N

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

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Nielsen TR, Anderse Disord 2013; 36: 354		al. Validat	ion of the RUDAS f	for multicultura	I screening in Danisl	n memory o	linics. Dement Ger	iatr Cogn
Inclusion criteria	People referred to with suspected der			ation of possible	e dementia. After Marc	h 2012 sele	ctive inclusion of imn	nigrants
Exclusion criteria	After a March 2012	people fror	n a non-immigrant b	ackground with	suspected dementia v	vere exclude	ed.	
Sex	52.6% male							
Age	Dementia median a	age 77 years	s (Q1-Q3= 71.5-81);	non-dementia 6	61 years (50.5-70).			
Presentation	Suspected dement	ia						
Reference standard	Dementia diagnose	ed according	to the DSM-IV-TR	criteria; patients	with MCI included in t	he non-dem	entia group.	
Dementia versus no	dementia							
Index Test: Rowland	d Universal Dement	ia Assessm	ent Scale, RUDAS	(<22)				
RUDAS (Rowland Un	iversal Dementia As	sessment S	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		ople with im			immigrant backgroun ntly younger than Dan			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Rowland RUDAS (Rowland Un				(<23)				
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

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Nielson TP Anderso	n BB Coffman H of	tal Validat	ion of the BUDAC	or multiquiture	Legraphing in Daniel	momonica	linice Domant Car	iatr Coan
Nielsen TR, Anderse Disord 2013; 36: 354		i ai. vaiidat	ion of the RUDAS 1	or municultura	i screening in Danisi	i memory c		atr Cogn
	selection:				standard:		timing:	
Overall risk of bias		ople with im			immigrant backgroun ntly younger than Dani			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Rowland			•	(<24)				
RUDAS (Rowland Un								
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		ople with im			immigrant backgroun ntly younger than Dani			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Rowland RUDAS (Rowland Un			•	(<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

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Nielsen TR, Anderse Disord 2013; 36: 354		t al. Validat	ion of the RUDAS f	or multicultura	l screening in Danish	n memory o	linics. Dement Ger	iatr Cogn
Disoru 2013, 30. 334	selection:				standard:		timing:	
Overall risk of bias		ople with im			immigrant backgroun ntly younger than Dani			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Rowland RUDAS (Rowland Un			· ·	(<26)				
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		ople with im			immigrant backgroun ntly younger than Dani			
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	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

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Nielsen TR, Anderse	en BB, Gottrup H, e	t al. Validati	ion of the RUDAS f	or multicultura	l screening in Danish	n memory o	linics. Dement Ger	iatr Cogn
Disord 2013; 36: 354					o formal and a		Alma la au	
	selection:				standard:		timing:	
Overall risk of bias		ople with im			f immigrant backgroun ntly younger than Dani			
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 lacke	ed MMSE da	ata and so were excl	uded from the a	nalysis by the authors			
Risk of bias	Patient selection:	High	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias		ople with im			f immigrant backgroun ntly younger than Dani			
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

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Disord 2013; 36: 354					otom dord		4imin a	
	selection:				standard:		timing:	
Overall risk of bias		ople with im			immigrant backgroun ntly younger than Dani			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	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 lacke	ed MMSE da	ata and so were excl	uded from the a	nalysis by the authors			
Risk of bias	Patient selection:	High	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias		ople with im			immigrant backgroun ntly younger than Dani			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE, <27/30	<27)							
Results	True positives:	63	False negatives:	8	False positives:	22	True negatives:	38
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

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	selection:				standard:		timing:
Overall risk of bias		ople with im					non-immigrants during this pants; the test threshold
	Detient	Laur	Indov tooti	Low	Reference	Laur	
Indirectness	Patient selection:	LOW	Index test:	Low	standard:	Low	

P.1.15 O

Study type	Prospective Cohort						
Country	UK						
Setting	Old age psychiatry service						
Inclusion criteria	People referred to the clinic for	or diagnostic investiga	ation of dementia	or depression.			
Exclusion criteria	People with uncertain diagno	ses or cases where a	standard (not ar	ngled) CT scan was c	arried out.		
Sex	42.2% male						
Age	Mean age 79.2 years (SD 7.0)					
Presentation	Suspected dementia or depre	ssion					
Reference standard	AD was diagnosed using the depression using DSM-IV.	NINCDS-ADRDA crit	eria; VaD using I	NINDS-AIREN; DLB u	sing the cor	nsensus criteria (Mck	(eith) and
Dementia versus no	dementia						
degrees C caudal to the section that corre	ed out using an IGE CT 9800 he the orbito-meatal line. The med sponded most closely to that pa r margins of the brain stem was	ium width of the mediassing through the mi	al temporal line (d-point of the ter	(MTL) was measured nporal lobes. The med	from hard c	opies using callipers,	, through
		•					

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			negatives:					
Additional comme nts	Subgroup analysis	was not car	ried out for DLB as	the numbers of	patients was very sma	ll (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								
ndex Test: CT CT scans were carrie degrees C caudal to t	he orbito-meatal line	. The mediu	m width of the medi	al temporal line	ugh the temporal lobes (MTL) was measured mporal lobes. The med	from hard o	copies using callipers,	throug
Index Test: CT CT scans were carrie degrees C caudal to t the section that corres anterior and posterior	he orbito-meatal line sponded most closely	The mediu y to that pas stem was c	m width of the medi sing through the mi chosen for analysis. False	al temporal line d-point of the te Cut off < 11.5m	(MTL) was measured mporal lobes. The med	from hard o	copies using callipers,	throug side of t
Index Test: CT CT scans were carrie degrees C caudal to t the section that corres anterior and posterior Results Additional comme	he orbito-meatal line sponded most closel margins of the brain True positives:	The mediu y to that pas stem was o	m width of the medissing through the michosen for analysis. False negatives:	al temporal line d-point of the tel Cut off < 11.5m 34	(MTL) was measured mporal lobes. The med m.	from hard of dium width	copies using callipers, of the MTL on either s	through side of t
Index Test: CT CT scans were carrie degrees C caudal to t the section that corres anterior and posterior Results Additional comme nts	he orbito-meatal line sponded most closel margins of the brain True positives:	The mediu y to that pas stem was c 35 was not car	m width of the medissing through the michosen for analysis. False negatives:	al temporal line d-point of the te Cut off < 11.5m 34 the numbers of	(MTL) was measured mporal lobes. The med m. False positives:	from hard of dium width	copies using callipers, of the MTL on either s	through side of t
Index Test: CT CT scans were carrie degrees C caudal to t the section that corres anterior and posterior Results Additional comme nts Risk of bias	he orbito-meatal line sponded most closely margins of the brain True positives: Subgroup analysis Patient selection:	The mediu y to that pas stem was o 35 was not car Unclear	m width of the medi sing through the mi chosen for analysis. False negatives: ried out for DLB as	al temporal line d-point of the te Cut off < 11.5m 34 the numbers of Low	(MTL) was measured mporal lobes. The med m. False positives: patients was very sma Reference	from hard of dium width of the following the	copies using callipers, of the MTL on either s True negatives: Flow and	through side of t
ndex Test: CT CT scans were carried degrees C caudal to the section that corresonterior and posterior Results Additional comments Risk of bias Overall risk of bias	he orbito-meatal line sponded most closely margins of the brain True positives: Subgroup analysis Patient selection:	The mediu y to that pas stem was o 35 was not car Unclear analysis wit	Im width of the medissing through the michosen for analysis. False negatives: ried out for DLB as Index test:	al temporal line d-point of the te Cut off < 11.5m 34 the numbers of Low excluded)	(MTL) was measured mporal lobes. The med m. False positives: patients was very sma Reference	from hard of dium width of the following the	copies using callipers, of the MTL on either s True negatives: Flow and	through side of t
Index Test: CT CT scans were carrie degrees C caudal to t	he orbito-meatal line sponded most closely margins of the brain True positives: Subgroup analysis Patient selection: Serious (Subgroup Patient	The mediu y to that pas stem was o 35 was not car Unclear analysis wit	m width of the medissing through the michosen for analysis. False negatives: ried out for DLB as Index test:	al temporal line d-point of the te Cut off < 11.5m 34 the numbers of Low excluded)	(MTL) was measured mporal lobes. The med m. False positives: patients was very sma Reference standard: Reference	from hard of dium width of the following from the f	copies using callipers, of the MTL on either s True negatives: Flow and	throug side of t 8

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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.

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 car	ried out for DLB as	the numbers of p	oatients was very sma	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 with >10% population excluded)									
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									
O'Brien JT, McKeith The British Journal				accuracy of 123	BI-FP-CIT SPECT in p	ossible der	mentia 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	of dementia and	d possible dementia w	ith Lewy boo	dies ; an MMSE scor	e of 10 or		
Exclusion criteria	Parkinson's diseas	e with deme	entia; people with str	ructural imaging	ear before the onset of findings indicative of in ted to interact with stri	nfarction in t	he region of the basa	al ganglia,		
Sex	Not stated									
Age	Age range 55-90 y	ears (mean	age not stated)							
Presentation	possible DLB									
Reference standard	Clinician diagnosis DLB.	after 12 mc	nths follow-up using	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.

Alzheimers Dement	2010, 0. 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)

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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]	he 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			a consecutive or ranger preter with knowle		patients was enrolled a ence diagnosis.)	ind whether	inappropriate exclus	ions were				
Indirectness	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low						
Overall indirectness	Serious (It is unclea	ar whether t	he LeARN cohort co	nsisted of peopl	e with suspected cogr	nitive impairr	ment.)					

AD versus non-AD dementias

Index Test: FDG-PET

185 MBq of 18F-FDG was administered. Patients underwent a 10-minute transmission scan followed by a 15-minute emission scan using an ECAT Exact

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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]	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		ndex test wa	as interpreted with k		e of patients was enro reference diagnosis;							
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 peop	le with suspected cogr	nitive impairr	ment.)					

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).

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Alzheimers Dement Results	True positives:	38	False	27	False positives:	4	True negatives:	14		
Additional comme	, , ,			·	rated during the analys					
				, ,	s not extracted as this					
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High		
Overall risk of bias	were avoided; the i	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.)								
ndirectness	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low				
Overall indirectness	Serious (It is unclea	ar whether t	he LeARN cohort co	nsisted of peopl	e with suspected cogr	nitive impair	ment.)			
AD versus DLB										
Index Test: FDG-PE		Patients und	erwent a 10-minute	transmission sca	an followed by a 15-m	inute emissi	ion scan using an FC	AT Eva		
HR1 scanner (Siemer were analysed using used for coregistration and parietotemporal hygyrus), or dementia o	ns/CTI, Knoxville, TN the PMOD Alzheime n and segmentation. nypometabolism), FT ther (PSP: mesenche). Parametr r's discrimin [18F]FDG F D (frontoten	ic SUVr images wer ation (PALZ) tool.T1 PET scans were inte nporal metabolic imp	e extracted from -weighted MRI (rpreted as either pairment), DLB (d	the interval between (3T Signa HDxt; General or deviant an occipital hypometabolism; C	ral Electric, d suggestive ism with rela	ninutes after injection Milwaukee, WI) scar e for AD (posterior ci atively intact posterio	. Scans is were ngulate r cingul		
HR1 scanner (Siemel were analysed using used for coregistration and parietotemporal had been been to the bath with	ns/CTI, Knoxville, TN the PMOD Alzheime n and segmentation. nypometabolism), FT ther (PSP: mesenche). Parametr r's discrimin [18F]FDG F D (frontoten epalon, pref	ic SUVr images wer ation (PALZ) tool.T1 PET scans were inte nporal metabolic imp	e extracted from -weighted MRI (rpreted as either pairment), DLB (eus, and thalamu	the interval between (3T Signa HDxt; Gene r normal or deviant an occipital hypometabol	ral Electric, d suggestive ism with rela BD: asymm	ninutes after injection Milwaukee, WI) scar e for AD (posterior ci atively intact posterio	. Scans is were ngulate r cingula n with		
HR1 scanner (Siemer were analysed using used for coregistration and parietotemporal regyrus), or dementia of involvement of the baresults Additional comme	ns/CTI, Knoxville, TN the PMOD Alzheime in and segmentation. hypometabolism), FT ther (PSP: mesenchesal ganglia). True positives: The study population). Parametr r's discrimin [18F]FDG F D (frontoten epalon, pref 38	ic SUVr images wer ation (PALZ) tool.T1 PET scans were inte nporal metabolic imp rontal, caudate nucl False negatives: I of 2 groups that co	e extracted from -weighted MRI (rpreted as either pairment), DLB (eus, and thalamu 27 uld not be separ	the interval between (3T Signa HDxt; General or deviant an occipital hypometabolism; C False positives:	ral Electric, d suggestive ism with rela BD: asymm 4	ninutes after injection Milwaukee, WI) scar e for AD (posterior cir atively intact posterio etric hypometabolism True negatives:	. Scans is were ngulate r cingul n with		
were analysed using used for coregistration and parietotemporal h	ns/CTI, Knoxville, TN the PMOD Alzheime n and segmentation. nypometabolism), FT ther (PSP: mesenchesal ganglia). True positives: The study population The data for [11C]). Parametr r's discrimin [18F]FDG F D (frontoten epalon, pref 38	ic SUVr images wer ation (PALZ) tool.T1 PET scans were inte nporal metabolic imp rontal, caudate nucl False negatives: I of 2 groups that co	e extracted from -weighted MRI (rpreted as either pairment), DLB (eus, and thalame 27 uld not be separ	the interval between (3T Signa HDxt; Gene normal or deviant an occipital hypometabolism; C False positives:	ral Electric, d suggestive ism with rela EBD: asymm 4 sis. test is only	ninutes after injection Milwaukee, WI) scar e for AD (posterior cir atively intact posterio etric hypometabolism True negatives:	. Scans were ngulate r cingulate n with		

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Alzheimers Dement	2013; 9: 414–421.							
	selection:				standard:		timing:	
Overall risk of bias		ndex test w	as interpreted with k		e of patients was enro reference diagnosis;			
Indirectness	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low		
Overall indirectness	Serious (It is unclea	ar whether t	he LeARN cohort co	onsisted of peopl	e with suspected cogr	nitive impairr	ment.)	
FTD versus non- FT	D							
were analysed using	ns/CTI, Knoxville, TN the PMOD Alzheime	l). Parametr r's discrimin	ic SUVr images wer ation (PALZ) tool.T1	e extracted from l-weighted MRI (the interval between at Signa HDxt; Gene	45 and 60 m	Milwaukee, WÍ) scan	. Scans is were
were analysed using tused for coregistration and parietotemporal h gyrus), or dementia or	ns/CTI, Knoxville, TN the PMOD Alzheime n and segmentation. nypometabolism), FT ther (PSP: mesenche	l). Parametr r's discrimin [18F]FDG F D (frontoter	ic SUVr images wer ation (PALZ) tool.T1 PET scans were inte nporal metabolic imp	e extracted from l-weighted MRI (rpreted as either pairment), DLB (the interval between a 3T Signa HDxt; Gene normal or deviant and occipital hypometabol	45 and 60 m ral Electric, l d suggestive ism with rela	inutes after injection Milwaukee, WI) scan for AD (posterior cir tively intact posterior	i. Scans is were ngulate r cingulate
were analysed using tused for coregistration and parietotemporal had gyrus), or dementia or	ns/CTI, Knoxville, TN the PMOD Alzheime n and segmentation. nypometabolism), FT ther (PSP: mesenche	l). Parametr r's discrimin [18F]FDG F D (frontoten epalon, pref	ic SUVr images wer ation (PALZ) tool.T1 PET scans were inte nporal metabolic imp	e extracted from I-weighted MRI (rpreted as either pairment), DLB (eus, and thalam	the interval between a 3T Signa HDxt; Gene normal or deviant and occipital hypometabol	45 and 60 m ral Electric, d suggestive ism with rela BD: asymm	inutes after injection Milwaukee, WI) scan for AD (posterior cir tively intact posterior	i. Scans is were ngulate r cingulate
were analysed using to used for coregistration and parietotemporal had gyrus), or dementia or involvement of the ba	ns/CTI, Knoxville, TN the PMOD Alzheime in and segmentation. hypometabolism), FT ther (PSP: mesenchesal ganglia). True positives: The study population	I). Parametr r's discrimin [18F]FDG F D (frontoten epalon, pref	ic SUVr images wer ation (PALZ) tool.T1 PET scans were intenporal metabolic improntal, caudate nucleon False negatives:	e extracted from l-weighted MRI (rpreted as either pairment), DLB (eus, and thalam 12 uld not be separ	the interval between a 3T Signa HDxt; Gene normal or deviant an occipital hypometabol us hypometabolism; C False positives:	45 and 60 m ral Electric, d suggestive ism with related EBD: asymm	inutes after injection Milwaukee, WI) scan for AD (posterior circlively intact posterior etric hypometabolism	i. Scans is were ingulate r cingulate m with
were analysed using to used for coregistration and parietotemporal had gyrus), or dementia or involvement of the bankesults Additional comments	ns/CTI, Knoxville, TN the PMOD Alzheime in and segmentation. hypometabolism), FT ther (PSP: mesenchesal ganglia). True positives: The study population The data for [11C]	I). Parametr r's discrimin [18F]FDG F D (frontoten epalon, pref 6 on consisted Pittsburgh o	ic SUVr images wer ation (PALZ) tool.T1 PET scans were interporal metabolic improntal, caudate nucleon regatives: If of 2 groups that compound B ([11C] February)	e extracted from l-weighted MRI (rpreted as either pairment), DLB (eus, and thalame 12 uld not be separ	the interval between all Signa HDxt; Gene normal or deviant an occipital hypometabolism; Carlse positives: ated during the analysis not extracted as this	45 and 60 m ral Electric, d suggestive ism with relace EBD: asymm 12 sis.	inutes after injection Milwaukee, WI) scan for AD (posterior cir tively intact posterior etric hypometabolism True negatives:	i. Scans is were ingulate r cingulate n with 123 the UK.
were analysed using a used for coregistration and parietotemporal higher gyrus), or dementia or involvement of the backers. Additional comments Risk of bias	ns/CTI, Knoxville, TN the PMOD Alzheime n and segmentation. nypometabolism), FT ther (PSP: mesenchesal ganglia). True positives: The study population The data for [11C] Patient selection:	I). Parametr r's discrimin [18F]FDG F D (frontoter epalon, pref 6 on consisted Unclear	ic SUVr images wer ation (PALZ) tool.T1 PET scans were intenporal metabolic improntal, caudate nucleon false negatives: If of 2 groups that compound B ([11C] Findex test:	e extracted from l-weighted MRI (rpreted as either pairment), DLB (eus, and thalam 12 uld not be separ PIB) imaging was High	the interval between a ST Signa HDxt; Gene normal or deviant an occipital hypometabolism; C False positives: ated during the analysis not extracted as this Reference standard:	45 and 60 m ral Electric, d suggestive ism with related EBD: asymmatical asymmatical extension of the suggestive is asymmatical extension of the suggestion	inutes after injection Milwaukee, WI) scan for AD (posterior cir tively intact posterior etric hypometabolism True negatives: used for research in Flow and timing:	i. Scans is were ingulate r cingulate n with 123 the UK. Low
were analysed using a used for coregistration and parietotemporal	ns/CTI, Knoxville, TN the PMOD Alzheime n and segmentation. nypometabolism), FT ther (PSP: mesenche sal ganglia). True positives: The study population The data for [11C] Patient selection: Serious (It is uncleant	I). Parametr r's discrimin [18F]FDG F ID (frontoter epalon, pref 6 on consisted Unclear ar whether a	ic SUVr images wer ation (PALZ) tool.T1 PET scans were intenporal metabolic improntal, caudate nucleon false negatives: If of 2 groups that compound B ([11C] Findex test:	e extracted from l-weighted MRI (rpreted as either pairment), DLB (eus, and thalame 12 uld not be separ PIB) imaging was High dom sample of p	the interval between a ST Signa HDxt; Gene normal or deviant and occipital hypometabolism; C False positives: ated during the analysis not extracted as this Reference standard: atients was enrolled a	45 and 60 m ral Electric, d suggestive ism with related EBD: asymmatical asymmatical extension of the suggestive is asymmatical extension of the suggestion	inutes after injection Milwaukee, WI) scan for AD (posterior cir tively intact posterior etric hypometabolism True negatives: used for research in Flow and timing:	i. Scans is were ingulate r cingulate n with 123 the UK. Low
were analysed using a used for coregistration and parietotemporal higher gyrus), or dementia or involvement of the backers. Additional comments Risk of bias	ns/CTI, Knoxville, TN the PMOD Alzheime n and segmentation. hypometabolism), FT ther (PSP: mesenchesal ganglia). True positives: The study population The data for [11C] Patient selection: Serious (It is unclead avoided; the index	I). Parametr r's discrimin [18F]FDG F ID (frontoter epalon, pref 6 on consisted Unclear ar whether a	ic SUVr images wer ation (PALZ) tool.T1 PET scans were interporal metabolic improntal, caudate nucle report of 2 groups that compound B ([11C] Findex test:	e extracted from 1-weighted MRI (rpreted as either pairment), DLB (reus, and thalame 12 uld not be separ PIB) imaging was High dom sample of pedge of the refere	the interval between a ST Signa HDxt; Gene normal or deviant and occipital hypometabolism; C False positives: ated during the analysis not extracted as this Reference standard: atients was enrolled a	45 and 60 m ral Electric, d suggestive ism with related EBD: asymmatical asymmatical extension of the suggestive is asymmatical extension of the suggestion	inutes after injection Milwaukee, WI) scan for AD (posterior cir tively intact posterior etric hypometabolism True negatives: used for research in Flow and timing:	i. Scans is were ingulate r cingulate n with 123 the UK. Low

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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]	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		ndex test wa	as interpreted with k		e of patients was enro reference diagnosis;							
Indirectness	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low						
Overall indirectness	Serious (It is unclea	ar whether t	he LeARN cohort co	onsisted of peop	e with suspected cogr	nitive impairr	nent.)					

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

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Alzheimers Dement 2013; 9: 414-421.

used for coregistration and segmentation. [18F]FDG PET scans were interpreted as either normal or deviant and suggestive for AD (posterior cingulate and parietotemporal hypometabolism), FTD (frontotemporal metabolic impairment), DLB (occipital hypometabolism with relatively intact posterior cingulate gyrus), or dementia other (PSP: mesenchepalon, prefrontal, caudate nucleus, and thalamus hypometabolism; CBD: asymmetric hypometabolism with involvement of the basal ganglia).

Results	True positives:	6	False negatives:	12	False positives:	0	True negatives:	5			
Additional comme nts	The study population	on consisted	of 2 groups that co	uld not be separ	ated during the analys	sis.					
	The data for [11C]	e 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		ndex test wa	as interpreted with k		e of patients was enro reference diagnosis;						
Indirectness	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low					
Overall indirectness	Serious (It is unclea	ar whether t	he LeARN cohort co	nsisted of peopl	e with suspected cogr	nitive impair	ment.)				

DLB versus non-DLB

Index Test: FDG-PET

185 MBq of 18F-FDG was administered. Patients underwent a 10-minute transmission scan followed by a 15-minute emission scan using an ECAT Exact HR1 scanner (Siemens/CTI, Knoxville, TN). Parametric SUVr images were extracted from the interval between 45 and 60 minutes after injection. Scans were analysed using the PMOD Alzheimer's discrimination (PALZ) tool.T1-weighted MRI (3T Signa HDxt; General Electric, Milwaukee, WI) scans were used for coregistration and segmentation. [18F]FDG PET scans were interpreted as either normal or deviant and suggestive for AD (posterior cingulate and parietotemporal hypometabolism), FTD (frontotemporal metabolic impairment), DLB (occipital hypometabolism with relatively intact posterior cingulate gyrus), or dementia other (PSP: mesenchepalon, prefrontal, caudate nucleus, and thalamus hypometabolism; CBD: asymmetric hypometabolism with involvement of the basal ganglia).

Results	True positives:	1	False	4	False positives:	6	True negatives:	142
			negatives:					

Ossenkoppele R, Pri Verhey FR, Verbeek diagnostic process i Alzheimers Dement	MM, van Buchem N n a memory clinic.				se SF, Windhorst AD, s P, van Berckel BN:					
Additional comme nts	The study population			·	rated during the analys		16			
	The data for [11C]	Pittsburgh c	compound B ([11C] I	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 whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were voided; 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 unclea	ar whether t	he LeARN cohort co	onsisted of people	le with suspected cogr	nitive impair	ment.)			
DLB versus non-DLE	3 dementias									
Index Test: FDG-PET 185 MBq of 18F-FDG HR1 scanner (Siemer were analysed using tused for coregistration and parietotemporal high gyrus), or dementia of involvement of the base	was administered. For its construction was administered was admi). Parametr 's discrimin [18F]FDG F D (frontoten	ic SUVr images wer ation (PALZ) tool.T1 PET scans were inte nporal metabolic imp	e extracted from l-weighted MRI (rpreted as either pairment), DLB (the interval between 4 (3T Signa HDxt; Gene r normal or deviant and occipital hypometaboli	45 and 60 m ral Electric, d suggestive ism with rela	ninutes after injection Milwaukee, WI) scar e for AD (posterior ci atively intact posterio	i. Scans is were ngulate r cingulate		
Results	True positives:	1	False negatives:	4	False positives:	5	True negatives:	88		
Additional comme nts			.	·	ated during the analys		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					e of patients was enrol reference diagnosis;					

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Verhey FR, Verbe		/IA, Hoeksti				, Handels RL, Wolfs CA, Aalten P, Impact of molecular imaging on the
Alzheimers Deme	nt 2013; 9: 414–421.					
	>10% study popula	ition was ex	cluded.)			
Indirectness	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low
Overall indirectness	Serious (It is unclea	ar whether t	he LeARN cohort co	onsisted of peop	le with suspected cogr	nitive impairment.)

P.1.16 P

Panegyres PK, Rogers JM, McCarthy M, Campbell A, Wu JS. Fluorodeoxyglucose-Positron Emission Tomography in the differential diagnosis of early-onset dementia: a prospective, community-based study. BMC Neurology 2009; 9: 41-49.

Study type	Prospective cohort
Country	Australia
Setting	Young onset dementia clinic
Inclusion criteria	Individuals referred to a young onset dementia clinic (<65 years old) for specialist neurologic investigation of suspected dementia over the years from 1998 to 2006.
Exclusion criteria	Not stated
Sex	53.9% male
Age	Mean age of symptom onset was 60.0 years (SD 4.2)
Presentation	suspected dementia
Reference standard	A diagnosis of Dementia was made using the DSM-IV manual; FTD was diagnosed according to Neary (1998); AD according to the NINCDS-ADRDA criteria; DLB according to McKeith (1996); VaD according to NINDS-AIREN.

AD versus non-AD

Index Test: FDG-PET

18F FDG-PET was imaged using an Allegro GSO PET scanner. Brain images were attenuation corrected using the 137Cs attenuation source build into the Allegro camera system. Scatter and random correction was performed as part of the RAMLA-3D reconstruction algorithm as provided by the camera manufacturer, Phillips. The FDG PET images were displayed using the Siemens "cool" colour scale. Maximum cortical activity was extracted using the three-dimensional stereotactic surface projection (3D-SSP) method and the data sets were normalized to the average cerebral count for each patient. The 3D-SSP images were compared individually with age appropriate and modality appropriate normal databases generated in the PET centre. A statistically significant threshold, controlling for multiple pixel comparisons and shape of the stochastic process on 3D-SSP format, of Z = 4.53 (p < 0.05) was used.

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Panegyres PK, Rogers JM, McCarthy M, Campbell A, Wu JS. Fluorodeoxyglucose-Positron Emission Tomography in the differential diagnosis of early-onset dementia: a prospective, community-based study. BMC Neurology 2009; 9: 41-49.

The severity of the reductions in each of the lobes was evaluated using volumes of interest analysis. Depending on the pattern of cerebral metabolism, each case was classified as either: normal; possible AD; possible FTLD; possible LBD; possible PPA or possible depression.

Results	True positives:	38	False negatives:	11	False positives:	10	True negatives:	43
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Not serious							
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low		
Overall indirectness	Serious (The study	only recruit	ed people with early	onset dementia	a (<65 years old).)			

FTD versus not FTD

Index Test: FDG-PET

18F FDG-PET was imaged using an Allegro GSO PET scanner. Brain images were attenuation corrected using the 137Cs attenuation source build into the Allegro camera system. Scatter and random correction was performed as part of the RAMLA-3D reconstruction algorithm as provided by the camera manufacturer, Phillips. The FDG PET images were displayed using the Siemens "cool" colour scale. Maximum cortical activity was extracted using the three-dimensional stereotactic surface projection (3D-SSP) method and the data sets were normalized to the average cerebral count for each patient. The 3D-SSP images were compared individually with age appropriate and modality appropriate normal databases generated in the PET centre. A statistically significant threshold, controlling for multiple pixel comparisons and shape of the stochastic process on 3D-SSP format, of Z = 4.53 (p < 0.05) was used. The severity of the reductions in each of the lobes was evaluated using volumes of interest analysis. Depending on the pattern of cerebral metabolism, each case was classified as either: normal; possible AD; possible FTLD; possible LBD; possible PPA or possible depression.

Results	True positives:	9	False negatives:	8	False positives:	4	True negatives:	81
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Not serious							
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	Low		
Overall indirectness	Serious (The study	only recruit	ed people with early	onset dementia	a (<65 years old).)			
DLB versus not DLE	3							

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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 recruit	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

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Panegyres PK, Roge of early-onset deme						mography in the differential diagnosis
Overall risk of bias	Not serious					
Indirectness	Patient selection:	High	Index test:	Low	Reference standard:	
Overall indirectness	Serious (The study	only recruit	ted people with early	onset dementia	(<65 years old).)	

	nical Neuropsychologist, 2014; 28: 994–1007.
Study type	Prospective cohort
Country	France
Setting	Five secondary referral hospital centres in France
Inclusion criteria	Consecutive ambulatory patients with memory complaints who visited a memory consultation for the first time between March 2011 and December 2011 were recruited.
Exclusion criteria	Inability to read or write or understand French, known dementia, and major depressive disorder.
Sex	32.0% male
Age	Mean age 76.0 (SD 10.0)
Presentation	Memory complaints
Reference standard	A consensus diagnosis of dementia was made according to DSM-IV criteria.

Dementia versus no dementia

Index Test: Test Your Memory, TYM (≤39)

Test Your Memory (F-TYM Test), French version. Cross-cultural adaptation was needed for the sentence to be copied and this adaptation respected the author's requirements. In the verbal fluency test, names of animals beginning with "S" were replaced by names beginning with "C" as there are more animals whose name starts with "C" than with "S" in French. Cut-off ≤ 39.

Results	True positives:	61	False negatives:	7	False positives:	40	True negatives:	93
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Serious (Optimised	l cut-off was	used; the study wa	s not downgrade	ed for exclusions as <1	0% populat	ion was excluded)	

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Postel-Vinay N, Hand Population. The Clin				ation of the Tes	st Your Memory (FTY	M Test) in a	a French Memory C	linic
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MMSE (< MMSE, French langua	•							
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 wa	s not downgrade	ed for exclusions as <1	10% populati	on was excluded)	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

P.1.17 R

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

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Reference standard	Pathology (brain bi	opsy or pos	t-mortem brain path	ology)				
FTD versus non-FTI								
Index Test: 99mTc-H 99mTc-HMPAO SPE headed camera.		ecified; four	patterns emerged, o	each correspo	nding to a distinct patho	ogical ent	ry. Images taken with a	a single
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-H 99mTc-HMPAO SPE headed camera. Results			patterns emerged, of False negatives:		nding to a distinct patho False positives:		ry. Images taken with a	a single
Risk of bias	Patient selection:	Unclear	Index test:	Unclear	Reference standard:	Low	Flow and timing:	High
Overall risk of bias			ed with >10% study ate exclusions avoid		cluded; unclear whether	random c	or consecutive patient e	enrolme
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
	00.000.0111				o turruur ur			

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Study type	Retrospective coho	ort							
Country	Czech Republic								
Setting	National Reference	Laboratory	for Diagnostics of H	luman Prion Dis	eases, Thomayer Hos	pital, Prag	ue		
Inclusion criteria					feldt-Jakob disease; C analysis of T-tau, P-ta				
Exclusion criteria	Not stated	Not stated							
Sex	45.7% male	45.7% male							
Age	Mean age at death	66.3 years	(SD 9.1)						
Presentation	Suspected dement	ia, including	possible/probable (CJD)					
Reference standard		ion protein.			cal examination and w gene (PRNP) was ana				
CJD versus not CJD									
Index Test: Total Ta	~								
Total tau analysed us									
Results	True positives:	28	False negatives:	8	False positives:	7	True negatives:	16	
	Patient	Low	Index test:	Unclear	Reference	Low	Flow and timing:	Low	
Risk of bias	selection:				standard:		uning.		
Risk of bias Overall risk of bias	selection: Serious (It was und without knowledge	of the result		tandard; a pre-s	of patients was enrolle pecified cut-off was us		x test results were int		
	selection: Serious (It was und without knowledge	of the result ere interpret	ts of the reference s	tandard; a pre-s ge of the index to	of patients was enrolle pecified cut-off was us		x test results were int		

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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							

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

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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			Γ alone versus final Our analysis uses the		al diagnosis and for S results.	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		
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			Γ alone versus final Our analysis uses the		al diagnosis and for S results.	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		

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Overall indirectness	Not serious							
FTD versus AD								
	CT. SPECT imaging				on values according to initially determined to			
					retation of images take			
Results	True positives:	9	False negatives:	3	False positives:	0	True negatives:	23
Additional comme nts			alone versus final our analysis uses the		al diagnosis and for Sl esults.	PECT with c	clincal 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	ere >10% study por	pulation exclude	d)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

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)

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Presentation	Suspected dement	ia						
Reference standard	DSM-IV with Clinic	al Dementia	Rating, neuropsych	nological tests a	nd research diagnostic	criteria fo	r MCI, DLB and FTD.	
Dementia versus no	n-dementia (includi	ing MCI)						
Index Test: Clock Di	rawing Test, CDT, s	coring met	hod unclear (<8)					
Clock Drawing Test, 0	CDT <8 out of 10 (fre	e- hand- dra	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	Not serious							

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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.

was 00 5005.								
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							

Sakamoto F, Shiraishi S, Yoshida M, Tomiguchi S, Hirai T, Namimoto T, Hashimoto M, Ikeda M et al.Diagnosis of dementia with Lewy bodies: diagnostic performance of combined 123I-IMP brain perfusion SPECT and 123I-MIBG myocardial scintigraphy. Ann Nucl Med, 2014; 28:203–211.

Study type	Retrospective cohort
Country	Japan
Setting	Kumamoto University Hospital
Inclusion criteria	Patients with suspected DLB who underwent both 123I-IMP brain perfusion SPECT and 123I-MIBG myocardial scintigraphy studies at Kumamoto University Hospital between January 2007 and December 2012. Patients with well-controlled diabetes or hypertension treated with small doses of ACE inhibitors or beta blockers were included although their 123I-MIBG myocardial scintigraphy findings may have been affected.
Exclusion criteria	Patients with possible DLB were excluded because both DLB and other types of dementia were included in this category. Patients with congestive heart failure or taking antipsychotic drugs (tricyclic antidepressants, reserpine) that would affect the results of 123I-MIBG myocardial scintigraphy were also excluded.
Sex	43.0% male
Age	Mean age 72.5 years (SD 10.4)
Presentation	suspected DLB

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Sakamoto F, Shiraishi S, Yoshida M, Tomiguchi S, Hirai T, Namimoto T, Hashimoto M, Ikeda M et al.Diagnosis of dementia with Lewy bodies: diagnostic performance of combined 123I-IMP brain perfusion SPECT and 123I-MIBG myocardial scintigraphy. Ann Nucl Med, 2014; 28:203–211.

Reference standard

A diagnosis of DLB was made according to McKeith (2006), other criteria are not stated.

DLB versus not DLB

Index Test: 123I-IMP SPECT and 123I-MIBG cardiac scintigraphy combined

123I -IMP SPECT imaging was carried out using a two-head gamma camera (Millennium VG, GE) equipped with a low-energy general-purpose collimator. Transaxial images were reconstructed with filtered back projection using a Butterworth filter. The reconstructed 123I-IMP SPECT images were analyzed with Neurostat/(3D-SSP) and data were normalized to the mean global activity. Using the SEE method, the whole brain was divided into segments. The parietal lobe hypoperfusion score used here.

123I-MIBG cardiac scintigraphy. Planar scans were acquired using a two-head gamma camera (Millennium VG, GE) equipped with a medium-energy general-purpose collimator. Using the region of interest (ROI) method, we calculated the early and delayed 123I-MIBG heart-to-mediastinum uptake (H/M) ratios on anterior views of the planar images. An irregular circular ROI was manually drawn on the left ventricle and a square ROI was placed in the upper mediastinum area. The early H/M ratio used for analysis here.

The formula for calculating the combined index for estimation group was: - 4:72 - 2:48x early H/M +1:07 x parietal lobe hypoperfusion + 0:10 x age

Results	True positives:	23	False negatives:	3	False positives:	10	True negatives:	64
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias			er the study avoided of the results of the		clusions or whether th	e reference	standard results we	re
Indirectness	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

DLB versus not DLB

Index Test: 123I-MIBG cardiac scintigraphy

123I-MIBG cardiac scintigraphy. Planar scans were acquired using a two-head gamma camera (Millennium VG, GE) equipped with a medium-energy general-purpose collimator. Using the region of interest (ROI) method, we calculated the early and delayed 123I-MIBG heart-to-mediastinum uptake (H/M) ratios on anterior views of the planar images. An irregular circular ROI was manually drawn on the left ventricle and a square ROI was placed in the upper

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

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					miguchi S et al. Diag Radiol 2017; 90: 2010		emetia with Lewy bo	odies:
Study type	Prospective cohort							
Country	Japan							
Setting	Kumamoto Univers	ity Hospital.						
Inclusion criteria			no had undergone be between January 20		ain perfusion SPECT a 2014.	ınd 123I-MIE	3G myocardial scinti	graphy at
Exclusion criteria	Congestive heart father the resulst of the M			cardiomyopathy	and diabetes, and pa	tients taking	antipsychotic drugs	that affect
Sex	41.6% male							
Age	Mean age 76.0 year	ars (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								
	cintigraphy, early hea	art-to-media ourpose colli		layed imaging w	cquired with a dual-heras performed at 15 mi	n and 3 hrs		ff <2.0.
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 varial	oles.	
Risk of bias	Patient selection:	Low	Index test:	Unclear	Reference standard:	Unclear	Flow and timing:	Low
Overall risk of bias	were interpreted wi	ithout knowl	edge of the results of	of the reference	tcome variables and it standard; whether the ether the test cut-off w	reference s	tandard results were	est results
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

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Study type	Retrospective coho	rt						
Country	Germany							
Setting	Magnetic Resonan	ce/Compute	ed Tomography Insti	tute Hamburg				
Inclusion criteria	All cases reported	o the Germ	an CJD surveillance	unit				
Exclusion criteria	Not stated							
Sex	For the CJD positiv	e group 31.	5% male, not stated	I for CJD negtive	group			
Age	Mean age 65.5 yea	rs (range 3	8-86) for the CJD po	sitive group, CJ	D negative not stated			
Presentation	Rapidly progressive	e dementia	leading to suspected	d CJD				
Reference standard	92 patients underw according to Will (1		diagnosis accordin	g to Kretzschma	ır (1996); 70 patients v	vere diagno	osed using neuropath	ology
CJD versus non-CJ	<u> </u>							
	ט							
	<u> </u>							
Index Test: MRI MRI scans were mad				gers. The follow	ing MRI scans were pe	erformed: T	1-weighted, T2 weigh	nted,
Index Test: MRI MRI scans were mac proton density- weigl	le with either 1.0-T or				ing MRI scans were pe		1-weighted, T2 weigh	
Index Test: MRI MRI scans were mad proton density- weigh Results	le with either 1.0-T or nted and fluid attenua	tion inversion	on recovery.					
Index Test: MRI MRI scans were mad proton density- weigh Results Risk of bias	le with either 1.0-T or nted and fluid attenua True positives: Patient	tion inversion 109	n recovery. False negatives:	53	False positives:	4	True negatives:	53
Index Test: MRI MRI scans were mad	le with either 1.0-T or nted and fluid attenua True positives: Patient selection:	tion inversion 109	n recovery. False negatives:	53	False positives:	4	True negatives:	53

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

Study type Prospective cohort

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2010; 30: 411–6. Country	The Netherlands							
Setting	Alzheimer Centre a	ıt a Universi	ity Hospital					
Inclusion criteria	Patients visiting the	Alzheimer	Centre at the VU Ur	niversity Medical	Centre between 2004	and 2007		
Exclusion criteria	Not stated							
Sex	56.4% male							
Age	mean age 68.4 yea	rs (SD 8.8)						
Presentation	Suspected dement	ia						
Reference standard	Petersen criteria fo complaints.	r MCI, NINC	CDS-ADRDA for der	nentia. All remai	ning patients were cla	ssified as ha	aving subjective men	nory
AD versus subjectiv	e memory complain	nts (no dem	nentia group)					
Index Test: Information IQCODE (Dutch, 16 in		_	Decline, IQCODE (16 item, >3.2)				
Results	True positives:	173	False negatives:	7	False positives:	52	True negatives:	37
Additional comme nts	Data for 2x2 table of	obtained fro	m Harrison et al. (20	015) Cochrane R	eview. Not is an acce	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					ion excluded (MCl grovledge 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: Informai		Cognitive	Decline, IQCODE (16 item, >3.3)				
Results	True positives:	172	False	8	False positives:	47	True negatives:	42

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2010; 30: 411–6. Additional comme	Data for 2x2 table of	obtained fro	m Harrison et al. (20)15) Cochrane R	eview. Not is an acce	ssible forma	t in original paper	
nts	Data for EXE table (m riamom et al. (20	roj Godinano i	eview. Not is all adde.		it in original paper.	
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Unclear	Flow and timing:	High
Overall risk of bias					ion excluded (MCl grovledge 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: Informa IQCODE (Dutch, 16	nt Questionnaire on item) 3.5	Cognitive	Decline, IQCODE (16 item, >3.4)				
Results	True positives:	165	False	15	False positives:	33	True negatives:	56
			negatives:				gaareer	
	Data for 2x2 table of	obtained fro	_	015) Cochrane R	eview. Not is an acce			
Additional comme nts Risk of bias	Data for 2x2 table of Patient selection:		_	·	Review. Not is an acce Reference standard:			High
nts	Patient selection: Very serious (Use	Low of subgroup	m Harrison et al. (20 Index test: analysis where >10	High % study populat	Reference	ssible forma Unclear	it in original paper. Flow and timing:	High
nts Risk of bias	Patient selection: Very serious (Use	Low of subgroup and reference	m Harrison et al. (20 Index test: analysis where >10	High % study populated without know	Reference standard: ion excluded (MCI gro	ssible forma Unclear	it in original paper. Flow and timing:	High
nts Risk of bias Overall risk of bias	Patient selection: Very serious (Use of unclear that index a Patient	Low of subgroup and reference	Index test: analysis where >10 be tests are interpret	High % study populated without know	Reference standard: ion excluded (MCI gro rledge of each other.) Reference	ssible forma Unclear oup); lack of	it in original paper. Flow and timing:	High
nts Risk of bias Overall risk of bias Indirectness Overall indirectness	Patient selection: Very serious (Use of unclear that index a Patient selection: Not serious nt Questionnaire on	Low of subgroup and reference Low	Index test: analysis where >10 ce tests are interpret Index test:	High % study populated without know Low	Reference standard: ion excluded (MCI gro rledge of each other.) Reference	ssible forma Unclear oup); lack of	it in original paper. Flow and timing:	High

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nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Unclear	Flow and timing:	High
Overall risk of bias					tion excluded (MCI grovledge 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: Informar IQCODE (Dutch, 16 it		Cognitive	Decline ,IQCODE (16 item, >3.6)				
Results	True positives:	154	False negatives:	26	False positives:	23	True negatives:	66
Additional comme nts	Data for 2x2 table	obtained fro	m Harrison et al. (20	115) Cochrane F	Review. 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					tion excluded (MCI gro owledge of each other.		a pre-specified test	threshold
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
	Not serious							
Overall indirectness	selection: Not serious						evaluation of demer	ntia;
regional brain metal			. JAMA. 2001; 286:	2120-7.				
Study type	Prospective cohort							
Country	USA and Germany	1						
Setting	Neurology, psychia	atry and PFT	facilities associated	d with 7 academ	ic centres in USA and	1 in Germa	nv	

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Silverman DHS, Sm regional brain meta					sitron emission tomo	graphy in e	valuation of demer	ntia;		
Inclusion criteria		People presenting with symptoms of dementia at one of the academic centres								
Exclusion criteria	Not stated									
Sex	51.4% male									
Age	Mean age 67.0 yea	ırs (10.0)								
Presentation	Suspected dement	ia								
Reference standard	Using the methods	and criteria	standard to each in	stitution at the ti	me of pathological exa	amination- de	etails not provided.			
Dementia versus no	dementia									
Siemens ECAT EXA	arried out using (prior CT HR or HR+ scann	er.			931 scanner or (begin	-		solution		
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-PE 18 -FDG- PET was c Siemens ECAT EXAC	arried out using (prior		1996) a Siemens/C	CTI ECAT 831 or	931 scanner or (begin	nning Octobe	er 1996) a higher res	solution		
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

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Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall indirectness	Not serious									
	ong V, Nako A, Choti Assoc Thia 2006; 89			P et al. Use of H	lachinski Ischemic S	core in the	memory clinic: Th	ai		
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	l dementia							
Exclusion criteria	Not stated	ot stated								
Sex	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	ard tests and neuro	imaging as need	led.					
VaD and mixed den	nentia (VaD with AD	versus AD)							
	ski Ischemic Score, Score (HIS), cut-off 5.	• •								
Results	True positives:	73	False negatives:	12	False positives:	35	True negatives:	94		
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	High		
Overall risk of bias	the index test resul	ts were inte		wledge of the res	optimised test-threshouts of the reference s					
Indirectness	Patient		Index test:	Low	Reference	Low				

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Siritho S, Senanarong V, Nako A, Chotinaiwattarukul W, Jamjumrus P et al. Use of Hachinski Ischemic Score in the memory clinic: Thai
experience. J Med Assoc Thia 2006; 89: 1822-1827.

Overall indirectness

Not serious

Skinner S, Adewale AJ, I	DeBlock L, Gill MJ, Power C. Neurocognitive screening tools in HIV/AIDS: comparative performance among patients
exposed to antiretroviral	therapy. HIV Medicine, 2009; 10: 246–252.

Study type	Prospective cohort
Country	Canada
Setting	Northern and Southern Alberta neurology clinics
Inclusion criteria	HIV+ people undergoing evaluation for neuropsychological deficits as part of a neurological consultation.
Exclusion criteria	Not stated
Sex	89.1% male
Age	Mean age 49.3 years (SD 7.9)
Presentation	HIV+ with suspected dementia
Reference standard	American Academy of Neurology algorithm for HIV-1 associated cognitive/motor disorder

HAND versus other neurological disorder in HIV+ people

Index Test: HIV dementia scale, HDS (<10)

HIV dementia scale (HDS) (<10)

The dementia scale (i	, , ,			_				40
Results	True positives:	6	False negatives:	/	False positives:	4	True negatives:	16
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

Index Test: HIV dementia scale, HDS (<11)

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exposed to antiretro				Screening too	is in m <i>vr</i> aids, comp	arative pe	erformance among pa	inenis
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	reshold.)					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: Internat International HIV Der		•	6) (<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							

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

Study type Prospective cohort

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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 fulfi 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	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 M	Index Test: Seven Minute Screen (P>0.7)								

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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-specifi	ed.)		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

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

Index Test: Syndrom Kurztest (≥7)

Syndrom Kurztest consists of nine subtests assessing episodic memory (free and cued recall and recognition) and information processing speed (naming items, reading numbers, ordering numbers, shifting numbers, symbol counting, interference). Here raw scores were adjusted for age. Three SKT scores were calculated according to the manual: a memory subscore that includes the scaled scores for three subtests (I, XIII and IX); an attention subscore that includes the scaled scores for the other subtests; and, finally, a total score that includes all scaled scores. According to the manual, a total SKT score of 9 to 13 indicates "mild organic mental or cognitive disorder, possible dementia," and higher scores indicate more advanced cognitive impairment. Cut -off ≥ 7.

Results	True positives:	49	False negatives:	20	False positives:	12	True negatives:	14
Additional 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	dard one and th	at was not pre-specifi	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 ≥ 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

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Setting

Inclusion criteria

Skjerev A, , Nordhus Kurztest among elde					PK. Validation of the S B; 20: 4, 807–814.	Seven Minu	ite Screen and Synd	drom
Overall risk of bias	Serious (Use of an	alternative t	threshold to the stan	idard one and th	nat was not pre-specifi	ed.)		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
items, reading number were calculated accommodudes the scaled so	nsists of nine subtest ers, ordering numbers ding to the manual: cores for the other su	s, shifting nua a memory s obtests; and	umbers, symbol cour ubscore that include , finally, a total score	nting, interferences the scaled scaled scaled scaled scaled at that includes a	ecall and recognition) a ce). Here raw scores we bres for three subtests Il scaled scores. Accor scores indicate more a	vere adjuste (I, XIII and ding to the	ed for age. Three SKT IX); an attention sub- manual, a total SKT	scores that score of 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, Hortoba					agnosis of Dementia	with Lewy	Bodies versus	
Study type	Prospective cohort							
Country	Norway							

New diagnosis of dementia at the study sites between 2005 and 2007, plus patients referred from other Neurology clinics. MMSE ≥

Specialist outpatient clinic and an old age psychiatry service in Hordland and Rogaland.

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neuropathology. Jo											
		20 and/or CDR ≤ 1; no acute delirium, terminal illness, major somatic or psychiaric illness with effects on cognition. Between 2007 and 2013 only DLB and PDD patients were included to increase sample size.									
Exclusion criteria	None stated										
Sex	48% male	48% male									
Age	Mean age 74.0 yea	ars (SD 8.2)									
Presentation	People have previous	ously been d	liagnosed with deme	entia							
Reference standard		ng to interna	tional consensus cri		accordance with publis d AD (including Brakk						
DLB and PDD versu	s other dementias										
Index Test: Internati	onal Consensus DI	_B diagnos	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	selectivey recruited p	participants with	a DLB or PDD diagno	sis to incre	ase the sample size f	or these			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
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 diffe	erential dementia diagnosis. Int J Geriatr Psychiatry 2015; 30: 864–869.
Study type	Prospective cohort

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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	F, Versijpt J, Hauth L, Goeman J, Martin J-J, Se Deyn PP and Engelborghs S. Diagnostic value of MIBG cardiac erential dementia diagnosis. Int J Geriatr Psychiatry 2015; 30: 864–869.
	or (ii) autopsy confirmation of the clinical diagnosis.
Exclusion criteria	Not stated, but people were not excluded for concomitant diseases and conditions like diabetes mellitus, arterial hypertension, hyperlipidemia, ischemic heart disease, and heart failure as well as pharmacological treatments at the time of MIBG scanning.
Sex	61.0% male
Age	Mean age 76.0 years (SD 8.0)
Presentation	Clinically ambiguous dementia (DLB or AD)
Reference standard	Clinical diagnosis of probable AD was made according to the NINCDS-ADRDA; probable DLB was diagnosed according to the criteria of McKeith (2005). In case consenting patients died, autopsy was performed in order to establish a definite dementia diagnosis. For the neuropathological diagnosis of AD, the criteria of Braak (1991, 2006) were applied as described earlier (Le Bastard, 2013).
DLB versus not-DLE	
Index Test: 123I-MIE	BG cardiac scintigraphy
(GE) scanner, both w	raphy data for 67 patients was acquired with a Philips XCT scanner, whereas for 18 patients, the data was acquired with a Varicam rith a low-energy, high-resolution collimator. Both cameras had similar hardware characteristics (LEHR collimator, large field doublese same settings of acquisition parameters. MIBG uptake was determined by calculating the heart-to-mediastinum-uptake (H/M) ratio.

Results	True positives:	16	False negatives:	0	False positives:	1	True negatives:	3
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	High	Flow and timing:	Low
Overall risk of bias	Serious (The diagn	osing physic	cians were not blind	to the index tes	t results.)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

	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

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Setting	Memory Clinic of th	ne University	y Department of Ger	iatrics in Bern.						
Inclusion criteria	Patients referred to	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 yea	ars (SD 11.0))							
Presentation	Cognitive complain	ıts								
Reference standard			ording to DSM-IV TR rment (Winblad, 200		is diagnosed using crit	teria set by t	the International Wor	king		
Dementia versus no	dementia									
Index Test: Short sr	nell test	ed abnorma	I if patients closed th	neir eyes and co	uld not identify instant	coffee power	der in a can when it v	was hel		
Index Test: Short sr Short smell test (SST 5–10 cm under their i	mell test i). This was considered		False	•	uld not identify instant False positives:	·	der in a can when it v	was hel		
Index Test: Short sr	nell test). This was considerence.	9	·	•	ŕ	·				
Index Test: Short sr Short smell test (SST 5–10 cm under their i Results Risk of bias	nell test). This was considered nose. True positives: Patient selection:	9 Low	False negatives: Index test:	8 Low	False positives:	34 Low	True negatives:	103		
Index Test: Short sr Short smell test (SST 5–10 cm under their i Results Risk of bias	nell test). This was considered nose. True positives: Patient selection:	9 Low and to have o	False negatives: Index test:	8 Low , but normal MM	False positives: Reference standard:	34 Low	True negatives:	103		
Index Test: Short sr Short smell test (SST 5–10 cm under their i Results	nell test). This was considered nose. True positives: Patient selection: Serious (Patients here) Patient selection:	9 Low and to have of High	False negatives: Index test: cognitive complaints Index test:	8 Low , but normal MM Low	False positives: Reference standard: ISE and CDT tests at Reference	Low baseline.)	True negatives: Flow and timing:	103		
Index Test: Short sr Short smell test (SST 5–10 cm under their in Results Risk of bias Overall risk of bias Indirectness Overall indirectness	nell test). This was considered nose. True positives: Patient selection: Serious (Patients here) Serious (Patients here) Serious (Patients here)	9 Low and to have of High	False negatives: Index test: cognitive complaints Index test:	8 Low , but normal MM Low	False positives: Reference standard: ISE and CDT tests at Reference standard:	Low baseline.)	True negatives: Flow and timing:	103		
Index Test: Short sr Short smell test (SST 5–10 cm under their in Results Risk of bias Overall risk of bias Indirectness Overall indirectness Index Test: Palmo-N	nell test). This was considered nose. True positives: Patient selection: Serious (Patients here) Serious (Patients here) Serious (Patients here) Mental Reflex (PMR). Considered	9 Low and to have of the High and to have of the ha	False negatives: Index test: cognitive complaints Index test: cognitive complaints	8 Low , but normal MM Low , but score as no	False positives: Reference standard: ISE and CDT tests at Reference standard:	34 Low baseline.) Low and CDT tests	True negatives: Flow and timing:	103 Low		

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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	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							
palm at the base of the instant coffee powde	he thumb) elicited a ur r in a can when it was	inilateral chi s held 5–10	n muscle twitch. SS cm under their nose	T was considere	ive if brushing the thured abnormal if patients	closed their	eyes and could not	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	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-I	Mental Reflex and SI	hort smell t	est, both positive					
palm at the base of the		ınilateral chi	n muscle twitch. SS	T was considere	ive if brushing the thured abnormal if patients			
Results	True positives:		False negatives:		False positives:	9	True negatives:	128

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Palmo-Mental Reflex	Test: an observati	ional study.	BMC Geriatrics. 2	015; 15:90-95.				
Additional comme nts								
Risk of bias	Patient selection:		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:	U	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 Alzh	heimer's Disease in a Memory Clinic Setting. Journal of Alzheimer's Disease, 2015; 44: 183–193.
Study type	Retrospective cohort
Country	Switzerland
Setting	Memory clinic of the StadtspitalWaid in Zurich.
Inclusion criteria	Patients were included, when (i) a clinical diagnosis was obtained according to the standard diagnostic procedure of the Stadtspital Waid and was clearly stated in the report and (ii) high-resolution MR imaging had been performed.
Exclusion criteria	No further selection criteria were applied. In particular, there was no exclusion criterion with respect to the MR image quality
Sex	Not stated
Age	Mean age 74.6 years (SD not stated)
Presentation	Memory complaints
Reference standard	Diagnoses are made in consensus by an interdisciplinary board using established clinical criteria to identify AD (NINCDS-ADRDA), mild cognitive impairment (Petersen criteria, 1999).

AD (probable) versus no AD (including possible AD diagnosis and unclear cases)

Index Test: MRI Hippocampal grey matter volume left, HVL. Cut- off 2.69 ml

MRI Hippocampal volume, HVL. MRI was carried out using Siemens Avanto 1.5 T (Siemens Erlangen, Germany) deploying 3D T1-weighted magnetization prepared rapid gradient echo (MPRAGE). MR images were segmented and stereotactically normalized to the Montreal Neurological

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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			r the index test resu d using ROC analys		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 Hippocampal grey matter volume right, HVR. Cut off 2.70ml.

MRI Hippocampal grey matter volume right, HVR. MRI was carried out using Siemens Avanto 1.5 T (Siemens Erlangen, Germany) deploying 3D T1-weighted magnetization prepared rapid gradient echo (MPRAGE). MR images were segmented and stereotactically normalized to the Montreal Neurological Institute (MNI) space using a combined segmentation and registration approach. Hippocampal GM volume (HV) was calculated by multiplying the subject's GM component image with a predefined binary mask from a freely available atlas and then summing over all voxel intensities. Masks for the left and the right hemisphere were used separately yielding two sub-volumes for each brain hemisphere, HVL and HVR, respectively. Total HV was obtained by summing the GM volume within both masks. Cut off 2.70ml.

Results	True positives:	33	False negatives:	11	False positives:	13	True negatives:	43
Additional comme nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias			r the index test result using ROC analysi		eted without knowledge	e of the resu	ilts of the reference s	standard;
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		

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Suppa P, Anker U, S for Detection of Alzh					et al. Fully Automate er's Disease, 2015; 4			olumetry
Overall indirectness	Not serious	_						
Index Test: MRI Tota	al Hippocampal gre	y matter vo	lume, Hv. Cut off 4	.95ml.				
weighted magnetization Neurological Institute multiplying the subject	on prepared rapid gr (MNI) space using a t's GM component ir the right hemisphere	adient echo combined s nage with a e were used	(MPRAGE). MR image segmentation and repredefined binary mage separately yielding	ages were segm gistration appro- ask from a freel two sub-volume	nto 1.5 T (Siemens Erlented and stereotaction ach. Hippocampal GM y available atlas and the for each brain hemis	cally normali volume (H\ hen summin	zed to the Montreal /) was calculated by g over all voxel inter	nsities.
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			r the index test resu d using ROC analysi		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							
MRI Hippocampal gre	ey matter volume left.	total grey n	natter volume, (HVL	/GMV). MRI was	_/GMV). Cut-off 4.69 carried out using Sie	mens Avant		langen,
normalized to the Morwas calculated by mu	ntreal Neurological Ir Itiplying the subject's ks for the left and the was obtained by su	nstitute (MN) GM compo e right hemis mming the (space using a con ment image with a p sphere were used se	nbined segmentared binary eparately yielding	GE). MR images were ation and registration a mask from a freely aver two sub-volumes for aff 4.69 per mille	approach. H vailable atlas each brain	ippocampal GM volus and then summing hemisphere, HVL an	over all nd HVR,
Results	True positives:	35	False negatives:	9	False positives:	19	True negatives:	37
Additional comme								

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nts								
Risk of bias	Patient selection:	Low	Index test:	High	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	•		er the index test result d using ROC analysi	•	ted without knowledge	e of the res	ults of the reference s	standard
ndirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Germany) deploying normalized to the Mo	3D T1-weighted mag ntreal Neurological Ir	netization p nstitute (MN	repared rapid gradie I) space using a con	ent echo (MPRA) nbined segmenta	as carried out using Sig GE). MR images were ation and registration a	segmented approach. H	l and stereotactically lippocampal GM volu	ıme (H\
Germany) deploying normalized to the Mo	3D T1-weighted mag ntreal Neurological Ir	netization p nstitute (MN	repared rapid gradie I) space using a con	ent echo (MPRA) nbined segmenta	GE). MR images were	segmented approach. H	nto 1.5 T (Siemens E I and stereotactically lippocampal GM volu	ıme (H\
Germany) deploying normalized to the Mowas calculated by muvoxel intensities. Mas	3D T1-weighted mag ntreal Neurological Ir ultiplying the subject's	netization pastitute (MN) GM composeright hemis	repared rapid gradie I) space using a con onent image with a p sphere were used se	ent echo (MPRA) nbined segmenta redefined binary eparately yielding	GE). MR images were ation and registration at mask from a freely aver two sub-volumes for	segmented approach. F vailable atla	nto 1.5 T (Siemens E I and stereotactically lippocampal GM volu s and then summing	ıme (H\ over al
Germany) deploying normalized to the Mowas calculated by muoneel intensities. Mas	3D T1-weighted mag ntreal Neurological Ir altiplying the subject's sks for the left and the	netization p nstitute (MN s GM compo e right hemis mming the 0	repared rapid gradie I) space using a con onent image with a p sphere were used se	ent echo (MPRA) nbined segmenta redefined binary eparately yielding oth masks. Cut-o	GE). MR images were ation and registration at mask from a freely aver two sub-volumes for	segmented approach. Hailable atla each brain	nto 1.5 T (Siemens E I and stereotactically lippocampal GM volu s and then summing	ime (H\ over al id HVR
Germany) deploying normalized to the Mowas calculated by muzoxel intensities. Massespectively. Total HVResults	3D T1-weighted mag ntreal Neurological Ir ultiplying the subject's ks for the left and the / was obtained by su	netization p nstitute (MN s GM compo e right hemis mming the 0	repared rapid gradie I) space using a concent image with a posphere were used second volume within be False	ent echo (MPRA) nbined segmenta redefined binary eparately yielding oth masks. Cut-o	GE). MR images were ation and registration at mask from a freely aver two sub-volumes for the first two for mille.	segmented approach. Hailable atla each brain	nto 1.5 T (Siemens E I and stereotactically lippocampal GM volu s and then summing hemisphere, HVL an	ime (H\ over al id HVR
Germany) deploying normalized to the Mowas calculated by muyoxel intensities. Mas respectively. Total H	3D T1-weighted mag ntreal Neurological Ir ultiplying the subject's ks for the left and the / was obtained by su	netization p netitute (MN s GM compo e right hemis mming the 0	repared rapid gradie I) space using a concent image with a posphere were used second volume within be False	ent echo (MPRA nbined segmenta redefined binary eparately yielding oth masks. Cut-c	GE). MR images were ation and registration at mask from a freely aver two sub-volumes for the first two for mille.	segmented approach. Hailable atla each brain	nto 1.5 T (Siemens E I and stereotactically lippocampal GM volu s and then summing hemisphere, HVL an	ime (H\ over al id HVR
Germany) deploying normalized to the Mowas calculated by muyoxel intensities. Mastespectively. Total HVResults Additional comments	3D T1-weighted mag ntreal Neurological Ir ultiplying the subject's sks for the left and the was obtained by su True positives: Patient selection: Serious (It was und	netization p nstitute (MN s GM compose right hemis mming the 0 35 Low	repared rapid gradie I) space using a concent image with a posphere were used so GM volume within both False negatives: Index test:	ent echo (MPRA) hbined segmenta redefined binary eparately yielding oth masks. Cut-o 9 High	GE). MR images were ation and registration as mask from a freely as two sub-volumes for off 4.54 per mille. False positives: Reference	segmented approach. He vailable atla each brain	nto 1.5 T (Siemens E I and stereotactically lippocampal GM volus s and then summing hemisphere, HVL an True negatives: Flow and timing:	ume (H\ over al dd HVR 45
Germany) deploying normalized to the Movas calculated by muroxel intensities. Massespectively. Total HVResults Additional comments Risk of bias	3D T1-weighted mag ntreal Neurological Ir ultiplying the subject's sks for the left and the was obtained by su True positives: Patient selection: Serious (It was und	netization p netitute (MN s GM composeright hemis mming the 0 35 Low clear whether deductions are the composeries and the composeries are the co	repared rapid gradie I) space using a concent image with a posphere were used so GM volume within bo False negatives: Index test:	ent echo (MPRA) hbined segmenta redefined binary eparately yielding oth masks. Cut-o 9 High lits were interpre	GE). MR images were ation and registration are mask from a freely as two sub-volumes for off 4.54 per mille. False positives: Reference standard:	segmented approach. He vailable atla each brain	nto 1.5 T (Siemens E I and stereotactically lippocampal GM volus s and then summing hemisphere, HVL an True negatives: Flow and timing:	ome (H\ over al dd HVR 45

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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	`		r the index test resu d using ROC analys	•	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							

P.1.19 T

Tagliapietra M, Zanusso G, Fiorini M, Bonetto N, Zarantonello G, Zambon A, Ermani M, Monaco S et al. Accuracy of diagnostic criteria for sporadic Creutzfeldt-Jakob Disease among rapidly progressive dementia. Journal of Alzheimer's disease 2013; 1: 231-238.

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

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Presentation	Suspected CJD du	e to rapidly	progressive dement	ia				
Reference standard	Clinician diagnosis	using Europ	pean sCJD (EUROC	JD) consortium	criteria (Zerr, 2009) fo	r probable	e or possible CJD	
CJD versus not C	JD							
	DWI IR images were taken. <i>i</i> either DWI or FLAIR im				hyperintensities in bot	h caudate	and 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 bia	Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
	R images were taken. A				hyperintensities in bot	h caudate	and putamen and /or i	n two
	True positives:	4	False	6	False positives:	4	True negatives:	16
Results	True positivos:		negatives:					
Additional comm			negatives:					
Additional commonts		Unclear	negatives:	Low	Reference standard:	Low	Flow and timing:	Low
Additional commonts Risk of bias	Patient selection:	Unclear		Low	Reference	Low		Low
Results Additional comments Risk of bias Overall risk of bia Indirectness	Patient selection:	Unclear		Low	Reference	Low		Low

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sporadic Creutzfeldt Index Test: EEG	t-Jakob Disease am	ong rapidly	y progressive dem	entia. Journal d	t Alzheimer's diseas	e 2013; 1: 2	231-238.	
EEG. The presence a and response of basic			llowing were conside	ered: periodic sh	arp-wave complexes,	epileptic ac	tivity, slowing of the r	hythms,
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	_							
Results	True positives:	11	False negatives:	0	False positives:	13	True negatives:	10
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: Total tau	ı							
Total tau, measured b	y ELISA (Bioscource	e Human To	otal tau kit), cut-off 1	300pg/ml.				

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Tagliapietra M, Zanu sporadic Creutzfeldt	-Jakob Disease am	ong rapidly	y progressive demo	entia. Journal o	f Alzheimer's diseas	e 2013; 1: 2	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							

Talbot PR, Lloyd JJ, Snowden JS, Neary D, Testa HJ. A clinical role for 99mTc-HMPAO SPECT in the investigation of dementia? Journal of Neurology, Neurosurgery, and Psychiatry 1998;63:306-13.

Study type	Prospective cohort
Country	UK
Setting	Cerebral function unit at hospital (memory clinic)
Inclusion criteria	Patients referred to clinic with suspected dementia
Exclusion criteria	Not stated
Sex	46.5% male
Age	Mean age 63.2 years (SD 8.0) (of 5 largest diagnostic groups)
Presentation	Suspected dementia
Reference standard	NINCDS-ADRDA (AD), VaD by Roman (1993) criteria, FTD by Brun (1994) criteria; pathological confirmation of AD was established in eight patients (Mann, 1993).
ETD versus non ETI	

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.

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Results	True positives:	21	False negatives:	37	False positives:	21	True negatives:	235
Additional comme nts	Data obtained from	Archer et a	I, (2015) Cochrane	review as not pre	esented in a useful for	mat in origir	nal paper.	
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Unclear	Flow and timing:	High
Overall risk of bias	knowledge of the in	idex test and	d whether the index	test was carried	whether the reference out without knowledg cal diagnosis group is	e of referen	ce test result; no pre	
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
	HMPAO SPECT							
plus unilateral posteri images. SPECT FTD	CT; threshold: not proior CBF abnormality (pattern indicative of	SPECT indi FTD: bilater	cative of FTLD). Vis al anterior brain hyp	ual interpretation operfusion.	scale: bilateral anterion with image analysis;	single- hea	ded camera used to	take
Index Test: 99mTc-l 99mTc-HMPAO SPE plus unilateral posteri images. SPECT FTD	CT; threshold: not proior CBF abnormality (SPECT indi FTD: bilater	cative of FTLD). Vis	ual interpretation operfusion.		single- hea		
Index Test: 99mTc-l 99mTc-HMPAO SPE plus unilateral posteri images. SPECT FTD Results Additional comme	CT; threshold: not proior CBF abnormality (pattern indicative of True positives:	SPECT indi FTD: bilater 37	cative of FTLD). Vis al anterior brain hyp False negatives:	ual interpretation operfusion.	n with image analysis;	single- head	True negatives:	take
Index Test: 99mTc-l 99mTc-HMPAO SPE plus unilateral posteri images. SPECT FTD Results Additional comme nts	CT; threshold: not proior CBF abnormality (pattern indicative of True positives:	SPECT indi FTD: bilater 37	cative of FTLD). Vis al anterior brain hyp False negatives:	ual interpretation operfusion. 43 review as not pre	n with image analysis; False positives:	single- head	True negatives:	take
Index Test: 99mTc-li 99mTc-HMPAO SPE plus unilateral posteri images. SPECT FTD Results Additional comme nts Risk of bias	CT; threshold: not project CBF abnormality (pattern indicative of True positives: Data obtained from Patient selection: Very serious (Uncle	SPECT indi FTD: bilater 37 Archer et a Unclear ear if avoide idex test and	cative of FTLD). Vis al anterior brain hyp False negatives: I, (2015) Cochrane Index test: d inappropriate excl d whether the index	review as not pre High usions; unclear viest was carried	False positives: esented in a useful for Reference standard: whether the reference out without knowledg	21 mat in origin Unclear standard re	True negatives: al paper. Flow and timing: sults were interprete	take 57 High d withou
Index Test: 99mTc-I 99mTc-HMPAO SPE plus unilateral posteri	CT; threshold: not project content of the content o	SPECT indi FTD: bilater 37 Archer et a Unclear ear if avoider idex test and t; subgroup	cative of FTLD). Vis al anterior brain hyp False negatives: I, (2015) Cochrane Index test: d inappropriate excl d whether the index	review as not pre High usions; unclear v test was carried >10% study popu	False positives: esented in a useful for Reference standard: whether the reference out without knowledg	21 mat in origin Unclear standard re	True negatives: al paper. Flow and timing: sults were interprete	take 57 High d withou

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Talbot PR, Lloyd JJ, Neurology, Neurosu				or 99mTc-HMP	AO SPECT in the inv	estigation o	of dementia? Journ	al of	
indirectness									
FTD versus AD									
Index Test: 99mTc-H	IMPAO 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	Archer et a	I, (2015) Cochrane	review as not pro	esented in a useful for	mat in origin	al paper.		
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Unclear	Flow and timing:	High	
Overall risk of bias	Very serious (Unclear if avoided inappropriate exclusions; unclear whether the reference standard results were interpreted without knowledge of the index test and whether the index test was carried out without knowledge of reference test result; no pre-specified index test threshold; subgroup analysis used with >10% study population excluded.)								
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								

Terpening Z, Cordato NJ, Hepner IJ, Lucas SK, Lindley RI. Utility of the Addenbrooke's Coginitive Examination- Revised for the diagnosis of dementua syndromes. Australas J Ageing. 2011; 30: 113-8.

Study type	Prospective Cohort
Country	Australia
Setting	Cognition clinic
Inclusion criteria	People referred to a cognition clinic
Exclusion criteria	Failure to complete all components of ACE-R.
Sex	58.2% male
Age	Mean age 68.7 years (SD9.9)

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Presentation	Suspected dementia								
Reference standard	DSM-IV for demen consensus criteria	•	S/ADRDA for AD, NI	NDS-AIREN for	VaD, Neary et al (199	8) criteria fo	r FTD, McKeith et al.	(1999)	
Dementia versus r	o dementia								
	brooke's Cognitive Enitive Examination-Re		•	•	ex 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								
	brooke's Cognitive Enitive Examination-Re		•	•	;				
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)				
ndirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			

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Addenbrooke's Cogni	tive Examination-Re	vised, ACE-	R, 88/100 standard	cut off from inde	x paper			
Results	True positives:	75	False negatives:	7	False positives:	13	True negatives:	27
Additional comme								
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 clir	ical diagnosis were	excluded from the	ne analysis)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not Serious							

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

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Indirectness

Overall indirectness

Patient Low

selection:

Not serious

Thomas AJ, Attems diagnosis of DLB. N			Keith I, Walker R et	al. Autopsy va	lidation of 123I-FP-C	IT dopamin	ergic neuroimaging	g for the	
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:		Index test:	Low	Reference standard:	Low	Flow and timing:	Low	
Overall risk of bias	Not serious								

Reference Low

standard:

Index test: Low

Toledo JB, Brettsch	neider J, Grossman	M, Arnold	SE, Hu, WT, Xie S	X, Lee VM-Y, SI	naw LM, Trojanowski	JQ.					
Study type	Retrospective cohort										
Country	USA										
Setting	Penn Centre for Ne	Penn Centre for Neurodegenerative Disease Research Integrated Neurodegenerative Disease database									
Inclusion criteria	Autopsy confirmation	on of a diag	nosis of AD, DLB, F	TD; available MI	MSE and CDR scores	and CSF bid	omarker data.				
Exclusion criteria	Not stated	Not stated									
Sex	Not reported	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	a 1-42 ELISA										
Results	True positives:	64	False negatives:	7	False positives:	5	True negatives:	24			

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Risk of bias

Overall risk of bias

Toledo JB, Brettsch	ineider J, Grossmar	n M, Arnold	SE, Hu, WT, Xie S	X, Lee VM-Y, SI	haw LM, Trojanowski	JQ.		
Risk of bias	Patient selection:	Low	Index test:	Unclear	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Serious (>10% pop specified)	oulation excl	uded from analysis;	the index test th	nresholds used are not	stated and	it is unclear if they w	ere pre-
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Toledo JB, Brettsch	ıneider							
Study type	Retrospective coho	ort						
Country	USA							
Setting	Penn Centre for Ne	eurodegene	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	MSE and CDR scores	and CSF bid	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					
AD versus FTD								
Index Test: p-tau 18 p-tau 181, Luminex	31							
Results	True positives:	71	False negatives:	0	False positives:	4	True negatives:	25

specified)

Patient Low

selection:

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

Reference Low

standard:

Flow and High

timing:

Index test: Unclear

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

G.Treglia, E.Cason, P.Cortelli, A.Gabellini, R.Liguori, A.Bagnato, A.Giordano, G.

Fagioli, Iodine-123metaiodobenzylguanidine scintigraphy and iodine-123 ioflupane single photon emission computed tomography in Lewy body diseases: complementary or alternative techniques? J. Neuroimaging 24 (2012) 149–154.

would under the con-	.p.o
Study type	Prospective cohort
Country	Italy
Setting	Unit of Nuclear Medicine, Maggiore Hospital, Bologna
Inclusion criteria	Patients who underwent both 123I-MIBG scintigraphy and 123I-FP-CIT SPECT within 2 months for differential diagnosis between DLB and other dementias
Exclusion criteria	Patients taking drugs interfering with myocardial 123I-MIBG or striatal 123I-FP-CIT uptake; heart diseases, diabetes, previous cardiotoxic therapy, or other diseases which may interfere with myocardial 123I-MIBG uptake; pregnancy and breastfeeding; inability to cooperate with the scintigraphic procedures
Sex	58.1% male
Age	Mean age 66.1 years (SD11.4)
Presentation	Clinically ambiguous dementia (CAD)
Reference standard	Specific criteria used not stated

DLB vs non-DLB dementia

Index Test: 123I-MIBG cardiac scintigraphy

123I-MIBG scintigraphy: after i.v. injection of 111 MBq of 123IMIBG, planar images of the chest in anterior view are obtained twice for 5 minutes, starting at 15 minutes after radiopharmaceutical injection (early image) and then at 240 minutes after radiopharmaceutical injection (delayed image). 123I-MIBG myocardial uptake was determined calculating the heart to mediastinum uptake ratio (H/M) which was compared with a control group.

Results	True positives:	18	False negatives:	2	False positives:	1	True negatives:	10
Risk of bias	Patient selection:	Low	Index test:	Unclear	Reference standard:	Unclear	Flow and timing:	Low

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Overall risk of bias	Not serious (Specif	ic criteria us	ed as the reference	standard not re	ported)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall ndirectness	Not serious							
determined by evalua digital evaluation (usi	ting the cerebral striang regions of interest	atal (caudate	e and putamen)/pos ared with a control g	terior striatum bi group.	SPECT images are ob Inding ratio of 123I-FP	-CIT, semi-c	quantitatively assess	ed by
Results	True positives:	18	False negatives:	2	False positives:	1	True negatives:	10
Additional comme nts								
nts	Patient selection:	Low	Index test:	Unclear	Reference standard:	Unclear	Flow and timing:	Low
	selection:		Index test: ed as the reference	0 1101001	standard:	Unclear		Low
nts Risk of bias	selection:	ic criteria us		standard not re	standard:	Unclear		Low

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
India

Setting Dementia diagnostic clinic
Inclusion criteria All referrals for SPECT perfusion

Exclusion criteria None stated.

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	Tripathi M, Tripathi M, Vibha, Gowda N, Bal C, Malhotra A. Tc-99 ethylctsteinate dimer SPECT in the differential diagnosis of dementias. Neurology India, 2010; 58:857-862.								
Sex	68.4% male								
Age	Mean age 63.2 years (9.8)								
Presentation	Clinically ambiguous dementia								
Reference standard	NINS-ADRDA for AD; NINDS-AIREN for VaD, DLB consensus criteria for DLB, Lund- Manchester criteria for DLB.								

AD versus non-AD

Index Test: 99mTc-ECD SPECT, visual assessment method

Tc -99m ECD SPECT. Images were acquired on a dual-head gamma camera (Varicam, Elscint) using a high-resolution low-energy or fan beam collimator. Acquisition parameters were 25 seconds per stop, 128X128 matrix, circular orbit of 180° each head, step, and shoot mode. Data were reconstructed using a Butterworth filter order 10, cut-off 0.5 cycles/pixel. These were corrected for gamma ray attenuation using Chang attenuation coefficient of 0.11/cm. Transaxial, coronal, and sagittal sections were reconstructed with 2 pixel slice thickness. Images were viewed on a monitor. A coloured display (brain-fit or brain-french, Xpertpro/Entegra workstation-GE) was used, ranging from blue as the lowest through magenta and orange to white as the highest. Perfusion was considered abnormal if the area of deficit was below the halfway point of this scale on more than two sections. Standard diagnostic patterns were used.

Results	True positives:	71	False negatives:	5	False positives:	2	True negatives:	39
Risk of bias	Patient selection:	Low	Index test:	Unclear	Reference standard:	Low	Flow and timing:	Unclear
Overall risk of bias			ere lost to follow up		eive 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							

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

Standard diagnostic p		dered abilon	nam me area or de	nicit was below t	he halfway point of thi	s scale on	more than two section	15.
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			ere lost to follow up dge of the reference		eive a reference standa	ard; it is un	clear whether the inde	ex test
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Tschampa HJ, Kalle disease: a study on					al. MRI in the diagnos	sis of spor	adic Creutzfeldt-Jak	ob
Study type	Retrospective coho	ort						
Country	Germany							
Setting	German surveilland	ce programn	пе					

Study type	Retrospective cohort										
Country	Germany										
Setting	German surveillance programme										
Inclusion criteria	Referred to the German CJD surveillance programme										
Exclusion criteria	Not stated										
Sex	Not stated										
Age	Not stated										
Presentation	Suspected CJD										
Reference standard	60 patients were diagnosed by autopsy using Kretzschmar (1996) and 84 were diagnosed using by clinicians using the WHO criteria.										
CJD versus not CJD (excluding possible CJD)											
Index Test: MRI	Index Test: MRI										
MRI, typical and non-	typical MRI patterns listed in paper. Hyperintense grey matter on MRI.										
Results	True positives: 86 False 58 False positives: 6 True negatives: 32										

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			negatives:							
Additional comme nts	Three independent observers.	observers r	rated 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: EEG EEG, Periodic sharp	wave complexes, sta	ndard proce	ess for surveillance ι	ınit.						
Results	True positives:	12	False	01	False positives:	2	True negatives:	30		
	True positives:	72	negatives:	91	raise positives.	2	True negatives.	30		
Additional comme			negatives:		sed the median sensit					
	Three independent	observers r	negatives:							
nts	Three independent observers.	observers r	negatives: rated the index test of	data. We have u	sed the median sensit Reference	ivity and spe	ecificity data for the 3	}		
nts Risk of bias	Three independent observers. Patient selection:	observers r	negatives: rated the index test of	data. We have u	sed the median sensit Reference	ivity and spe	ecificity data for the 3	}		
nts Risk of bias Overall risk of bias	Three independent observers. Patient selection: Not serious Patient	observers r	negatives: rated the index test of the index test:	data. We have u	sed the median sensit Reference standard: Reference	ivity and spe	ecificity data for the 3	}		
nts Risk of bias Overall risk of bias Indirectness Overall	Three independent observers. Patient selection: Not serious Patient selection: Not serious	observers r	negatives: rated the index test of the index test:	data. We have u	sed the median sensit Reference standard: Reference	ivity and spe	ecificity data for the 3	}		
nts Risk of bias Overall risk of bias Indirectness Overall indirectness Index Test: CSF 14-	Three independent observers. Patient selection: Not serious Patient selection: Not serious	observers r Low Low	negatives: rated the index test of the index test:	data. We have u	sed the median sensit Reference standard: Reference	ivity and spe	ecificity data for the 3	}		

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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									

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	rt							
Country	Belgium								
Setting	Laboratory of neuro	Laboratory of neurobiology, University of Antwerp							
Inclusion criteria	Clinical symptoms	compatible v	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	rs (SD 8.0)							
Presentation	suspected CJD								
Reference standard	Clinical diagnosis a	ccording to	Weber (2000) with	neuropathologic	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	

	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	3-3 and Amyloid Be	ta 1-42						
14-3-3, Amyloid Beta kDa. Amyloid Beta 1-4					for the presence or ab	sence of a	n immunoreactive ban	d at 30
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 Tau Tau, INNOTEST ELIS		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							

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ndirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall ndirectness	Not serious							
Index Test: Amyloid Tau and Amyloid beta og/ml cut-off.			NNOTEST ELISA, c	eut-off 1300pg/m	nl; Amyloid Beta 1-42 v	vas detecte	d using an ELISA wit	h a 400
Results	True positives:	45	False negatives:	7	False positives:	4	True negatives:	194
Additional comme								
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	Low
Overall risk of bias	Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

Van Everbroeck B, patients.J Neurol. 2	Dobbeleir I, De Waele M, De Deyn P, Martin JJ, Cras P. Differential diagnosis of 201 possible Creutzfeldt-Jakob disease 004; 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

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Reference standard	Autopsy using the	detection of	prion proteins by im	munocytochemi	stry for CJD.			
CJD versus not CJD								
Index Test: Total Ta	u							
Tau >1300pg/ml, by I	NNOTEST ELISA							
Results	True positives:	45	False negatives:	7	False positives:	2	True negatives:	79
Additional comme nts	Data for Periodic si reference diagnosi	•	omplexes (PSWCs)	in EEG and 14-	3-3- protein were not a	analysed as	s 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% po	pulation exc	luded from analysis)					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
Index Test: MRI MRI, presence of CJE	O typical lesions in th	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 si reference diagnosis		omplexes (PSWCs)	in EEG and 14-	3-3- protein were not	analysed as	s 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% po	pulation exc	luded from analysis))				
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

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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.

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					rithout knowledge of th sults interpreted witho			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

Index Test: 99mTc-HMPAO SPECT (FTD pattern)

99mTc-HMPAO SPECT imaging carried out in another specialist department. 72 images of tracer distribution with 24 images per scan with image

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

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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	interpreted without	ery serious (Subgroup analysis where >10% study population excluded and it was unclear whether: the index test results were erpreted without knowledge of the results of the reference standard; the index test threshold was pre-specified or the reference and ard 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	interpreted without	ery serious (Subgroup analysis where >10% study population excluded and it was unclear whether: the index test results were terpreted without knowledge of the results of the reference standard; the index test threshold was pre-specified or the reference tandard results interpreted without knowledge of the results of the index test.)								
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall	Not serious									

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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	interpreted without	ery serious (Subgroup analysis where >10% study population excluded and it was unclear whether: the index test results were terpreted without knowledge of the results of the reference standard; the index test threshold was pre-specified or the reference andard 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									

	Is A, Krudop WA, Peters A, Kerssens CJ, van Berckel BNM, Wattjes MP et al. Diagnostic Accuracy of the Frontotemporal us 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

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	s Criteria in the Lat dementia, and (8) I	//RI contrain	dications.						
Sex	80.0% male								
Age	Mean age 62.0 yea	ean age 62.0 years (SD 6.9)							
Presentation	suspected bvFTD								
Reference standard	repeated, and a fin dementia (Gorno-T	al multidisci _l empini, 201	olinary diagnosis wa 1, for PPA; NINCDS	as established. D S-ADRDA for AD	europsychological test Diagnoses were based I; NINCDS-AIREN for ' It psychiatric criteria (E	on the publi VaD; McKei	ished consensus gui th, 2005, for DLB; D	delines	
bvFTD versus not b	vFTD								
the neuropsychologic	al test battery and ne	euroimaging	results). A consens		neurological examina tween the neurologist	and the psy	chiatrist was made.		
Results	True positives:	23	False negatives:	4	False positives:	65	True negatives:	24	
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Unclear	Flow and timing:	High	
Overall risk of bias					s unclear whether a coreted without knowled				
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								
bvFTD versus not b	vFTD								
	sible and probable by	FTD (uses			neurological examina tween the neurologist			sults of	
Results	True positives:	23	False negatives:	4	False positives:	16	True negatives:	73	
Risk of bias	Patient selection:	Low	Index test:	Low	Reference	Unclear	Flow and	High	

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Overall risk of bias					s unclear whether a co reted without knowled				
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								
					t al. Diagnostic Accu havioral Changes. Jo				
Study type	Prospective cohort								
Country	The Netherlands								
Setting	VU medical centre	Alzheimer C	Centre and the Depa	ertment of Old A	ge Psychiatry of the G	GZInGeest, A	msterdam.		
Inclusion criteria	between April 2011	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	rs (SD 6.6)							
Presentation	suspected bv-FTD								
Reference standard		11, for AD;	NINDS-AIREN for V	aD; McKeith, 20	dementia (Rascovsky, 005, for DLB and DSM				
	hy ETD								
bv-FTD versus non-	טע-רוט								
	T s were made on an E				JFDG-PET-scans were sm based on the sumn			ted by a	

negatives:

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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							
T2* susceptibility seq (GCA) using a 4-point	uence, and diffusion t scale and classified	-recovery (F weighted im as consiste	LAIR) fast spin-ech naging/EPI were car ent with frontotempo	o with axial reforied out. The im ral dementia or	rmats, a transverse T2 ages were evaluated v not.	-weighted f	to global cortical atro	sverse ophy
T2* susceptibility seq (GCA) using a 4-point 18-F FDG-PET scans	uence, and diffusion t scale and classified were made on an E	recovery (F weighted im as consiste CAT EXAC n frontal and	ELAIR) fast spin-ech- naging/EPI were car ent with frontotempo F HR+ scanner (Sied d/or anterior tempora False	o with axial refo ried out. The im ral dementia or mens/CTI). [18F al hypometaboli	rmats, a transverse T2 ages were evaluated v	-weighted f with respect e assessed med images	fast spin-echo, a trans to global cortical atro visually and interpret	sverse ophy ted by ar
T2* susceptibility seq (GCA) using a 4-point 18-F FDG-PET scans experienced nuclear r Results Additional comme	uence, and diffusion t scale and classified were made on an E medicine physician o	recovery (F weighted im as consiste CAT EXAC n frontal and	ELAIR) fast spin-ech naging/EPI were can ent with frontotempo F HR+ scanner (Sie d/or anterior tempora	o with axial refo ried out. The im ral dementia or mens/CTI). [18F al hypometaboli	rmats, a transverse T2 ages were evaluated v not. FJFDG-PET-scans were sm based on the sumr	-weighted f with respect e assessed med images	fast spin-echo, a trans to global cortical atro visually and interpret s of all the frames.	sverse ophy ted by ar
T2* susceptibility seq (GCA) using a 4-point 18-F FDG-PET scans experienced nuclear results Additional comments	uence, and diffusion t scale and classified were made on an E medicine physician o	-recovery (F weighted im as consiste CAT EXAC n frontal and 26	ELAIR) fast spin-ech- naging/EPI were car ent with frontotempo F HR+ scanner (Sied d/or anterior tempora False	o with axial refo ried out. The im ral dementia or mens/CTI). [18F al hypometaboli	rmats, a transverse T2 ages were evaluated v not. FJFDG-PET-scans were sm based on the sumr	-weighted f with respect e assessed med images	fast spin-echo, a trans to global cortical atro visually and interpret s of all the frames.	sverse ophy ted by ar
T2* susceptibility seq (GCA) using a 4-point 18-F FDG-PET scans experienced nuclear results Additional comments Risk of bias	uence, and diffusion t scale and classified were made on an E medicine physician o True positives: Patient selection: Serious (19% study	recovery (F weighted im as consiste CAT EXAC [*] n frontal and 26 Unclear	TLAIR) fast spin-echinaging/EPI were can ent with frontotempo T HR+ scanner (Sied/or anterior temporal False negatives: Index test: was excluded from	o with axial reforied out. The imral dementia or mens/CTI). [18Fal hypometabolical formula in the content of th	rmats, a transverse T2 ages were evaluated v not.]FDG-PET-scans were sm based on the sumn False positives: Reference	e assessed med images 23 High	fast spin-echo, a trans to global cortical atro visually and interpret of all the frames. True negatives: Flow and timing: or random group of pa	sverse ophy ted by an 61 High atients
T2* susceptibility seq (GCA) using a 4-point 18-F FDG-PET scans experienced nuclear r	uence, and diffusion to scale and classified to were made on an Emedicine physician of the positives: Patient selection: Serious (19% study was enrolled or whom to scale and classified	recovery (F weighted in as consiste CAT EXAC n frontal and 26 Unclear y population ether inappr	TLAIR) fast spin-echinaging/EPI were can ent with frontotempo T HR+ scanner (Sied/or anterior temporal False negatives: Index test: was excluded from	o with axial reforied out. The imral dementia or mens/CTI). [18Fal hypometabolical formula in the content of th	rmats, a transverse T2 ages were evaluated v not. FJFDG-PET-scans were sm based on the summ False positives: Reference standard: s unclear whether a co	e assessed med images 23 High	fast spin-echo, a trans to global cortical atro visually and interpret of all the frames. True negatives: Flow and timing: or random group of pa	sverse ophy ted by a final High atients

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

P.1.21 W

Walker Z, Jaros E, Walker RWH, Lee L, Costa DC, Livingston, G et al. Dementia with Lewy bodies: a comparison of clinical diagnosis, FP-CIT single photon emission computed tomography imaging and autopsy. J Neurol Neurosurg Psychiatry 2007;78:1176–1181.

Single photon emiss	single photon emission computed tomography imaging and autopsy. 5 Neuron Neurosurg Esychiatry 2007,76.1170–1161.						
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						

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	E, Walker RWH, Lee L, Costa DC, Livingston, G et al. Dementia with Lewy bodies: a comparison of clinical diagnosis, FP-CIT nission computed tomography imaging and autopsy. J Neurol Neurosurg Psychiatry 2007;78:1176–1181.
Age	Mean age 77.3 years (SD 9.0)
Presentation	Suspected dementia
Reference standard	The neuropathological diagnostic criteria employed for AD included the following: CERAD (Consortium to Establish a Registry for Alzheimer's Disease) score and diagnosis, Braak stage18 and NIA-RI (National Institute on Aging and Reagan Institute) AD diagnosis. The neuropathological diagnostic criteria employed for DLB were those recommended by the Third report of the DLB Consortium (McKeith, 2005).

DLB versus non-DLB dementias

Index Test: 123I-FP-CIT SPECT

FP-CIT SPECT, visual rating of scans. Imaged using a Strichman Medical Equipment 810. The Strichman camera consists of 12 individual detectors, each equipped with a focusing collimator.

Results	True positives:	7	False negatives:	1	False positives:	2	True negatives:	10
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Unclear	Flow and timing:	Low
Overall risk of bias	Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

Index Test: 123I-FP-CIT SPECT

FP-CIT SPECT, semi-quantitatively analysed scans. Imaged using a Strichman Medical Equipment 810. The Strichman camera consists of 12 individual detectors, each equipped with a focusing collimator. For the analysis of striatal binding, the ratio of specific to non-specific binding was calculated. An abnormal scan, signifying a more likely diagnosis of DLB, was defined as a scan with semi-quantitative binding in the posterior putamen (right and left), which was more than 2 SDs below the mean of the controls.

Results	True positives:	7	False negatives:	1	False positives:	0	True negatives:	12
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Unclear	Flow and timing:	Low
Overall risk of bias	Not serious							
Indirectness	Patient	Low	Index test:	Low	Reference	Low		

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Walker Z, Jaros E, Walker RWH, Lee L, Costa DC, Livingston, G et al. Deme	ntia 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 Not serious indirectness

Index Test: 123I-FP-CIT SPECT

FP-CIT SPECT, semi-quantitatively analysed scans with abnormal binding on one side allowed. Imaged using a Strichman Medical Equipment 810. The Strichman camera consists of 12 individual detectors, each equipped with a focusing collimator. For the analysis of striatal binding, the ratio of specific to non-specific binding was calculated. An abnormal scan, signifying a more likely diagnosis of DLB, was defined as having posterior putamen binding on just one side (either right or left) more than 2 SDs below the mean of the controls (ie, ,2.91).

Results	True positives:	8	False negatives:	0	False positives:	1	True negatives:	11
Risk of bias	Patient selection:	Unclear	Index test:	Low	Reference standard:	Unclear	Flow and timing:	Low
Overall risk of bias	Not serious							
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

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

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	Walker RWH, Walker Z. Dopamine transporter single photon emission computerized tomography in the diagnosis of dementia with Lewy bodies. Movement Disorders 2009; 24: S754–9.					
Age	Not stated					
Presentation	Patients with previously diagnosed DLB or AD					
Reference standard	The neuropathological diagnostic criteria employed for AD included the following: CERAD (Consortium to Establish a Registry for Alzheimer's Disease) score and diagnosis, Braak stage and NIA-RI (National Institute on Aging and Reagan Institute) AD diagnosis.					
	The neuropathological diagnostic criteria employed for DLB were those recommended by the Third report of the DLB Consortium.					

DLB vs no-DLB

Index Test: 123I-FP-CIT SPECT

123I-FP-CIT SPECT scan using a Strichman Medical Equipment 810 camera. Scanning took place 3 to 4 hours after injection of DaTscanT M. All scans were subject to a semi-quantitative analysis, interpreted by a specialist in nuclear medicine. An abnormal scan on semi-quantitative analysis was defined as having binding > 2 SDs below that of healthy controls in the posterior putamen on 1 or both sides.

Results	True positives:	10	False negatives:	0	False positives:	1	True negatives:	12
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High
Overall risk of bias	Serious (Some of t	he included	individuals had a pr	esumed dement	ia diagnosis at baselin	ie)		
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							

P.1.22 Y

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

Study type	Prospective cohort
Country	Germany
Setting	Memory clinic

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					A, Muller MJ. Cerebr		id Tau Protein Leve	els and 1			
F-Fluorodeoxygluco Inclusion criteria	Consecutive referra			ntial Diagnosis	of Alzheimer's Disea	ise.					
Exclusion criteria	Not stated	מוז נט נווכ וווי	erriory chiric.								
Sex	60.0% male										
Age		re (SD 10.0	١								
Presentation	-	Mean age 67.0 years (SD 10.9) Suspected dementia									
Reference standard	Patients were diagnosed with AD according to NINCDS-ADRDA criteria; MCI according to Petersen criteria; vascular dementia according to NINDS-AIREN criteria; frontotemporal dementia according to Lund-Manchester criteria.										
AD versus no deme											
Index Test: Total Ta CSF total tau (INNOT		A), cut-off >	520ng/l								
Results	True positives:	11	False negatives:	13	False positives:	1	True negatives:	21			
Additional comme nts	p-tau 181 data not sharing the same to			mentia and AD v	ersus other dementias	do not have	e the same sensitivit	y despite			
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	sis with >10% popula	ation excluded; ι	ise of optimised thresh	olds for test	t)				
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										
AD versus non-AD	dementias (excludes	s MCI)									
Index Test: Total Ta		م), cut-off >،	440ng/l								
Results	True positives:	13	False negatives:	11	False positives:	1	True negatives:	12			
Additional comme	p-tau 181 data not sharing the same to			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			

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	selection:				standard:		timing:			
Overall risk of bias	Very serious (Subg	roup analys	is with >10% popula	ation excluded; ι	ise of optimised thresh	nolds for test	i)			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
Overall ndirectness	Not serious									
AD versus no deme	entia (excludes MCI)									
ealignment and spa SSP) technique. The	tial normalization, gre findings were finally	y matter act rated as AD	ivities were extracte -typical or not AD-ty	d to predefined pical.	scans were processed surface pixels using a	3-D stereota	actic surface projecti	on (3D-		
Results	True positives:	19	False negatives:	5	False positives:	2	True negatives:	20		
p-tau 181 data not analysed as AD versus non-dementia and AD versus other dementias do not have the same sensitivity despite sharing the same test cut-off (>65ng/l)										
Risk of bias	Patient selection:	Low	Index test:	Low	Reference standard:	Low	Flow and timing:	High		
Overall risk of bias	Serious (Subgroup	analysis wif	th >10% population	excluded)						
ndirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low				
	Not serious									
ndirectness	dementias (excludes	s MCI)								
Overall ndirectness AD versus non-AD ndex Test: FDG-PE	•	s MCI)								
ndirectness AD versus non-AD ndex Test: FDG-PE FDG-PET images ta realignment and spa	ET ken using a Siemens	ECAT EXAC	ivities were extracte	d to predefined	cans were processed surface pixels using a					

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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)				
ndirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall indirectness	Not serious							
AD versus other gro	oups (non-AD deme	ntias and n	o dementia, exclud	des MCI)				
SSP) technique. The	findings were finally	rated as AD	-typical or not AD-ty	rpical.	,		, ,	Ì
					surface pixels using a	3-D stereot	actic surface projecti	on (3D-
Results	True positives:	19	False negatives:	5	False positives:	2	True negatives:	33
	sharing the same to	est cut-off (>	-65ng/I)		versus other dementias MCI results in AD vers			y despit
nts	sharing the same to	est cut-off (> h different c	-65ng/I)	ould not include				y despit High
nts Risk of bias	sharing the same to Data presented wit Patient selection:	est cut-off (> h different c Low	·65ng/l) ut-offs for MCI so co	ould not include Low	MCI results in AD vers	sus all other	groups comparison. Flow and	
nts Risk of bias Overall risk of bias	sharing the same to Data presented wit Patient selection:	est cut-off (> h different c Low analysis wit	-65ng/l) ut-offs for MCI so co Index test:	ould not include Low excluded)	MCI results in AD vers	sus all other	groups comparison. Flow and	
Additional comments Risk of bias Overall risk of bias Indirectness Overall indirectness	sharing the same to Data presented with Patient selection: Serious (Subgroup Patient	est cut-off (> h different c Low analysis wit	e65ng/l) ut-offs for MCI so co Index test: th >10% population	ould not include Low excluded)	MCI results in AD vers Reference standard: Reference	sus all other Low	groups comparison. Flow and	
nts Risk of bias Overall risk of bias Indirectness Overall indirectness	sharing the same to Data presented with Patient selection: Serious (Subgroup Patient selection: Not serious	est cut-off (> h different c Low analysis wit Low	checker of the state of the sta	ould not include Low excluded) Low	MCI results in AD vers Reference standard: Reference	cus all other Low Low	groups comparison. Flow and timing:	High
Risk of bias Overall risk of bias Indirectness Overall indirectness	sharing the same to Data presented with Patient selection: Serious (Subgroup Patient selection: Not serious	est cut-off (> h different c Low analysis wit Low Low Low Low Kong. Hon	checker of the state of the sta	ould not include Low excluded) Low	MCI results in AD vers Reference standard: Reference standard:	cus all other Low Low	groups comparison. Flow and timing:	High

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Setting	Cognition clinic and	d memory cl	inic of a								
	public hospital in H	ong Kong									
Inclusion criteria	Cantonese-speakir consent, were recru	•	adults aged 60 year	s or above, who	were seen for suspec	ted cognitive	e impairment and ga	ve			
Exclusion criteria	system infection, be major depression of barriers such as de	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	rs (SD 7.5)									
Presentation	Suspected dement	Suspected dementia									
Reference standard	The DSM-IV criteria	a was used	to diagnose dement	ia and the Peter	sen criteria (1999) for	MCI.					
Dementia versus no	dementia (includin	g MCI)									
Index Test: Montrea Hong-Kong version o		•	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	optimal index test t	hresholds w	ere determined duri	ng the study; it i	ecutively or whether in s unclear whether the						
	Patient	Patient Low Index test: Low Reference standard:									
Indirectness	selection:				Stariuaru.						

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	f 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	avoided; the optima	al index test	thresholds were de	termined during	consecutively or whet the study; it is unclear subgroup analysis was	whether the	e index test results a	nd
ndirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low		
Overall Indirectness	Not serious							
index Test: MMSE (MMSE (
Results	True positives:	124	False negatives:	6	False positives:	5	True negatives:	44
Additional comme nts					is no dementia and Mo cificity is not consisten			
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Unclear	Flow and timing:	High
Overall risk of bias	avoided; the optima	al index test	thresholds were de	termined during	consecutively or whet the study; it is unclear subgroup analysis wa	whether the	e index test results a	nd
	Patient	Low	Index test:	Low	Reference	Low		

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P.1.23 Z

Study type	Prospective cohort										
Country	Germany										
Setting	German National S	urveillance	unit								
Inclusion criteria	People referred for	People referred for diagnosis with suspected CJD									
Exclusion criteria	Not stated	Not stated									
Sex	28.4% male	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 based on Masters et al. (1979), Will et al. (1998), Zerr (1996) and Steinhoff et al. (1996)										
CJD (including pos	sible CJD) versus no	ot-CJD									
Index Test: CSF 14-	3-3 immunoblotting										
CSF 14-3-3 protein d	etected by immunoble	otting with a	ıny 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 susp	ected CJD at baseline						
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Unclear	Flow and timing:	High			
Overall risk of bias	inappropriate exclu	sions avoid	ed; the index test re	sults were interp	ner: a consecutive or r preted without knowled ge of the results of the	ge of the re	sults of the reference				
	Patient	r the reference standard results were interpreted without knowledge of the results of the index test.) Patient Low Index test: Low Reference standard:									
Indirectness	selection:				standard:						

Zerr I, Bodemer M, G Ann Neurol 1998; 43		ection of 14	4-3-3 protein in the	cerebrospinal	fluid supports the di	agnosis of (Creutzfeldt-Jakob o	disease.			
Index Test: CSF 14-3-3 immunoblotting CSF 14-3-3 protein detected by immunoblotting with any ambiguous results defined as positive											
Results	True positives:	132	False negatives:	13	False positives:	7	True negatives:	97			
Additional comme The healthy control group was excluded as they did not have suspected CJD at baseline ats											
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Unclear	Flow and timing:	High			
Overall risk of bias	unclear whether: a results were interpr	consecutive eted withou	or random sample	of patients was esults of the refe	analysis was carried of enrolled or inappropria erence standard or the	ite exclusion	is avoided; the index	test			
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										

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)

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Zerr I, Pocchiari M, C 2000; 55: 811–815.	Collins S, et al. Ana	lysis of EE	G and CSF 14-3-3 բ	proteins as aids	to the diagnosis of	Creutzfeldt-	-Jakob disease. Ne	urology			
CJD versus not CJD	CJD versus not CJD										
Index Test: CSF 14-3-3 immunoblotting CSF 14-3-3 protein detected by immunoblotting											
Results	True positives:	497	False negatives:	114	False positives:	34	True negatives:	358			
Risk of bias	Patient selection:	Unclear	Index test:	Unclear	Reference standard:	Low	Flow and timing:	Low			
Overall risk of bias					dependently of the refo opriate exclusions avo						
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low					
Overall indirectness	Not serious										

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

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	n 2009: 132; 2659–2						A.B. 1 455		
Reference standard			brain pathology or l athogenic prion prot		nosis using the criteria	for probable	e CJD, codon 129 ge	enotyping	
CJD versus no CJD									
Index Test: WHO CJ	D criteria								
WHO criteria for spora test positive for CJD.	adic CJD. 14-3-3 wa	s detected b	y immunoblotting a	nd EEG (periodi	c sharp wave complex	es) were me	easured. EEG typica	l & 14-3-:	
Results	True positives:	95	False negatives:	8	False positives:	15	True negatives:	37	
Risk of bias	Patient selection:	Unclear	Index test:	High	Reference standard:	Low	Flow and timing:	High	
Overall risk of bias Very serious (Unclear whether patients were selected randomly or consecutively or whether inappropriate exclusions were avoided; the optimal index test thresholds were determined during the study and a subgroup analysis was used to determine test sensitivity and specificity.)									
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	Low			
Overall indirectness	Not serious								
Index Test: New crit	eria for sporadic C	JD							
	MRI a standardized p				ed by immunoblotting a al cortex regions. Curre				
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	

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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										

	n FH, Konijnberg E, van der Flier WM, et al. Diagnostic impact of [18F]flutemetamol PET in early-onset dementia. ch & Therapy 2017; 9: 2
Study type	Prospective cohort
Country	Netherlands
Setting	Memory clinic
Inclusion criteria	Consecutive series of patients visiting a memory clinic with suspected mild dementia (defined as Mini Mental State Examination (MMSE) score ≥ 18) or early-onset dementia (defined by age at diagnosis ≤ 70 years), who had no firm diagnosis after the standardized dementia evaluation or persisting diagnostic uncertainty (defined as pre-PET diagnostic confidence < 90% as measured by a standardised study questionnaire).
Exclusion criteria	People with suspected dementia and diagnostic confidence after standardised work-up > 90%.
Sex	55% male
Age	Mean age 62 years (SD 6)
Presentation	Suspected dementia
Reference standard	Clinical diagnosis was established using clinical criteria (Roman et al. 1993, McKeith et al 2005, Boeve etal 2003, Litvan et al 1996) without knowledge of PET or CSF results or APOE carrier status.
45	

AD versus non-AD

Index Test: [18F] flutemetamol PET

[18F] flutemetamol PET scans were made on a Gemini TF-64 PET/CT scanner. Patients underwent a low-dose CT scan followed by a 20-minute (i.e., 4 frames of 5 minutes) PET scan. Scans were checked for movement and frames were summed to obtain a static (20-minute) image for each patient. Scans were visually assessed and dichotomously rated as either amyloid positive or amyloid-negative by the local nuclear medicine physician, who completed the training program for visual interpretation of [18F]flutemetamol images.

Results	True positives:	110	False negatives:	34	False positives:	23	True negatives:	44
Risk of bias	Patient selection:		Index test:	Low	Reference standard:	Low	Flow and timing:	Low

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Zwan MD, Bouwman Alzheimer's Researc			er WM, et al. Diagn	ostic impact of	[18F]flutemetamol P	PET in early-onset dementia.
Overall risk of bias	Not serious					
Indirectness	Patient selection:	Low	Index test:	Low	Reference standard:	
Overall indirectness	Not serious					

P.2 GRADE tables

P.2.1 Dementia versus no dementia

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%Cl)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Apolipario 2015)	Dragnostiva	220	0.60 (0.50, 0.77)	0.04 (0.00, 0.07)	LR+	10.67 (5.40, 21.12)	Serious	n/a	Serious	Not serious		LOW
1 study (Apolinario 2015)	Prospective	230	0.69 (0.59, 0.77)	0.94 (0.88, 0.97)	LR-	0.33 (0.25, 0.44)	Serious	n/a	Serious	Not serious	-	LOW

Notes on risk of bias

Apolinario 2015: Optimised thresholds were calculated and people with moderate to severe dementia were excluded from the study.

Notes on indirectness

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 study (Austinasia 0045)	Description	000	0.04 (0.00, 0.07)	0.00 (0.54, 0.00)	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 ≥ 60 years old and had on average only 4.7 years of schooling

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Apolipario 2015)	Droopoetivo	230	0.07 (0.03, 0.00)	0.40 (0.33, 0.40)	LR+	1.63 (1.40, 1.89)	Serious	n/a	Serious	Not serious		LOW
1 study (Apolinario 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

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P.2.1.4 6 item screener (≥0)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Callahan	Prospective	054	4.00 (0.00, 4.00)	0.00 (0.00, 0.03)	LR+	1.00 (0.99, 1.01)	Serious	n/a	Not serious	Not serious		MODERATE
2002)	Prospective	651	1.00 (0.98, 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 bias

Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.

P.2.1.5 6 item screener (≥1)

		l .				Summary	of bias	sistency	ctness	Imprecision	derations	
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	of findings (95%CI)	Risk o	Incons	Indire	Impre	Other consider	Quality
SECONDARY CAR	RE											
1 study (Callahan	Prospective	651	0.07 (0.04, 0.09)	0.52 (0.49, 0.50)	LR+	2.07 (1.84, 2.34)	Serious	n/a	Not serious	Serious		LOW
2002)	Frospective	001	0.97 (0.94, 0.98)	0.53 (0.48, 0.59)	LR-	0.06 (0.03, 0.11)	Serious	n/a	Not serious	Not serious		MODERATE

Notes on risk of bias

Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.

P.2.1.6 6 item screener (≥2)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Callahan	Prospective	054	0.00 (0.00 0.00)	0.70 (0.75, 0.04)	LR+	4.35 (3.48, 5.44)	Serious	n/a	Not serious	Not serious		MODERATE
2002)	Prospective	651	0.90 (0.86, 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 bias

Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.

P.2.1.7 6 item screener (≥3)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Callahan	Prospective	651	0.91 (0.76, 0.94)	0.01 (0.97, 0.04)	LR+	8.81 (6.16, 12.58)	Serious	n/a	Not serious	Not serious		MODERATE
2002)	riospective	001	0.81 (0.76, 0.84)	0.91 (0.87, 0.94)	LR-	0.21 (0.17, 0.27)	Serious	n/a	Not serious	Not serious	_	MODERATE

Notes on risk of bias

Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.

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P.2.1.8 6 item screener (≥4)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Callahan	Prospective	651	0.68 (0.62, 0.72)	0.06 (0.03, 0.08)	LR+	17.22 (9.84, 30.13)	Serious	n/a	Not serious	Not serious		MODERATE
2002)	riospective	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 bias

Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.

P.2.1.9 6 item screener (≥5)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Callahan	Prospective	651	0.40 (0.44, 0.54)	0.00 (0.07, 1.00)	LR+	37.47 (14.07, 99.80)	Serious	n/a	Not serious	Not serious		MODERATE
2002)	Prospective	651	0.49 (0.44, 0.54)	0.99 (0.97, 1.00)	LR-	0.52 (0.47, 0.57)	Serious	n/a	Not serious	Serious	-	LOW

Notes on risk of bias

Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.

P.2.1.10 6 item screener (≥6)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAI	RE											
1 study	Prognactiva	651	0.30 (0.26, 0.35)	0.00 (0.07.1.00)	LR+	46.57 (11.59, 187.06)	Serious	n/a	Not serious	Not serious		MODERATE
(Callahan 2002)	Prospective	001	0.30 (0.26, 0.33)	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 bias

Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 atudu (Abdal A== 2045)	Dunamantiiva	045	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	JS	HIGH

P.2.1.12 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA												
1 study (Dahart 2005)	Dragnostivo	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
1 study (Dobert 2005)	Prospective	24	0.89 (0.65, 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 Dobert 2005: It is unclear wh	nether a consecutiv	ve or rand	lom sample of patie	nts was enrolled and	d whether in	appropriate exclusion	ns were a	oided.				

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Larner 2007)	Dragnostiva	205	0.05 (0.79, 0.00)	0.02 (0.76, 0.00)	LR+	4.93 (3.43, 7.09)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Larner 2007)	Prospective	285	0.85 (0.78, 0.90)	0.83 (0.76, 0.88)	LR-	0.18 (0.12, 0.27)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Larner 2007;	2 ×	424	0.91 (0.67, 0.98)	0.84 (0.29, 0.98)	LR+	5.62 (0.81, 39.07)	Serious	Serious	Not serious	Serious		VERY LOW
Mathuranath 2000)	prospective	424	0.91 (0.07, 0.98)	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 Mathuranath 2000: Optimis	sed test-threshol	d used a	nd it was unclear wh	ether the index test	results were	interpreted without k	nowledge	of the resu	Its of the refere	ence standard.		

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Larner 2007;	2 ×	404	0.00 (0.74, 4.00)	0.50 (0.00, 0.00)	LR+	2.18 (1.23, 3.85)	Serious	Serious	Not serious	Serious		VERY LOW
Mathuranath 2000)	prospective	424	0.98 (0.71, 1.00)	0.56 (0.29, 0.80)	LR-	0.04 (0.00, 0.42)	Serious	Serious	Not serious	Not serious	-	LOW
Notes on risk of bias Mathuranath 2000: Optimise	ed test-threshold	used and	d it was unclear whe	ether the index test r	esults were	interpreted without k	knowledge	of the resu	Its of the refere	ence standard.		

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (lubb 2015)	Drooppotivo	50	0.94 (0.64, 0.02)	0.07 (0.91.1.00)	LR+	26.65 (3.83, 185.32)	Serious	n/a	Serious	Not serious		LOW
1 study (Jubb 2015)	Prospective	59	0.81 (0.61, 0.92)	0.97 (0.81, 1.00)	LR-	0.20 (0.09, 0.44)	Serious	n/a	Serious	Not serious	-	LOW

Notes on risk of bias

Jubb 2015: Optimised threshold used for analysis.

Notes on indirectness

Jubb 2015: Study population was confined to >75 years

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

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
OLOGINDAN TOAKL			1									
1 atudy (lubb 2015)	Prospective	59	0.91 (0.61, 0.02)	0.70 (0.52, 0.92)	LR+	2.67 (1.54, 4.62)	Not serious	n/a	Serious	Serious		LOW
1 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

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 atualy (light 2045)	Dragagativa	50	0.00 (0.74, 0.00)	0.04 (0.42, 0.70)	LR+	2.34 (1.51, 3.63)	Serious	n/a	Serious	Serious		VERY LOW
1 study (Jubb 2015)	Prospective	59	0.92 (0.74, 0.98)	0.61 (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 threshold used for analysis.

Notes on indirectness

Jubb 2015: Study population was confined to >75 years

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

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
OZGGND/IIII G/IIIZ			1									
1 study (Jubb 2015)	Prospective	60	0.96 (0.77, 0.99)	0.50 (0.34, 0.66)	LR+	1.92 (1.36, 2.71)	Not serious	n/a	Serious	Serious		LOW
1 Study (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

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

Addenbiooke 3 C		A CATTONIA	au on Roviou	,710 <u>2</u> R (4 I)								
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Hannak 2011)	Droopoetiyo	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
1 study (Hancock 2011)	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												
Hancock 2011: Optimised	test threshold.											

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Bastide	2 ×	442	0.87 (0.69, 0.95)	0.72 (0.61, 0.92)	LR+	3.04 (2.48, 3.73)	Serious	Not serious	Not serious	Not serious		MODERATE
2012; Terpening 2011)	prospective	442	0.07 (0.09, 0.95)	0.73 (0.61, 0.82)	LR-	0.18 (0.08, 0.39)	Serious	Serious	Not serious	Not serious	-	LOW

Notes on risk of bias

Terpening 2011: Patients lacking a clinical diagnosis were excluded from the analysis Bastide 2012: Optimised test cut-offs used.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
4 atualy (Tamanina 2014)	Dana a a ativa	400	0.05 (0.70, 0.04)	0.00 (0.05, 0.00)	LR+	4.27 (2.28, 7.98)	Serious	n/a	Not serious	Not serious		MODERATE	
1 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													

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atualy (Tamanina 2011)	Dunanastiva	400	0.04 (0.02, 0.00)	0.00 (0.50, 0.00)	LR+	2.81 (1.79, 4.42)	Serious	n/a	Not serious	Serious		LOW
1 study (Terpening 2011)	Prospective	122	0.91 (0.83, 0.96)	0.68 (0.52, 0.80)	LR-	0.13 (0.06, 0.27)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of bias Terpening 2011: Patients la	acking a clinical	diagnosis	s were excluded fron	n the analysis								

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P.2.1.24 AD8 (≥2)

ABG (22)						Summary	of bias	nsistency	ectness	ecision	Other considerations	
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	of findings (95%CI)	Risk	Incon	Indire	Impre	Other	Quality
SECONDARY CARE												
1 study (Larner 2015)	Prospective	212	0.97 (0.89, 0.99)	0.11 (0.07, 0.17)	LR+	1.09 (1.02, 1.17)	Not serious	n/a	Not serious	Not serious		HIGH
1 Study (Lattlet 2015)	riospective	212	0.37 (0.09, 0.99)	0.11 (0.07, 0.17)	LR-	0.26 (0.06, 1.10)	Not serious	n/a	Not serious	Serious	-	MODERATE

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Flicker	Dunamantiva	200	0.07 (0.04, 0.00)	0.20 (0.40, 0.20)	LR+	1.34 (1.17, 1.54)	V. serious	n/a	Not serious	Not serious		LOW
1997) Prospective 299	0.97 (0.94, 0.99)	0.28 (0.19, 0.38)	LR-	0.10 (0.04, 0.24)	V. serious	n/a	Not serious	Not serious	-	LOW		

Notes on risk of bias

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

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

Studies PRIMARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	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
1997)	study (Flicker Prospective 299 0.58 (0.52, 0	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	

Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Flicker	Prospective	299	0.73 (0.66, 0.78)	0.71 (0.60, 0.80)	LR+	2.51 (1.78, 3.56)	V. serious	n/a	Not serious	Serious		VERY LOW
1997)	riospective	299	0.73 (0.00, 0.78)	0.71 (0.00, 0.00)	LR-	0.38 (0.30, 0.50)	V. serious	n/a	Not serious	Not serious		LOW

Notes on risk of bias

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

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

Studies PRIMARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
1 study (Flicker			0.00 (0.00 0.01)	0 -0 (0 10 0 00)	LR+	1.86 (1.47, 2.35)	V. serious	n/a	Not serious	Serious		VERY LOW
1997)	Prospective	299	0.88 (0.82, 0.91)	0.53 (0.42, 0.63)	LR-	0.24 (0.16, 0.35)	V. serious	n/a	Not serious	Not serious	-	LOW

Notes on risk of bias

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

P.2.1.29 Amyloid Beta 1-42 and total tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
1 study (Frisoni	Prophostivo	94	0.42 (0.31, 0.55) 0.79 (0.60,	0.70 (0.60, 0.00)	LR+	1.98 (0.92, 4.25)	Serious	n/a	Not serious	Serious		LOW
2009)		94	0.42 (0.31, 0.33)	0.79 (0.60, 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.

P.2.1.30 Applause sign (<3)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 atudu (Danalla 2040)	Description	075	0.54 (0.40, 0.67)	0.05 (0.00, 0.00)	LR+	3.64 (2.43, 5.45)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Bonello 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

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Beinhoff	Dragnactive	232	0.20 (0.29, 0.52)	0.03 (0.99, 0.06)	LR+	5.94 (3.12, 11.33)	Serious	n/a	Not serious	Not serious		MODERATE
2005) Prospec	Prospective	232	0.39 (0.28, 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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	(E											
1 study (Beinhoff	Prophostivo	222	0.55 (0.43, 0.66)	0.94 (0.77, 0.90)	LR+	3.35 (2.23, 5.05)	Serious	n/a	Not serious	Not serious		MODERATE
2005)	Prospective 232 0.55 (0.43, 0.66) 0	0.84 (0.77, 0.89)	LR-	0.54 (0.41, 0.71)	Serious	n/a	Not serious	Serious	-	LOW		

Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%Cl)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	E											
1 study (Beinhoff	Prophostivo	232	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)	0.63 (0.55, 0.70)	LR-	0.46 (0.31, 0.68)	Serious	n/a	Not serious	Serious	_	LOW

Notes on risk of bias

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P.2.1.34 Brief Neuropsychological Test Battery

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Coutinho 2012)	Propositivo	131	0.01 (0.70, 0.06)	0.92 (0.72 0.00)	LR+	5.43 (3.28, 8.99)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Coutinho 2013)	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

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

Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
RE											
Dragnostiva	222	0.96 (0.76, 0.03)	0.52 (0.45, 0.60)	LR+	1.81 (1.51, 2.19)	Serious	n/a	Not serious	Serious		LOW
Prospective	232	0.00 (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
	•	Design N	Design N (95%CI)	Design N (95%CI) (95 ⁵ %CI)	Design N (95%CI) (95%CI) Measure RE Prospective 232 0.86 (0.76, 0.93) 0.52 (0.45, 0.60)	Design N Sens (95%CI) Spec (95%CI) Measure Offindings (95%CI)	Design Total Sens Spec Measure Summary of findings (95%CI) ER	Total Sens Spec Measure Summary of findings 95%CI) RE	Total N Sens (95%CI) Spec (95%CI) Measure Summary of findings (95%CI) Serious Seri	Total N Sens (95%CI) Spec (95%CI) Measure Summary of findings (95%CI) Serious Seri	Total Sens (95%CI) Spec (95%CI) Measure Summary of findings (95%CI) Serious Seriou

Notes on risk of bias

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Beinhoff	Danamantinia	222	0.74 (0.50, 0.04)	0.00 (0.00 0.00)	LR+	5.91 (3.81, 9.17)	Serious	n/a	Not serious	Not serious		MODERATE
2005)	Prospective	232	0.71 (0.59, 0.81)	0.88 (0.82, 0.92)	LR-	0.33 (0.22, 0.48)	Serious	n/a	Not serious	Not serious	-	MODERATE

Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
2 studies (Beinhoff 2005;	1xprospectiv e 1x retrospectiv	734	0.55 (0.13, 0.91)	0.97 (0.94, 0.99)	LR+	15.66 (6.85, 35.82)	Serious	Not serio us	Not serious	Not serious	_	MODERATE
Milian 2012)	e e				LR-	0.41 (0.13, 1.28)	Serious	Serio us	Not serious	Serious		VERY LOW

Notes on risk of bias

Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other. Milian 2012: Unclear whether inappropriate exclusions were avoided; whether the patients were a random or consecutive sample and whether the reference standard result was interpreted without knowledge of the results of the index test.

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

Olock Blawing	, 1001, 001,	onann.	an occining in	otiloa (° o)									
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Berger	Dunamantina	400	0.00 (0.00 0.00)	0.50 (0.40, 0.05)	LR+	2.06 (1.69, 2.51)	Serious	n/a	Not serious	Serious		LOW	
2008)	Prospective	462	0.90 (0.86, 0.93)	0.56 (0.48, 0.65)	LR-	0.18 (0.12, 0.25)	Serious	n/a	Not serious	Not serious	-	MODERATE	
Notes on risk of bia	Notes on risk of bias												
Berger 2008: People	who received a fir	nal diagno	osis of FTD, DLB or	MCI were excluded	from the stu	dy.							

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

Olock Blawing I	oot, ob 1, 11	atoon v	sooning moune	a (* 1)								
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Pargar 2009)	Prophostivo	462	0.72 (0.67, 0.76)	0.64 (0.55, 0.72)	LR+	2.00 (1.57, 2.54)	Serious	n/a	Not serious	Serious		LOW
1 study (Berger 2008)	Prospective	402	0.72 (0.67, 0.76)	0.64 (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.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Parger 2009)	Prophostivo	462	0.59 (0.52, 0.62)	0.01 (0.74, 0.07)	LR+	3.10 (2.14, 4.49)	Serious	n/a	Not serious	Not serious		MODERATE
1 study (Berger 2008)	Prospective	402	0.58 (0.53, 0.63)	0.81 (0.74, 0.87)	LR-	0.52 (0.44, 0.60)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of bias Berger 2008: People wh	no received a fina	al diagno	sis of FTD, DLB or M	CI were excluded fro	m the study.							

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 abody (Carrar 2000)	Description	204	0.70 (0.00 0.77)	0.02 (0.74, 0.00)	LR+	4.10 (2.68, 6.28)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Sager 2006)	Prospective	364	0.72 (0.66, 0.77)	0.83 (0.74, 0.89)	LR-	0.34 (0.28, 0.42)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
4 -tudy (D	December	400	0.04 (0.77, 0.05)	0.00 (0.54, 0.00))	LR+	2.04 (1.64, 2.54)	Serious	n/a	Not serious	Serious		LOW	
1 study (Berger 2008)	Prospective	462	0.81 (0.77, 0.85)	0.60 (0.51, 0.68))	LR-	0.31 (0.24, 0.41)	Serious	n/a	Not serious	Not serious	-	MODERATE	
Notes on risk of bias Berger 2008: People wh	Notes on risk of bias Berger 2008: People who received a final diagnosis of FTD, DLB or MCI were excluded from the study												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Pargar 2009)	Propositivo	462	0.03 (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	
1 study (Berger 2008)	Prospective	402	0.93 (0.90, 0.95)	0.37 (0.29, 0.45)	LR-	0.19 (0.12, 0.30)	V. serious	n/a	Not serious	Not serious	-	LOW	
Notes on risk of bias Berger 2008: People wh	lotes on risk of bias lerger 2008: People who received a final diagnosis of FTD, DLB or MCI were excluded from the study and an optimised threshold was used.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 atudu (Damas 2000)	Duagnactive	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
1 study (Berger 2008)	Prospective	462	0.88 (0.84, 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			: (570.010. •	101								

Berger 2008: People who received a final diagnosis of FTD, DLB or MCI were excluded from the study.

P.2.1.45 CERAD battery

	,											
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	E.											
1 study	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

Notes on risk of bias

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

P.2.1.46 Computed Tomography, CT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (O'Prion 2000)	Proppostivo	116	0.54 (0.45, 0.64)	0.77 (0.49, 0.02)	LR+	2.36 (0.86, 6.46)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (O'Brien 2000)	Prospective	110	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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
PRIMARY CARE													
1 study (Cruz-Orduna 2012)	Propositivo	160	0.87 (0.59, 0.97)	0.82 (0.75, 0.87)	LR+	4.83 (3.24, 7.22)	Serious	n/a	Not serious	Not serious		MODERATE	
1 Study (Gruz-Orduna 2012)	Prospective	100	0.67 (0.59, 0.97)	0.62 (0.75, 0.67)	LR-	0.16 (0.04, 0.59)	Serious	n/a	Not serious	Serious	_	LOW	
Notes on risk of bias Cruz-Orduna 2012: Threshold	Notes on risk of bias Cruz-Orduna 2012: Thresholds were not pre-specified but were calculated to give optimum sensitivity and specificity.												

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P.2.1.48 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	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
Frisoni 2009: Silverman	prospective	386	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.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 at refer (Marrier and 2042)	Dunamantina	4.45	0.70 (0.00, 0.05)	0.00 (0.70, 0.00)	LR+	7.66 (3.31, 17.69)	V. serious	n/a	Not serious	Not serious		LOW
1 study (Mormont 2012)	Prospective	145	0.78 (0.69, 0.85)	0.90 (0.78, 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% popula	tion at an	alysis and use of opt	imised test threshold	S.							

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Garcia	2 ×	436	0.03 (0.00, 0.06)	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, 0.96)	0.65 (0.27, 0.91)	LR-	0.12 (0.07, 0.18)	Serious	Not serious	Not serious	Not serious	-	MODERATE

Notes on risk of bias

Garcia 2002: Inappropriate exclusions at patient selection stage.

Knaefelc 2003: Unclear whether all patients were included in the analysis; unclear interval between index and reference tests; lack of a pre-specified threshold.

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

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

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE	E											
2 studies (Flicker 1997; Hancock	2 ×	443	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	443	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.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Cruz-Orduna	Dusanastiva	100	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) Prospec	Prospective	160	0.93)	0.83)	LR-	0.26 (0.09, 0.72)	Serious	n/a	Not serious	Serious		LOW
SECONDARY CARE												
4 ahudu (Fliakaa 4007)	Dusanastiva	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
1 study (Flicker 1997)	Prospective	299	0.86)	0.71)	LR-	0.30 (0.22, 0.42)	V. serious	n/a	Not serious	Not serious		LOW
ALL EVIDENCE POOLED \	V. serious											
2 studies (Cruz-Orduna	2x	459	0.81 (0.76,	0.70 (0.53,	LR+	2.63 (1.65, 4.20)	V. serious	Serious	Not serious	Serious		VERY LOW
	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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY C	ARE											
1 study (Flicker	Prospostivo	200	0.78 (0.72, 0.83)	0.65 (0.54, 0.75)	LR+	2.23 (1.65, 3.01)	V. serious	n/a	Not serious	Serious		VERY LOW
1997)		0.76 (0.72, 0.63)	0.65 (0.54, 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.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY C	ARE											
1 study (Flicker	Prospective	299	0.75 (0.68, 0.80)	0.71 (0.60, 0.80)	LR+	2.58 (1.82, 3.64)	V. serious	n/a	Not serious	Serious		VERY LOW
1997)	Fiospective	299	0.73 (0.08, 0.80)	0.71 (0.00, 0.00)	LR-	0.36 (0.27, 0.47)	V. serious	n/a	Not serious	Not serious		LOW

Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
1 study (Flicker	Description	200	0.70 (0.04, 0.70)	0.75 (0.04, 0.02)	LR+	2.78 (1.90, 4.07)	V. serious	n/a	Not serious	Serious		VERY LOW
1997)	Prospective	299	0.70 (0.64, 0.76)	0.75 (0.64, 0.83)	LR-	0.40 (0.31, 0.50)	V. serious	n/a	Not serious	Serious	-	VERY LOW

Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY C	ARE											
1 study (Flicker	Prognactiva	200	0.65 (0.58, 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)	Flospective		0.05 (0.56, 0.71)	0.80 (0.69, 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.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
1 study (Flicker	Prospective	299	0.59 (0.52, 0.65)	0.83 (0.74, 0.90)	LR+	3.46 (2.12, 5.65)	V. serious	n/a	Not serious	Not serious		LOW
1997)	riospective	299	0.58 (0.52, 0.65)	0.63 (0.74, 0.90)	LR-	0.50 (0.42, 0.60)	V. serious	n/a	Not serious	Serious		VERY LOW

Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Beinhoff	Prospective	232	0.12 (0.06, 0.22)	0.00 (0.05, 1.00)	LR+	10.06 (2.19, 46.14)	Serious	n/a	Not serious	Not serious		MODERATE
2005)	Prospective	232	0.12 (0.06, 0.22)	0.99 (0.95, 1.00)	LR-	0.89 (0.81, 0.97)	Serious	n/a	Not serious	Not serious	-	MODERATE

Notes on risk of bias

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAL	RE											
1 study (Beinhoff	Dunamantika	000	0.44 (0.22, 0.50)	0.03 (0.00, 0.00)	LR+	6.08 (3.30, 11.18)	Serious	n/a	Not serious	Not serious		MODERATE
2005)	Prospective	232	0.44 (0.33, 0.56)	0.93 (0.88, 0.96)	LR-	0.60 (0.49, 0.75)	Serious	n/a	Not serious	Serious	-	LOW

Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Beinhoff	Dunamantiva	222	0.00 (0.00 0.00)	0.00 (0.04, 0.75)	LR+	2.56 (1.99, 3.31)	Serious	n/a	Not serious	Serious		LOW
2005)	Prospective	232	0.80 (0.69, 0.88)	0.69 (0.61, 0.75)	LR-	0.29 (0.17, 0.47)	Serious	n/a	Not serious	Not serious	_	MODERATE

Notes on risk of bias

P.2.1.62 Mini-ACE (<26)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Larger 2017)	Dragnostiva	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
1 study (Larner 2017)	Prospective	200	0.98 (0.85, 1.00)	0.35 (0.29, 0.42)	LR-	0.07 (0.01, 0.46)	Not serious	n/a	Not serious	Not serious	-	HIGH

P.2.1.63 Mini-Cog (≤2)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnera Darde 2012)	Dragnactive	142	0.00 (0.96, 1.00)	0.40 (0.34, 0.50)	LR+	1.65 (1.39, 1.95)	Serious	n/a	Not serious	Not serious		MODERATE
1 study (Carnero-Pardo 2013)	Prospective	142	0.99 (0.86, 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 the	hreshold was no	ot pre-sp	ecified, but was opti	mised based on the	data obtaine	ed.						

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

Studies SECONDARY O	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
1 study (Milian		500	0.07 (0.02.0.00)	0.00 (0.00 4.00)	LR+	112.68 (7.12, 1782.71)	Serious	n/a	Not serious	Not serious		MODERATE
2012)	Retrospective	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 bias

Milian 2012: Unclear whether inappropriate exclusions were avoided; whether the patients were a random or consecutive sample and whether the reference standard result was interpreted without knowledge of the results of the index test.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
4 study (Company Davids 2011)	Description	447	0.00 (0.77, 0.00)	0.00 (0.74, 0.07)	LR+	4.78 (3.09, 7.39)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Carnero-Pardo 2011)	Prospective	117	0.93 (0.77, 0.98)	0.80 (0.71, 0.87)	LR-	0.08 (0.02, 0.32)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies	Design	Tota I N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnero-	Description	447	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)	Prospective	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	Description	000	0.82 (0.71,	0.81 (0.75,	LR+	4.38 (3.13, 6.14)	Serious	n/a	Not serious	Not serious		MODERATE
2005)	Prospective	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 ×	240	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)	rnero-Pardo prospective 349	349	0.98)	0.85)	LR-	0.14 (0.03, 0.57)	Serious	Serious	Not serious	Serious	-	VERY LOW

Notes on risk of bias

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Beinhoff	Danamantika	222	0.00 (0.70, 0.04)	0.70 (0.62, 0.76)	LR+	2.92 (2.28, 3.74)	Serious	n/a	Not serious	Not serious		MODERATE
2005)	Prospective	232	0.88 (0.78, 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 bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Beinhoff	Prospective	232	0.02 (0.02.0.07)	0.62 (0.45, 0.60)	LR+	1.97 (1.65, 2.34)	Serious	n/a	Not serious	Serious		LOW
2005)	Prospective	232	0.92 (0.83, 0.97)	0.53 (0.45, 0.60)	LR-	0.14 (0.06, 0.34)	Serious	n/a	Not serious	Not serious	-	MODERATE

Notes on risk of bias

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

Studies SECONDARY CAR	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	(E											
1 study (Beinhoff	Prophostivo	222	0.98 (0.90, 1.00)	0.22 (0.25, 0.20)	LR+	1.45 (1.30, 1.61)	Serious	n/a	Not serious	Not serious		MODERATE
2005)		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 bias

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

P.2.1.70 MMSE (<17)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carpara Darda 2012)	Dragnastiva	260	0.70 (0.50, 0.70)	0.03 (0.90, 0.05)	LR+	9.92 (6.35, 15.52)	Serious	n/a	Not serious	Not serious		MODERATE
1 study (Carnero-Pardo 2013)	Prospective	360	0.70 (0.59, 0.79)	0.93 (0.89, 0.95)	LR-	0.32 (0.23, 0.45)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of bias Carnero-Pardo 2013: Multiple to												

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MMSE (<18) P.2.1.71

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE	PRIMARY CARE											
4 4 4 40 0 4 0040	Prospective	360	0.81 (0.70, 0.88)	0.92 (0.88, 0.95)	LR+	9.91 (6.60, 14.88)	Serious	n/a	Not serious	Not serious		MODERAT E
1 study (Cruz-Orduna 2012)					LR-	0.21 (0.13, 0.33)	Serious	n/a	Not serious	Not serious	-	MODERAT E
SECONDARY CARE												
			9 0.50, 0.43, 0.57)	0.90 (0.82, 0.95)	LR+	5.19 (2.65, 10.16)	V. serious	n/a	Not serious	Not serious		LOW
1 study (Flicker 1997)	Prospective	299			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	0.50	0.67 (0.33,	0.92 (0.88,	LR+	7.59 (4.07, 14.17)	V. serious	Serious	Not serious	Not serious		VERY LOW
2012; Flicker 1997)	prospective	659	0.89)	0.94)	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

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P.2.1.72 MMSE (<19)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE	PRIMARY CARE											
2 studies (Carnero-Pardo	2x	500	520 0.87 (0.78, 0.92) 0.87 (0.83, 0.90)	0.87 (0.83,	LR+		Serious		Not serious	Not serious		MODERAT E
2013, Cruz-Orduna 2012)	prospective	520		Not serious	Not serious	-	MODERAT E					
SECONDARY CARE												
		299	0.56 (0.49,	0.97 (0.78, 0.93)	LR+	4.19 (2.39, 7.36)	V. serious	n/a	Not serious	Not serious		LOW
1 study (Flicker 1997)	Prospective		9 0.62)		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	242	0.76 (0.46,	0.87 (0.83,	LR+	5.95 (4.64, 7.62)	Serious	Not serious	Not serious	Not serious		MODERAT E
2013; Cruz-Orduna 2012; Flicker 1997)	prospective	819	0.93)	0.89)	LR-	0.26 (0.10, 0.70)	V. serious	Serious	Not serious	Serious	- L	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

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P.2.1.73 MMSE (<20)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnero-Pardo	Prospective	360	0.94 (0.85, 0.97)	0.82 (0.77, 0.86)	LR+	5.19 (4.02, 6.70)	Serious	n/a	Not serious	Not serious		MODERAT E
2013)					LR-	0.08 (0.03, 0.19)	Serious	n/a	Not serious	Not serious	-	MODERAT E
SECONDARY CARE												
4 ahudu (Fliakaa 1007)			0.62 (0.55,	0.84 (0.75, 0.91)	LR+	3.96 (2.38, 6.60)	V. serious	n/a	Not serious	Not serious		LOW
1 study (Flicker 1997)	Prospective	299	0.68)		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	050	0.82 (0.36,	0.82 (0.78,	LR+	4.92 (3.91, 6.18)	Serious	Not serious	Not serious	Not serious		MODERAT E
2013; Flicker 1997)	prospective	659	0.98)	0.86)	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

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P.2.1.74 MMSE (<21)

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

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P.2.1.75 MMSE (<22)

Studies PRIMARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
	Prospectiv		0.96 (0.89,	0.67 (0.61,	LR+	2.92 (2.46, 3.48)	Serious	n/a	Not serious	Not serious		MODERA TE
1 study (Carnero-Pardo 2013)	е	360	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; Carnero-Pardo 2013; Flicker	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	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

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P.2.1.76 MMSE (<23)

Studies	Design	Tot al N	Sens (95%CI)	Spec (95%CI)	Meas ure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
4 study (Corners Dords 2042)	1 ×	360	0.99 (0.91,	0.57 (0.51,	LR+	2.29 (2.00, 2.62)	Serious	n/a	Not serious	Serious		LOW
1 study (Carnero-Pardo 2013)	prospect 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)	prospect 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)	prospect 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.

P.2.1.77 MMSE (<24)

Studies PRIMARY CARE	Design	Tot al N	Sens (95%CI)	Spec (95%CI)	Meas ure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
4 shirth: (Correcte Double 2042)	Prospecti	200	0.99 (0.91,	0.46 (0.40,	LR+	1.84 (1.65 2.05)	Seriou s	n/a	Not serious	Serious		LOW
1 study (Carnero-Pardo 2013)	ve	360	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 ×	2,9	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;	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
Kukull 1994; Mathuranath 2000; Nielsen 2013; Postel-Vinay 2014; Sager 2006)	prospecti ve	5	0.84)	0.94)	LR-	0.29 (0.20, 0.38)	Seriou s	Serious	Not serious	Not serious	-	LOW

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Dementia

Appendix P: Diagnosis evidence tables & GRADE

		Tot al	Sens	Spec	Meas	Summary of findings	sk of bias	consistency	directness	precision	her nsiderations	
Studies	Design	N	(95%CI)	(95%CI)	ure	(95%CI)	Risk	lıc	밀	Ξ	₹ Ö Qual	ity

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

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P.2.1.78 MMSE (<25)

Studies PRIMARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measu re	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMART CARE												
1 study (Carnero-Pardo 2013)	1 × prospectiv	360	0.99 (0.91,	0.38 (0.33,	LR+	1.61 (1.46, 1.76)	Serious	n/a	Not serious	Not serious		MODER ATE
1 Study (Camero-Fardo 2013)	e	300	1.00)	0.44)	LR-	0.02 (0.00, 0.27)	Serious	n/a	Not serious	Serious	-	MODER ATE
SECONDARY CARE												
7 studies (Callahan 2002; Flicker 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	0.82 (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				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	0.85 (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

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Dementia

Appendix P: Diagnosis evidence tables & GRADE

Q4Viv.	D	Total	Sens	Spec	Measu	Summary of findings	Risk of bias	consistency	directness	ıprecision	ther onsiderations	0114
Studies	Design	N	(95%CI)	(95%CI)	re	(95%CI)	ë	Ĕ	<u>≅</u>	<u>=</u>	5 8	Quality

Notes on risk of bias

Kukull 1994: It is unclear whether the index test results were interpreted without knowledge of the results of the reference standard; multiple pre-specified cut-offs were used to determine the optimal cut-off; the index test result was known during the reference standard diagnosis.

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

Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.

Milian 2012: Unclear whether inappropriate exclusions were avoided; whether the patients were a random or consecutive sample and whether the reference standard result was interpreted without knowledge of the results of the index test.

Carnero-Pardo 2013: Multiple test thresholds were used

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

Yeung 2014: Unclear whether patients were selected randomly or consecutively or whether inappropriate exclusions were avoided; the optimal index test thresholds were determined during the study; it is unclear whether the index test results and reference test results were assessed independently of each other: subgroup analysis was carried out with >10% population (MCI) being excluded.

P.2.1.79 MMSE (<26)

11111102 (120)												
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE		•					·	·	·	·		
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
Flicker 1997; Milian 2012; Nielsen 2013)	1 × retrospective	1,583	0.91)	0.78 (0.53, 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.

P.2.1.80 MMSE (<27)

		Total	Sens	Spec	Measur	Summary of findings	Risk of bias	consistency	Indirectness	Imprecision	Other considerations	
Studies	Design	N	(95%CI)	(95%CI)	е	(95%CI)	ĕ	Ĕ	Ĕ	트	2 8	Quality
SECONDARY CARE												
4 studies (Bastide 2012; Callahan 2002; Mathuranath 2000; Nielsen	4 ×	1,241	0.86 (0.73,	0.75 (0.66,	LR+	3.43 (2.43, 4.85)	Serious	Serious	Not serious	Not serious		LOW
2013)	prospective	1,241	0.94)	0.82)	LR-	0.17 (0.09, 0.33)	Serious	Serious	Not serious	Not serious	-	LOW

Notes on risk of bias

Mathuranath 2000: Optimised test-threshold used and it was unclear whether the index test results were interpreted without knowledge of the results of the reference standard.

Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.

Bastide 2012: Optimised test cut-offs used.

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

P.2.1.81 MMSE (<28)

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDART CARE					m1							
2 studies (Callahan	2 ×	796	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	790	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.

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

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY C	ARE											
1 study (Yeung	Prognostivo	272	1.00 (0.04, 1.00)	0.27 (0.20, 0.45)	LR+	1.57 (1.39, 1.78)	Serious	n/a	Not serious	Not serious		MODERATE
2014)	Prospective	212	1.00 (0.94, 1.00)	0.37 (0.29, 0.45)	LR-	0.01 (0.00, 0.17)	Serious	n/a	Not serious	Not serious	-	MODERATE

Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 atualy (Calabatain 2044)	Dunamantiva	04	0.00 (0.70, 0.00)	0.24 (0.24, 0.45)	LR+	1.41 (1.16, 1.71)	Not serious	n/a	Serious	Not serious		MODERATE
1 study (Goldstein 2014)	Prospective	81	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.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Coldatain 2014)	Dragnostiva	81	0.09 (0.77, 1.00)	0.22 (0.14, 0.26)	LR+	1.27 (1.09, 1.48)	Not serious	n/a	Serious	Not serious		MODERATE	
1 study (Goldstein 2014)	Prospective	01	0.98 (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	Notes on indirectness Goldstein 2014: Study only recruited African Americans ≥ 50 years old.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Larger 2017)	Dragnostiva	260	0.00 (0.94, 1.00)	0.24 (0.25, 0.27)	LR+	1.43 (1.30, 1.57)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Larner 2017)	Prospective	260	0.99 (0.84, 1.00)	0) 0.31 (0.25, 0.37)	LR-	0.04 (0.00, 0.58)	Not serious	n/a	Not serious	Serious	-	MODERATE

P.2.1.87 MRI

IVIIXI							1					
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
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
	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.

P.2.1.88 Orientation, OR (<7)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAI	RE											
1 study (Beinhoff	Prospective	232	0.30 (0.39, 0.53)	0.00 (0.05, 1.00)	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 bias

P.2.1.89 Orientation, OR (<8)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAL	RE											
1 study (Beinhoff	Droopostivo	222	0.65 (0.53, 0.76)	0.00 (0.95, 0.04)	LR+	6.76 (4.11, 11.12)	Serious	n/a	Not serious	Not serious		MODERATE
2005)	Prospective	232	0.65 (0.53, 0.76)	0.90 (0.85, 0.94)	LR-	0.39 (0.28, 0.54)	Serious	n/a	Not serious	Serious	-	LOW

Notes on risk of bias

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

P.2.1.90 Palmo-Mental Reflex

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 at . d (Ctrait 2045)	Detresensetive	454	0.44 (0.04, 0.05)	0.00 (0.74, 0.07)	LR+	2.26 (1.16, 4.41)	Serious	n/a	Not serious	Serious		LOW
1 study (Streit 2015)	Retrospective	154	0.41 (0.21, 0.65)	0.82 (0.74, 0.87)	LR-	0.72 (0.48, 1.08)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of bias												

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

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

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDART CARE												
1 study (Streit 2015)	Potrospoctivo	154	0.71 (0.46, 0.87)	0.64 (0.55, 0.71)	LR+	1.93 (1.33, 2.82)	Serious	n/a	Not serious	Serious		LOW
1 Study (Strell 2015)	(Streit 2015) Retrospective 154 0.71 (0.46, 0.87) 0.64	0.04 (0.05, 0.71)	LR-	0.46 (0.22, 0.98)	Serious	n/a	Not serious	Serious	_	LOW		
Notes on risk of bias												

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Strait 2015)	Potroppostivo	154	0.24 (0.00, 0.40)	0.02 (0.00 0.07)	LR+	3.58 (1.24, 10.38)	Serious	n/a	Not serious	Serious		LOW
1 study (Streit 2015)	Retrospective	154	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.

P.2.1.93 Phototest (<27)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
4 atualis (Campana Danda 2014)	Dunanastiva	110	0.04 (0.00, 0.00)	0.00 (0.04, 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	0.81 (0.68, 0.90)	0.89 (0.81, 0.94)	LR-	0.21 (0.12, 0.38)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
ARE											
5 "	00.4	0.00 (0.50, 0.70)	0.00 (0.70, 0.00)	LR+	6.84 (2.95, 15.87)	Serious	n/a	Not serious	Not serious		MODERATE
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
	Design CARE Prospective	Design N	Design N (95%CI)	Design N (95%CI) (95%CI)	Design N (95%CI) (95%CI) Measure CARE Prospective 204 0.66 (0.58, 0.73) 0.90 (0.79, 0.96)	Design Total Sens Spec Measure Offindings (95%CI) CARE Prospective 204 0.66 (0.58, 0.73) 0.90 (0.79, 0.96) LR+ 6.84 (2.95, 15.87)	Design Total Sens (95%CI) Spec (95%CI) Measure Summary of findings (95%CI) Serious	Design Total Sens Spec Measure Summary of findings (95%CI) Serious N/a	Design Total Sens Spec Measure Summary of findings (95%CI) Design Total Sens (95%CI) Measure Summary of findings (95%CI) Design Total Sens Sens (95%CI) Design Total Sens Design Total Sens Spec Measure Summary of findings (95%CI) Serious Not serious Not serious Not serious Serious Not s	Total Sens (95%CI) Spec (95%CI) Measure Summary of findings (95%CI) Serious Seriou	

Notes on risk of bias

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

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

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Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
1 study	Drooppotivo	127	0.40 (0.37, 0.60)	0.01 (0.91.0.06)	LR+	5.27 (2.37, 11.70)	V. serious	n/a	Not serious	Not serious		LOW
(Nielsen 2013)	Prospective	137	0.49 (0.37, 0.60)	0.91 (0.81, 0.96)	LR-	0.57 (0.45, 0.72)	V. serious	n/a	Not serious	Serious	-	VERY LOW

Notes on risk of bias

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

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

Studies SECONDARY CA	D esign ARE	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
1 study (Nielsen	Dan and the	407	0.04 (0.50, 0.74)	0.00 (0.70, 0.00)	LR+	3.78 (2.14, 6.65)	V. serious	n/a	Not serious	Not serious		LOW
2013)	Prospective	137	0.64 (0.52, 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.

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

Studies SECONDARY CA	Design ARE	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
1 study (Nielsen	5 "	407	0.00 (0.50, 0.70)	0.00 (0.00 0.00)	LR+	3.47 (2.09, 5.78)	V. serious	n/a	Not serious	Not serious		LOW
2013)	Prospective	137	0.69 (0.58, 0.79)	0.80 (0.69, 0.88)	LR-	0.38 (0.26, 0.55)	V. serious	n/a	Not serious	Serious	-	VERY LOW

Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
1 study (Nielsen	Dragnostiva	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)		137	0.76 (0.65, 0.85)	0.66 (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.

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

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Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA												
1 study (Nielsen	Dragnastivo	127	0.92 (0.74, 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)		137	0.82 (0.71, 0.89)	0.65 (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.

P.2.1.100 Seven Minute Screen (P>0.6)

					1	1	1					
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Chiana 2000)	Dragnostiva	95	0.72 (0.64, 0.92)	0.65 (0.46, 0.94)	LR+	2.09 (1.21, 3.62)	Serious	n/a	Not serious	Serious		LOW
1 study (Skjerve 2008)	Prospective	95	0.72 (0.61, 0.82)	0.65 (0.46, 0.81)	LR-	0.42 (0.26, 0.68)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of bias												

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

P.2.1.101 Seven Minute Screen (P>0.7)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skionyo 2009)	Prophostivo	95	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
1 study (Skjerve 2008)	erve 2008) Prospective	90	0.72 (0.01, 0.02)	0.69 (0.49, 0.84)	LR-	0.40 (0.25, 0.63)	Not serious	n/a	Not serious	Serious	-	MODERATE

P.2.1.102 Seven Minute Screen (P>0.8)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 atualy (Okiamia 2000)	Dragonostica	05	0.74 (0.50, 0.00)	0.72 (0.52 0.07)	LR+	2.64 (1.38, 5.06)	Serious	n/a	Not serious	Serious		LOW
1 study (Skjerve 2008)	Prospective	95	0.71 (0.59, 0.80)	0.73 (0.53, 0.87)	LR-	0.40 (0.26, 0.61)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of bias Skjerve 2008: Use of an a	Iternative thresho	old to the	standard one and that	t was not pre-specifie	d.							

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P.2.1.103 Short smell test

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 -tt- (Otit 0045)	Determention	454	0.50 (0.00, 0.74)	0.75 (0.07.0.00)	LR+	2.13 (1.25, 3.64)	Serious	n/a	Serious	Serious		VERY LOW
1 study (Streit 2015)	Retrospective	154	0.53 (0.30, 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.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Malhotra	Droopostivo	107	0.70 (0.70, 0.96)	0.75 (0.54, 0.88)	LR+	3.15 (1.56, 6.34)	V. serious	n/a	Not serious	Serious		VERY LOW
2013)	Prospective	otive 127 0.79 (0.70, 0.86	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 bias

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

Notes on indirectness

Malhotra 2013: Participants had ≥ 6 years education

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 -to-to-(84-16-to-0040)	December	407	0.70 (0.00, 0.05)	0.75 (0.54, 0.00)	LR+	3.11 (1.54, 6.26)	Serious	n/a	Serious	Serious		VERY LOW
1 study (Malhotra 2013)	Prospective 127 0.78 (0.69, 0.85	0.78 (0.69, 0.85)	0.75 (0.54, 0.88)	LR-	0.30 (0.19, 0.46)	Serious	n/a	Serious	Not serious	-	LOW	

Notes on risk of bias

Malhotra 2013: It was unclear whether the study avoided inappropriate exclusions and optimised test cut-offs were used.

Notes on indirectness

Malhotra 2013: 60% participants had < 6 years education

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Malhotra	Dragnactiva	107	0.72 (0.62, 0.90)	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, 0.80)	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 bias

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

Notes on indirectness

Malhotra 2013: Participants had < 6 years education

P.2.1.107 Syndrom Kurztest (≥7)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skionyo 2009)	Prospective	95	0.71 (0.59, 0.80)	0.54 (0.35, 0.72)	LR+	1.54 (0.99, 2.39)	Serious	n/a	Not serious	Serious		LOW
1 study (Skjerve 2008)	Fiospective	90	0.71 (0.59, 0.60)	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 Skierve 2008: Use of an a	alternative thresh	old to the	standard one and tha	t was not pre-specifie	d.							

P.2.1.108 Syndrom Kurztest (≥8)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Chianya 2009)	Droopostivo	0.E	0.65 (0.53, 0.75)	0.65 (0.46, 0.94)	LR+	1.88 (1.08, 3.28)	Serious	n/a	Not serious	Serious		LOW
1 study (Skjerve 2008)	Prospective	95	0.65 (0.53, 0.75)	0.65 (0.46, 0.81)	LR-	0.53 (0.35, 0.82)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of bias Skjerve 2008: Use of an a	alternative thresh	old to the	standard one and tha	t was not pre-specifie	d.							

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P.2.1.109 Syndrom Kurztest (≥9)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Chiana 2000)	Droopoetivo	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
1 study (Skjerve 2008)	Prospective	95	0.58 (0.46, 0.69)	0.69 (0.49, 0.84)	LR-	0.61 (0.42, 0.89)	Not serious	n/a	Not serious	Serious	-	MODERATE

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Marmont 2012)	Dragnostiva	145	0.04 (0.70, 0.00)	0.00 (0.79, 0.06)	LR+	7.96 (3.45, 18.37)	V. serious	n/a	Not serious	Not serious		LOW
1 study (Mormont 2012)	Prospective	145	0.81 (0.72, 0.88)	0.90 (0.78, 0.96)	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	of >35% popula	tion at an	alysis and use of opt	imised test threshold	S.							

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 atrialis (Marranant 2042)	Description	4.45	0.75 (0.05, 0.00)	0.00 (0.05, 0.00)	LR+	18.38 (4.71, 71.75)	V. serious	n/a	Not serious	Not serious		LOW
1 study (Mormont 2012)	Prospective	145	0.75 (0.65, 0.83)	0.96 (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 Mormont 2012: Exclusion	of >35% popula	tion at ar	nalysis and use of op	timised test threshold	ds.							

P.2.1.112 Test Your Memory, TYM (≤30)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 -4	December	004	0.70 (0.00, 0.00)	0.00 (0.04, 0.00)	LR+	5.93 (3.77, 9.32)	Serious	n/a	Not serious	Not serious		MODERATE
1 study (Hancock 2011)	Prospective	224	0.73 (0.62, 0.82)	0.88 (0.81, 0.92)	LR-	0.31 (0.21, 0.44)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of bias Hancock 2011: Optimised	test threshold.											

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P.2.1.113 Test Your Memory, TYM (≤42)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 abody (Hanasak 2044)	December	004	0.05 (0.07, 0.00)	0.45 (0.07, 0.50)	LR+	1.73 (1.48, 2.02)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Hancock 2011)	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

P.2.1.114 Test Your Memory (≤39)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Postel-Vinay 2014)	Prospective	201	0.90 (0.80, 0.95)	0.70 (0.62, 0.77)	LR+	2.98 (2.27, 3.91)	Serious	n/a	Not serious	Not serious	_	MODERATE
1 Study (1 Oster-Villay 2014)	1 Tospective	201	0.90 (0.00, 0.93)	0.70 (0.02, 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 use	ed; the st	tudy was not downgr	aded for exclusions	as <10% po _l	oulation was exclude	ed					

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4	Dunamantina	204	0.05 (0.00, 0.00)	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)	Prospective	364	0.85 (0.80, 0.89)	0) 0.60 (0.50, 0.69)	LR-	0.25 (0.18, 0.35)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
RE											
Dragnostiva	222	0.05 (0.74, 0.02)	0.62 (0.56, 0.70)	LR+	2.31 (1.85, 2.89)	Serious	n/a	Not serious	Serious		LOW
Prospective	232	0.05 (0.74, 0.92)	0.03 (0.36, 0.70)	LR-	0.24 (0.13, 0.43)	Serious	n/a	Not serious	Not serious	-	MODERATE
	•	Design N	Design N (95%CI)	Design N (95%CI) (95 ['] %CI)	Design N (95%CI) (95%CI) Measure RE Prospective 232 0.85 (0.74, 0.92) 0.63 (0.56, 0.70) LR+	Design N Sens (95%CI) Spec (95%CI) Measure Offindings (95%CI)	Design Total Sens Spec Measure Summary of findings 95%CI) Prospective 232 0.85 (0.74, 0.92) 0.63 (0.56, 0.70) LR+ 2.31 (1.85, 2.89) Serious	Total Sens Spec Measure Summary of findings 95%CI) ER+ 2.31 (1.85, 2.89) Serious n/a	Total N Sens (95%CI) Spec (95%CI) Measure Summary of findings (95%CI) Serious Seri	Total N Sens (95%CI) Spec (95%CI) Measure Summary of findings (95%CI) Serious Seri	Total Sens (95%CI) Spec (95%CI) Measure Summary of findings (95%CI) Serious Seriou

Notes on risk of bias

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

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Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Beinhoff	Dragnostivo	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)	Prospective 232 0.94 (0.85, 0.98)	0.58 (0.50, 0.65)	LR-	0.10 (0.04, 0.27)	Serious	n/a	Not serious	Not serious	-	MODERATE		

Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAP	RE											
1 study (Beinhoff	Prognostivo	232	0.04 (0.95, 0.09)	0.52 (0.45, 0.60)	LR+	1.97 (1.66, 2.34)	Serious	n/a	Not serious	Serious		LOW
2005)	Prospective	232	0.94 (0.85, 0.98)	0.52 (0.45, 0.60)	LR-	0.12 (0.04, 0.30)	Serious	n/a	Not serious	Not serious	-	MODERATE

Notes on risk of bias

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

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Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Beinhoff	Dragnostivo	222	0.05 (0.97, 0.00)	0.46 (0.39, 0.53)	LR+	1.76 (1.52, 2.04)	Serious	n/a	Not serious	Serious		LOW
2005)		0.46 (0.38, 0.53)	LR-	0.10 (0.03, 0.30)	Serious	n/a	Not serious	Not serious	-	MODERATE		

Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Beinhoff	Prophostivo	232	0.97 (0.89, 0.99)	0.20 (0.21, 0.46)	LR+	1.58 (1.39, 1.79)	Serious	n/a	Not serious	Not serious		MODERATE
005) Prospective 23	232	0.97 (0.69, 0.99)	0.39 (0.31, 0.46)	LR-	0.08 (0.02, 0.31)	Serious	n/a	Not serious	Not serious	-	MODERATE	

Notes on risk of bias

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

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Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Beinhoff	Prospective	rospective 232 0.98 (0.90, 1.0	0.09 (0.00, 1.00)	0.24 (0.24, 0.29)	LR+	1.42 (1.28, 1.58)	Serious	n/a	Not serious	Not serious		MODERATE
2005)	Prospective	232	0.98 (0.90, 1.00)	0.31 (0.24, 0.38)	LR-	0.05 (0.01, 0.35)	Serious	n/a	Not serious	Not serious	-	MODERATE

Notes on risk of bias

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

P.2.2 AD versus DLB

P.2.2.1 Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
Latudy (Androgon 2001)	Droopoetiyo	170	0.65 (0.57, 0.72)	0.67 (0.22, 0.90)	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

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P.2.2.2 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Prospective	70	0.58 (0.46, 0.70)	0.20 (0.03, 0.69)	LR+	0.73 (0.45, 1.19)	V. serious	n/a	Serious	Serious	_	VERY LOW
	Frospective	70	0.30 (0.40, 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.

P.2.2.3 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Prognactive	270	0.29 (0.24, 0.35)	0.72 (0.59, 0.92)	LR+	1.05 (0.64, 1.75)	Serious	n/a	Not serious	Not serious		MODERATE
Koikkalainen 2016)	Prospective	210	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.

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P.2.3 AD versus FTD

P.2.3.1 99mTc-HMPAO SPECT

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

Notes on risk of bias

Launes 1991: Subgroup analysis used with >10% study population excluded.

Velakoulis 1997: Subgroup analysis where >10% study population excluded and it was unclear whether: the index test results were interpreted without knowledge of the results of the reference standard; the index test threshold was pre-specified or the reference standard results interpreted without knowledge of the results of the index test.

Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded

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P.2.3.2 Amyloid Beta 1-42 and Total Tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	nconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE			. ,	. ,		· , ,						
4 atudu (Talada 2042)	Detuces estive	100	0.00 (0.04, 0.05)	0.03 (0.05, 0.03)	LR+	5.23 (2.35, 11.65)	Serious	n/a	Not serious	Not serious		MODERATE
1 study (Toledo 2012)	Retrospective	100	0.90 (0.81, 0.95)	0.83 (0.65, 0.93)	LR-	0.12 (0.06, 0.25)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of bias												

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

P.2.3.3 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Prospective	83	0.58 (0.46, 0.70)	0.78 (0.54, 0.91)	LR+	2.63 (1.08, 6.39)	V. serious	n/a	Serious	Serious		VERY LOW
(Ossenkoppele 2013)	Flospective	03	0.38 (0.40, 0.70)	0.76 (0.34, 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.

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P.2.3.4 MRI

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Droopootivo	315	0.29 (0.24, 0.35)	0.77 (0.69, 0.95)	LR+	1.28 (0.83, 1.96)	Serious	n/a	Not serious	Not serious		MODERATE
Koikkalainen 2016)	Prospective	313	0.29 (0.24, 0.33)	0.77 (0.68, 0.85)	LR-	0.92 (0.80, 1.06)	Serious	n/a	Not serious	Not serious	-	MODERATE

Notes on risk of bias

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

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P 100												
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 -tudy (Talada 2042)	Detreserentive	100	0.00 (0.00 4.00)	0.05 (0.00, 0.04)	LR+	6.62 (2.82, 15.52)	Serious	n/a	Not serious	Not serious		MODERATE
1 study (Toledo 2012)	Retrospective	100	0.99 (0.90, 1.00)	0.85 (0.68, 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

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P.2.4 AD versus no dementia

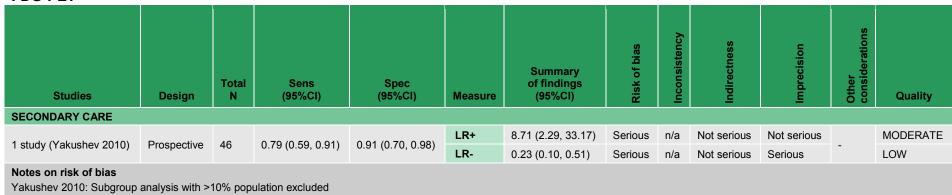
P.2.4.1 Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE	E											
1 study	Dragnostiva	70	0.94 (0.72, 0.02)	0.94 (0.64, 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.

P.2.4.2 FDG-PET



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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Marmont 2012)	Dragnostiva	110	0.94 (0.70, 0.90)	0.00 (0.96, 1.00)	LR+	81.45 (5.15, 1287.53)	V. serious	n/a	Not serious	Not serious		LOW
1 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% popula	ation at a	nalysis and use of o	otimised test thresho	lds.							

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

Studies SECONDARY CA	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDART CA	AKE											
1 study (Sikkes	Droopoetivo	260	0.06 (0.02, 0.08)	0.42 (0.32, 0.52)	LR+	1.64 (1.38, 1.96)	V. serious	n/a	Not serious	Not serious		LOW
2010)	Prospective	269	0.96 (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 bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Sikkes 2010)	Prospective	269	0.96 (0.91, 0.98)	0.47 (0.37, 0.58)	LR+	1.81 (1.48, 2.21)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.09 (0.05, 0.19)	V. serious	n/a	Not serious	Not serious		LOW

Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Sikkes 2010)	Prospective	269	0.92 (0.87, 0.95)	0.63 (0.52, 0.72)	LR+	2.47 (1.88, 3.25)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.13 (0.08, 0.22)	V. serious	n/a	Not serious	Not serious		LOW

Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
1 study (Sikkes	1 study (Sikkes Prospective	269	0.90 (0.94, 0.03)	0.60 (0.59, 0.77)	LR+	2.84 (2.08, 3.88)	V. serious	n/a	Not serious	Not serious		LOW
2010)	Prospective	209	0.89 (0.84, 0.93)	0.69 (0.58, 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.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
1 study (Sikkes	Prospective	269	0.86 (0.80, 0.90)	0.74 (0.64, 0.92)	LR+	3.31 (2.32, 4.73)	V. serious	n/a	Not serious	Not serious		LOW
2010)	riospective	209	0.60 (0.60, 0.90)	0.74 (0.64, 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.

P.2.5.6 MMSE (<28)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Marmant 2012)	Droopoetivo	110	0.09 (0.90, 1.00)	0.79 (0.64, 0.97)	LR+	4.38 (2.60, 7.38)	V. serious	n/a	Not serious	Not serious		LOW
1 study (Mormont 2012)	Prospective	110	0.98 (0.89, 1.00)	0.78 (0.64, 0.87)	LR-	0.02 (0.00, 0.15)	V. serious	n/a	Not serious	Not serious	-	LOW
Notes on risk of bias												

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

P.2.5.7 p-tau 181

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Maddalena	Dragnostiva	70	0.67 (0.52, 0.70)	0.63 (0.40, 0.94)	LR+	1.81 (0.97, 3.36)	Serious	n/a	Not serious	Serious		LOW
2003)	Prospective	70	0.67 (0.53, 0.78)	0.63 (0.40, 0.81)	LR-	0.53 (0.31, 0.89)	Serious	n/a	Not serious	Serious		LOW

Notes on risk of bias

Maddalena 2003: It was unclear whether inappropriate exclusions had been made; an optimised threshold was used for each test and within each test for different analyses; it was unclear whether the index and reference tests were interpreted independently of each other.

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

p-tuu/Amyloid							<u>o</u>	ncy	SS	c	ations	
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias Indirectness Imprecision		Imprecision	Other considerat	Quality	
SECONDARY CARE	■											
1 study	Droopootivo	70	0.90 (0.67, 0.90)	0.90 (0.66, 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 risk of bias

Maddalena 2003: It was unclear whether inappropriate exclusions had been made; an optimised threshold was used for each test and within each test for different analyses; it was unclear whether the index and reference tests were interpreted independently of each other.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Marmont 2012)	Dragnostivo	110	0.02 (0.02.0.07)	0.00 (0.79, 0.06)	LR+	9.00 (3.91, 20.71)	V. serious	n/a	Not serious	Not serious		LOW
1 study (Mormont 2012)	Prospective	110	0.92 (0.82, 0.97)	0.90 (0.78, 0.96)	LR-	0.09 (0.04, 0.21)	V. serious	n/a	Not serious	Not serious	-	LOW
Notes on risk of bias Mormont 2012: Exclusion of >35% population at analysis and use of optimised test thresholds.												

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P.2.5.10 Total Tau

Total Tau												
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atualy (Valuabay 2010)	Dunnanastiva	40	0.40 (0.07, 0.05)	0.05 (0.74, 0.00)	LR+	10.08 (1.42, 71.85)	V. serious	n/a	Not serious	Serious		VERY LOW
1 study (Yakushev 2010)	Prospective	46	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 Yakushev 2010: Subgroup analysis with >10% population excluded; use of optimised thresholds for test												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
4 - to de (M t 0040)	December	440	0.00 (0.00, 0.00)	0.00 (0.05, 0.00)	LR+	22.09 (5.67, 86.05)	V. serious	n/a	Not serious	Not serious		LOW	
1 study (Mormont 2012)	Prospective	110	0.90 (0.80, 0.96)	0.96 (0.85, 0.99)	LR-	0.10 (0.05, 0.22)	V. serious	n/a	Not serious	Not serious	-	LOW	
Notes on risk of bias Mormont 2012: Exclusion	Notes on risk of bias Mormont 2012: Exclusion of >35% population at analysis and use of optimised test thresholds.												

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P.2.6 AD versus non-AD dementia plus unclassifiable

P.2.6.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA												
1 study (Boutoleau-	Prospective	56	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
Bretonniere 2012)	Frospective	50	0.78 (0.54, 0.91)	0.66 (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

P.2.6.2 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Boutoleau-	Droopoetivo	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
retonniere 2012)	Prospective	50	0.33 (0.16, 0.57)	0.66 (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

P.2.7 AD versus non-AD

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 -tooks (Death- 004.4)	December	4.440	0.00 (0.00, 0.00)	0.70 (0.00 0.70)	LR+	3.10 (2.68, 3.57)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Duits 2014)	Prospective	1,149	0.86 (0.83, 0.89)	0.72 (0.68, 0.76)	LR-	0.19 (0.16, 0.24)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Prandt 2009)	Detroppediye	147	0.42 (0.20, 0.56)	0.00 (0.93, 0.04)	LR+	4.13 (2.10, 8.11)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Brandt 2008)	Retrospective	147	0.42 (0.29, 0.56)	0.90 (0.82, 0.94)	LR-	0.65 (0.51, 0.83)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
2 studies (Brandt	1x prospective,	205	0.00 (0.00 0.07)	0.00 (0.00 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

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMER	A											
2 studies (Kaneta	2x	000	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	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
Notes on risk of his	as											

Tripathi 2010: 14% of participants were lost to follow up and did not receive a reference standard; it is unclear whether the index test was interpreted without knowledge of the reference standard.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA												
1 study (Kaneta 2016)	Prospective	89	0.71 (0.57,	0.68 (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 index test.

P.2.7.6 99mTc-ECD SPECT, automated method

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA	A											
1 study (Kaneta	Prospective	89	0.40 (0.27, 0.54)	0.93 (0.69, 0.03)	LR+	2.32 (1.08, 4.96)	Not serious	n/a	Not serious	Serious		MODERATE
2016)	riospective	09	0.40 (0.27, 0.54)	0.83 (0.68, 0.92)	LR-	0.73 (0.56, 0.95)	Not serious	n/a	Not serious	Not serious	-	HIGH

P.2.7.7 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
5 studies (Bergman 1997; Holman 1992; Launes 1991;	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	303	0.70 (0.55, 0.81)	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 prospective				LR+	6.80 (1.98, 23.36)	Not serious	Not serious	Not serious	Serious		MODERATE
2005; Rollin-Sillaire 2012)	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
Holman 1992; Launes 1991; Masterman 1997:	prospective; 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

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.

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P.2.7.8 Amyloid Beta 1-42

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

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P.2.7.9 Amyloid Beta 1-42 and total tau

Studies SECONDARY C	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDART C	ARE											
1 study (Frisoni	Prognostivo	Prospective 94 0.71 (0.55, 0.83	0.71 (0.55, 0.92)	0.88 (0.76, 0.94)	LR+	5.68 (2.76, 11.70)	Serious	n/a	Not serious	Not serious		MODERATE
	(19) Prospective 9	94	0.7 1 (0.33, 0.63)	0.00 (0.70, 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.

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%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Duita 2014)	Dragnostiva	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
1 study (Duits 2014)	Prospective	1,149	0.74 (0.70, 0.77)	0.86 (0.83, 0.89)	LR-	0.30 (0.26, 0.35)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
2 studies (Gabelle	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
(117 (Lille), (Habelle	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.

P.2.7.12 Amyloid Beta 1-42/Total Tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
2 studies (Gabelle 2012 (Lille and	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.

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

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
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
ille); Dumurgier 2015 (Paris); umurgier 2015 (Montpellier))	prospective	367	0.94)	0.85)	LR-	0.22 (0.09, 0.54)	V. serious	Serious	Not serious	Serious	-	VERY LOW

Notes on risk of bias

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

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

P.2.7.14 EEG

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Engadal 2015)	Droopoetivo	272	0.70 (0.64, 0.77)	0.40 (0.24, 0.46)	LR+	1.16 (1.00, 1.35)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Engedal 2015)	Prospective	372	0.70 (0.61, 0.77)	0.40 (0.34, 0.46)	LR-	0.76 (0.56, 1.02)	Not serious	n/a	Not serious	Not serious	-	HIGH

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P.2.7.15 FDG-PET

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Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
6 studies (Dobert 2005; Frisoni 2009;	6 ×	544	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
Ossenkoppele 2013; Panegyres 2009; 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.

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P.2.7.16 FDG-PET/CT

15012170												
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
1 study (Motara	Detroppostive	00	0.07 (0.74, 0.04)	0.06 (0.96, 0.00)	LR+	22.61 (5.78, 88.40)	Serious	n/a	Serious	Not serious		LOW
2017)	Retrospective	98	0.87 (0.74, 0.94)	0.96 (0.86, 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

P.2.7.17 [18F] flutemetamol PET

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
020011271111 071112												
1 atudy (7wan 2017)	Dragnastiva	211	0.76 (0.60, 0.93)	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)	0.00 (0.54, 0.76)	LR-	0.36 (0.26, 0.51)	Not serious	n/a	Not serious	Serious	-	MODERATE

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P.2.7.18 Formula Hulstaert (biomarkers)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 -t. d. (D.:t- 2044)	Dragonactiva	1 1 1 0	0.02 (0.04.0.05)	0.74 (0.70, 0.77)	LR+	3.54 (3.06, 4.10)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Duits 2014)	Prospective	1,149	0.93 (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

P.2.7.19 Formula Mattson (biomarkers)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Duita 2014)	Droopoetivo	1 1 1 0	0.00 (0.77, 0.02)	0.05 (0.01.0.00)	LR+	5.26 (4.28,6.47)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Duits 2014)	Prospective	1,149	0.80 (0.77, 0.83)	3) 085 (0.81, 0.88) L	LR-	0.24 (0.20, 0.28)	Not serious	n/a	Not serious	Not serious	-	HIGH

P.2.7.20 Formula Mulder (biomarkers)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Duita 2014)	Droopoetivo	1 140	0.03 (0.04, 0.05)	0.72 (0.69, 0.76)	LR+	3.38 (2.93, 3.91)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Duits 2014)	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

P.2.7.21 Formula Schoonenboom (biomarkers)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Duita 2014)	Droopoetivo	1 140	0.04 (0.00, 0.03)	0.79 (0.74 0.94)	LR+	4.10 (3.48, 4.82)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Duits 2014)	Prospective	1,149	0.91 (0.88, 0.93)	3) 0.78 (0.74, 0.81)	LR-	0.12 (0.09, 0.15)	Not serious	n/a	Not serious	Not serious	-	HIGH

P.2.7.22 Mass Spectrometry

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 -tudy (Jaha 2014)	Description	00	0.07 (0.77, 0.04)	0.02 (0.02 0.02)	LR+	5.02 (2.05, 12.29)	Serious	n/a	Not serious	Serious		MODERATE
1 study (Jahn 2011)	Prospective	86	0.87 (0.77, 0.94)	0.83 (0.62, 0.93)	LR-	0.15 (0.08, 0.30)	Serious	n/a	Not serious	Serious	-	MODERATE

P.2.7.23 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Frisoni	2 ×	007	0.62 (0.00, 0.06)	0.70 (0.00, 0.04)	LR+	1.91 (1.56, 2.35)	Not serious	Not serious	Not serious	Serious		MODERATE
2009; Koikkalainen 2016)	prospective	637	0.62 (0.09, 0.96)	96) 0.72 (0.39, 0.91)	LR-	0.47 (0.13, 1.66)	Not serious	Serious	Not serious	Serious	-	LOW

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Cuppe 2015)	Datragnactive	100	0.64 (0.46, 0.74)	0.96 (0.74, 0.03)	LR+	4.30 (2.17, 8.50)	Serious	n/a	Not serious	Not serious		MODERATE
1 study (Suppa 2015)	Retrospective	100	0.61 (0.46, 0.74)	0.86 (0.74, 0.93)	LR-	0.45 (0.31, 0.66)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of bias Suppa 2015: It was und	lear whether the ir	ndex test	results were interpre	eted without knowled	ge of the resu	ults of the reference s	standard; as	ssay cu	it-offs were det	ermined using F	ROC anal	ysis.

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%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 atualy (Compa 2045)	Detuces estive	100	0.70 (0.50, 0.00)	0.74 (0.50, 0.00)	LR+	2.47 (1.56, 3.89)	Serious	n/a	Not serious	Serious		LOW
1 study (Suppa 2015)	Retrospective	100	0.70 (0.56, 0.82)	0.71 (0.58, 0.82)	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.

MRI Hippocampal grey matter volume left/ total grey matter volume (HVL/GMV). Cut-off 4.69 per mille. P.2.7.26

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Cuppa 2015)	Detroppostive	100	0.90 (0.65, 0.90)	0.66 (0.53, 0.77)	LR+	2.34 (1.58, 3.48)	Serious	n/a	Not serious	Serious		LOW
1 study (Suppa 2015)	Retrospective	100	0.80 (0.65, 0.89)	0.66 (0.53, 0.77)	LR-	0.31 (0.17, 0.57)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of bias				d		- 		66				

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.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Cuppe 2015)	Detroppositive	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
1 study (Suppa 2015)	Retrospective	100	0.75 (0.60, 0.86)	0.77 (0.64, 0.86)	LR-	0.33 (0.19, 0.55)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of bias												

Suppa 2015: It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; assay cut-offs were determined using ROC analysis.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Cuppa 201E)	Detroppediye	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
1 study (Suppa 2015)	Retrospective	100	0.80 (0.65, 0.89)	0.80 (0.68, 0.89)	LR-	0.25 (0.14, 0.46)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of bias	l a a u la a t la a u t la a . ; u					ulta af tha wafawanaa	-4		.t affaana alat	i	200	i.

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.

MRI Total hippocampal grey matter volume/total grey matter volume (HV/GMV). Cut-off 8.36 per mille. P.2.7.29

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Suppo 2015)	Potroppostivo	100	0.66 (0.51, 0.78)	0.99 (0.76, 0.04)	LR+	5.27 (2.55, 10.88)	Serious	n/a	Not serious	Not serious		MODERATE
1 study (Suppa 2015)	Retrospective	100	0.00 (0.51, 0.76)	0.88 (0.76, 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.

P.2.7.30 Olfactory Test ≥ 3 errors

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CA	ARE												
1 study			2 -2 (2 -2 2 2 4)		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	otes on risk of bias												
Christensen 2017	: Although the th	reshold	was not pre-specified	, data was presented	I for all possi	ble cut offs.							

P.2.7.31 Olfactory Test ≥ 4 errors

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality		
SECONDARY CA	ARE													
1 study	D "	50	0.50 (0.04.0.00)	0.70 (0.50 0.07)	LR+	1.86 (0.88, 3.93)	Not serious	n/a	Not serious	Serious		MODERATE		
(Christensen 2017)	Prospective	50	0.50 (0.31, 0.69)	0.73 (0.53, 0.87)	LR-	0.68 (0.43, 1.09)	Not serious	n/a	Not serious	Serious	-	MODERATE		
	Notes on risk of bias													
Christensen 2017	: Although the th	reshold v	was not pre-specified	, data was presented	l for all possi	ble cut offs.								

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Christensen 2017: Although the threshold was not pre-specified, data was presented for all possible cut offs...

P.2.7.32 Olfactory Test ≥ 5 errors

Ondotory 1		_										
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY C	ARE											
1 study			0.04 (0.00.0.44)	0.05 (0.05.0.04)	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	0.21 (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 hias											

P.2.7.33 p-tau 181

Studies ALL EVIDENCE POOLED	Design	Tot al N	Sens (95%CI)	Spec (95%CI)	Meas ure	Summar y of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
9 studies (Brandt 2008; Duits 2014; Dumurgier 2015 (Lille); Dumurgier 2015 (Paria); Dumurgier 2015 (Montaellier); Caballa 2012 (Lille and	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
2015 (Paris); Dumurgier 2015 (Montpellier); Gabelle 2012 (Lille and Paris); Gabelle 2012 (Montpellier); Knapskgog 2016; Mulder 2010)	2 × retrospe ctive	8	(0.62, 0.84)	(0.76, 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.

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P.2.7.34 p-tau and Amyloid Beta 1-42 combined then in case of discrepancy between p-tau and Amyloid Beta 1-42 the Amyloid Beta 42/40 ratio was used in place of Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	E											
1 study	Droopostivo	220	0.00 (0.00 0.00)	0.04 (0.96, 0.05)	LR+	10.29 (6.41, 16.50)	V. serious	n/a	Not serious	Not serious		LOW
(Dumurgier 2015)	Prospective	329	0.88 (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).

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	E											
1 study	Droopoetivo	303	0.97 (0.91, 0.02)	0.01 (0.96, 0.05)	LR+	9.79 (6.01, 15.93)	V. serious	n/a	Not serious	Not serious		LOW
(Dumurgier 2015)	Prospective	303	0.87 (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 bias

Dumurgier 2015: The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study; the timing of the reference and index tests is unclear and a subgroup analysis was carried out that excluded >10% population (with indeterminate results).

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

P-tad/Amyrold Bett		Total	Sens	Spec		Summary of findings	Risk of bias	consistency	Indirectness	Imprecision	rther onsiderations	Quality
Studies	Design	N	(95%CI)	(95%CI)	Measure	(95%CI)	<u>~</u>	<u> ۽</u>	드	=	5 8	Quality
SECONDARY CARE												
2 studies (Duits 2014;	2 ×	1 424	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).

P.2.7.37 Total Tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
ALL EVIDENCE POOLED												
9 studies (Brandt 2008; Duits 2014; Dumurgier (Lille) 2015; Dumurgier 2015	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.

P.2.7.38 Total Tau/Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Duita 2014)	Droopoetiyo	1 1 1 0	0.05 (0.02, 0.00)	0.02 (0.70, 0.05)	LR+	4.78 (3.96, 5.77)	Not serious	Not serious	Not serious	Not serious		HIGH
1 study (Duits 2014)	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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 at adv. (Candon an 2007)	Detrees estive	100	0.50 (0.40, 0.60)	0.72 (0.02 0.04)	LR+	2.15 (1.45, 3.19)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Goodman 2007)	Retrospective	168	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

P.2.8 AD versus other dementias

P.2.8.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
1 study	Dan and attitud	00	0.00 (0.50, 0.00)	0.74 (0.50, 0.05)	LR+	3.05 (1.57, 5.93)	V. serious	n/a	Not serious	Serious		VERY LOW
(Velakoulis 1997)		0.89 (0.50, 0.98)	0.71 (0.50, 0.85)	LR-	0.16 (0.02, 1.01)	V. serious	n/a	Not serious	Serious	-	VERY LOW	

Notes on risk of bias

Velakoulis 1997: Subgroup analysis where >10% study population excluded and it was unclear whether: the index test results were interpreted without knowledge of the results of the reference standard; the index test threshold was pre-specified or the reference standard results interpreted without knowledge of the results of the index test.

P.2.8.2 AD scale (≥6)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atd (Ctafaan 2010)	Dunamanting	100	0.00 (0.74, 0.07)	0.07 (0.70, 0.00)	LR+	6.18 (3.53, 10.82)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Gustafson 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												

Notes on hisk of blus

Gustafson 2010: The study was not downgraded for subgroup analysis as <10% population was excluded.

P.2.8.3 Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
3 studies (Boutoleau-Bretonniere	3 ×	249	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.

P.2.8.4 Amyloid Beta 1-42 and total tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY C	ARE											
1 study (Frisoni	dy (Frisoni Propostivo 66 0.74 (0.55.0.0	0.74 (0.55, 0.00)	0.00 (0.70, 0.00)	LR+	19.89 (2.87, 137.80)	V. serious	n/a	Not serious	Not serious		LOW	
2009)	Prospective	66	0.71 (0.55, 0.83)	0.96 (0.79, 0.99)	LR-	0.30 (0.18, 0.50)	V. serious	n/a	Not serious	Not serious	-	LOW

Notes on risk of bias

Frisoni 2009: Subgroup analysis with >10% population excluded; patients whose cognitive deficit reverted (regarded as primarily depressed with secondary cognitive impairment) were excluded from the study; unclear whether reference test was interpreted without knowledge of index test and unclear whether results of index test interpreted without knowledge of reference test.

P.2.8.5 Apo E (≥1 allele)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Mayouy 1009)	Detroppositive	2 100	0.65 (0.62, 0.67)	0.69 (0.64, 0.72)	LR+	2.03 (1.75, 2.34)	Not serious	n/a	Not serious	Serious		MODERATE
1 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

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

001 14 0 0, total 144			li .	l .					l .			
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE					•			•	•	•		
1 study (Boutoleau-	Drooppotive	4.4	0.97 (0.69,	0.69 (0.49,	LR+	3.09 (1.76, 5.42)	V. serious	n/a	Not serious	Serious		VERY LOW
Bretonniere 2012)	Prospective	44	1.00)	0.83)	LR-	0.04 (0.00, 0.60)	V. serious	n/a	Not serious	Serious	-	VERY LOW

Notes on risk of bias

Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.

P.2.8.7 Computed Tomography, CT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 atuativ (OIDsian 2000)	Dunamantina	100	0.54 (0.30, 0.03)	0.20 (0.24, 0.55)	LR+	0.82 (0.58, 1.17)	Serious	n/a	Not serious	Not serious		MODERATE
1 study (O'Brien 2000)	Prospective	103	0.51 (0.39, 0.62)	0.38 (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 >1	0% popu	ılation excluded									

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P.2.8.8 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
6 studies (Arslan 2015; Frisoni 2009; Hoffman 2000; Jagust 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.

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P.2.8.9 MRI

WITCH												
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE									·			·
2 studies (Frisoni 2009;	2 ×	471	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	4/1	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.

P.2.8.10 p-tau 181

p tau ioi												
Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	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
2012; Ibach 2006; Maddalena 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.

lbach 2006: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the test thresholds were not pre-specified and it is unclear whether the index test was interpreted without knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.

Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.

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

p												
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Ibach 2006;	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.

lbach 2006: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the test thresholds were not pre-specified and it is unclear whether the index test was interpreted without knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.

P.2.8.12 Total tau

										1		
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
3 studies (Boutoleau-Bretonniere 2012; Ibach 2006; Yakushev 2010)	3 × prospectiv e	205	0.71 (0.52, 0.85)	0.82 (0.63, 0.93)	LR+	4.28 (1.75, 9.99)	V. serious	Not serious	Not serious	Not serious		LOW
					LR-	0.38 (0.24, 0.61)	V. serious	Serious	Not serious	Serious	-	VERY LOW

Notes on risk of bias

Ibach 2006: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the test thresholds were not pre-specified and it is unclear whether the index test was interpreted without knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded. Yakushev 2010: Subgroup analysis with >10% population excluded; use of optimised thresholds for test

Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.

P.2.8.13 Total Tau/Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ibach 2006) Prospective	124	0.75 (0.64, 0.93)	0.75 (0.64, 0.95)	LR+	3.00 (1.81, 4.98)	V. serious	n/a	Not serious	Serious		VERY LOW	
	Fiospective	124	0.75 (0.64, 0.83)	0.75 (0.61, 0.85)	LR-	0.33 (0.22, 0.51)	V. serious	n/a	Not serious	Serious	-	VERY LOW

Notes on risk of bias

lbach 2006: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the test thresholds were not pre-specified and it is unclear whether the index test was interpreted without knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.

P.2.9 AD versus VaD

P.2.9.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
2 studies (Launes 1991; McMurdo 1994)	2 × prospective	97	0.61 (0.49, 0.72)	0.85 (0.69, 0.93)	LR+	4.13 (1.85, 9.21)	Serious	Not serious	Not serious	Serious		LOW
					LR-	0.45 (0.31, 0.66)	Serious	Not serious	Not serious	Serious	-	LOW
MULTIPLE CAMERA												
1 study (Boutoleau-Bretonniere 2012)	Prospective	26	0.78 (0.54, 0.91)	0.50 (0.20, 0.80)	LR+	1.56 (0.75, 3.25)	V. serious	n/a	Not serious	Serious		VERY LOW
					LR-	0.44 (0.15, 1.35)	V. serious	n/a	Not serious	Serious	-	VERY LOW
ALL EVIDENCE POOLED												
3 studies (Boutoleau-Bretonniere 2012; Launes 1991; McMurdo 1994)	3 × prospective	400	0.64 (0.53, 0.74)	0.74 (0.45, 0.91)	LR+	2.54 (1.19, 5.41)	V. serious	Not serious	Not serious	Serious		VERY LOW
		123			LR-	0.45 (0.32, 0.64)	Serious	Not serious	Not serious	Serious	-	LOW

Notes on risk of bias

Launes 1991: Subgroup analysis used with >10% study population excluded. McMurdo 1994: Subgroup analysis used with >10% study population discarded.

Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded

P.2.9.2 Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Androson 2001)	Prospective	186	0.65 (0.57, 0.72)	0.49 (0.20, 0.69)	LR+	1.25 (0.83, 1.87)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Andreasen 2001)	riospective	100	0.65 (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

P.2.9.3 Computed Tomography, CT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE							•	<u>'</u>				
4 -tt- (OID-i 0000)	Danasation	0.4	0.54 (0.00, 0.00)	0.00 (0.47, 0.50)	LR+	0.75 (0.52, 1.06)	Serious	n/a	Not serious	Not serious		MODERATE
1 study (O'Brien 2000)	Prospective	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 >1	0% popu	lation excluded									

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P.2.9.4 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Description	0.47	0.00 (0.04, 0.05)	0.00 (0.00 0.00)	LR+	2.33 (0.79, 6.85)	Serious	n/a	Not serious	Serious		LOW
(Koikkalainen 2016)	Prospective	247	0.29 (0.24, 0.35)	0.88 (0.68, 0.96)	LR-	0.81 (0.68, 0.96)	Serious	n/a	Not serious	Not serious	-	MODERATE

Notes on risk of bias

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

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

P.2.10.1 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE	≣											
1 study (Vijverberg	Droopostivo	111	0.90 (0.71, 0.06)	0.69 (0.67, 0.77)	LR+	2.77 (1.97, 3.88)	Serious	n/a	Not serious	Serious		LOW
2016b)	Prospective	111	0.89 (0.71, 0.96)	0.68 (0.57, 0.77)	LR-	0.16 (0.06, 0.48)	Serious	n/a	Not serious	Not serious	-	MODERATE

Notes on risk of bias

Vijverberg 2016b: 19% study population was excluded from analysis and it is unclear whether a consecutive or random group of patients was enrolled or whether inappropriate exclusions were avoided; all test results (including the index tests) were used to reach the clinical diagnosis.

P.2.10.2 FDG-PET and MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE	≣											
1 study (Vijverberg	Dragnostiva	111	0.06 (0.79, 0.00)	0.72 (0.62, 0.94)	LR+	3.52 (2.46, 5.02)	Serious	n/a	Not serious	Not serious		MODERATE
2016b)	Prospective	111	0.96 (0.78, 0.99)	0.73 (0.62, 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.

P.2.10.3 FTDC criteria for by FTD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 - 4	Detroconstitue	4.47	0.70 (0.00 0.07)	0.00 (0.00, 0.00)	LR+	18.48 (6.07, 56.26)	Serious	n/a	Not serious	Not serious		MODERATE
study (Harris 2013)	Retrospective	147	0.79 (0.69, 0.87)	0.96 (0.88, 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

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P.2.10.4 FTDC criteria for possible bvFTD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Vijverberg	Prospective	116	0.85 (0.67, 0.94)	0.27 (0.10, 0.27)	LR+	1.17 (0.95, 1.43)	Serious	n/a	Not serious	Not serious		MODERATE
2016a)	Frospective	110	0.65 (0.67, 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.

P.2.10.5 FTDC criteria for probable bvFTD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE	E											
1 study (Vijverberg	Droopootivo	116	0.95 (0.67, 0.04)	0.82 (0.73, 0.89)	LR+	4.74 (2.96, 7.59)	Serious	n/a	Not serious	Not serious		MODERATE
2016a)	Prospective	116	0.85 (0.67, 0.94)	0.62 (0.73, 0.69)	LR-	0.18 (0.07, 0.45)	Serious	n/a	Not serious	Not serious	-	MODERATE

Notes on risk of bias

Vijverberg 2016a: 19% study population was excluded from analysis and it is unclear whether a consecutive or random group of patients was enrolled or whether the reference standard results were interpreted without knowledge of the results of the index test.

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P.2.10.6 MRI

1411 (1												
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE	E											
1 study (Vijverberg	Droopostivo	111	0.70 (0.51, 0.94)	0.02 (0.05.0.07)	LR+	9.85 (4.39, 22.12)	Serious	n/a	Not serious	Not serious		MODERATE
2016b)	Prospective	111	0.70 (0.51, 0.84)	0.93 (0.85, 0.97)	LR-	0.32 (0.18, 0.57)	Serious	n/a	Not serious	Serious	-	LOW

Notes on risk of bias

Vijverberg 2016b: 19% study population was excluded from analysis and it is unclear whether a consecutive or random group of patients was enrolled or whether inappropriate exclusions were avoided; all test results (including the index tests) were used to reach the clinical diagnosis.

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

P.2.11.1 FDG-PET

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDAIL! CAILE												
1 study (Kerklaan 2014)	Retrospective	e 52 0.47 (0.24, 0.71) 0.92 (0.78, 0.9	0.92 (0.78, 0.97)	LR+	5.76 (1.71, 19.34)	Not serious	n/a	Not serious	Serious		MODERATE	
i Study (Nerkladii 2014)	Reliospective	32	0.47 (0.24, 0.71)	0.92 (0.76, 0.97)	LR-	0.58 (0.36, 0.94)	Not serious	n/a	Not serious	Serious	-	MODERATE

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P.2.12 CADASIL versus CADASIL-like syndromes

P.2.12.1 Skin biopsy

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ampuero 2009)	Droopoetiyo	00	0.06 (0.79, 0.00)	0.69 (0.56, 0.70)	LR+	3.03 (2.10, 4.39)	Not serious	n/a	Not serious	Not serious		HIGH
i study (Ambuero 2009)	Prospective	90	0.96 (0.78, 0.99)	0.68 (0.56, 0.79)	LR-	0.05 (0.01, 0.37)	Not serious	n/a	Not serious	Not serious	-	HIGH

P.2.13 CBD versus non-CBD

P.2.13.1 CBD consensus criteria

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 - 1 - 1 - (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

P.2.14 CJD versus non-CJD

P.2.14.1 Amyloid Beta 1-42 and total tau

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
1 study (Van Everbroeck	Determinantina	050	0.07 (0.74.0.00)	0.00 (0.05, 0.00)	LR+	42.84 (16.14, 113.67)	Not serious	n/a	Not serious	Not serious		HIGH
2003)	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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Fourier 2017)	Potroppostivo	268	0.04 (0.95, 0.07)	0.05 (0.01.0.00)	LR+	19.84 (10.46, 37.65)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Fourier 2017)	Retrospective	200	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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Tschampa	Detreserentive	474	0.04 (0.00, 0.05)	0.44 (0.20, 0.64)	LR+	1.64 (1.21, 2.21)	Not serious	n/a	Not serious	Serious		MODERATE
2005)	Retrospective	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

P.2.14.4 CSF 14-3-3 ELISA

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
2 studies (Kenney	1 × prospective;	000	0.94 (0.78,	0.96 (0.91,	LR+	22.61 (10.33, 49.47)	Serious	Not serious	Not serious	Not serious		MODERAT E
2000; Leitao 2016)	1 × retrospective	292	0.98)	0.98)	LR-	0.07 (0.02, 0.24)	Serious	Serious	Not serious	Not serious	-	LOW

Notes on risk of bias

Kenney 2000: The test threshold was not pre-specified and it was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test. Leitao 2016: It was unclear whether: a consecutive or random sample of patients was enrolled; the study avoided inappropriate exclusions; test thresholds were pre-specified.

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P.2.14.5 CSF 14-3-3 immunoblotting

Studies SECONDARY CARE	Design	Tot al N	Sens (95%CI)	Spec (95%CI)	Mea sure	Summa ry of finding s (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	
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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	RE											
1 study (Chohan	Detrespestive	444	0.00 (0.50, 0.00)	0.05 (0.00, 0.07)	LR+	11.72 (6.16, 22.29)	Serious	n/a	Not serious	Not serious		MODERATE
2010)		0.02 (0.56, 0.68)	0.95 (0.90, 0.97)	LR-	0.40 (0.34, 0.47)	Serious	n/a	Not serious	Not serious	-	MODERATE	

Notes on risk of bias

Chohan 2010: Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.

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

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
1 study (Van Everbroeck	D	050	0.00 (0.07.4.00)	0.00 (0.04.0.00)	LR+	43.81 (17.57, 109.24)	Not serious	n/a	Not serious	Not serious		HIGH
2003)	Retrospective	250	0.99 (0.87, 1.00)	0.98 (0.94, 0.99)	LR-	0.01 (0.00, 0.15)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies SECONDARY CA	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	KE											
1 study (Chohan	Retrospective	351	0.75 (0.69, 0.80)	0.88 (0.82, 0.93)	LR+	6.33 (3.97, 10.09)	Serious	n/a	Not serious	Not serious		MODERATE
2010)	Reliospective	331	0.73 (0.09, 0.60)	0.00 (0.02, 0.93)	LR-	0.28 (0.22, 0.36)	Serious	n/a	Not serious	Not serious	-	MODERATE

Notes on risk of bias

Chohan 2010: Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	RE											
1 study (Chohan	Detropportive	351	0.57 (0.50, 0.63)	0.06 (0.00, 0.08)	LR+	12.81 (5.81, 28.25)	Serious	n/a	Not serious	Not serious		MODERATE
2010) Re	Retrospective	331	0.57 (0.50, 0.63)	0.96 (0.90, 0.98)	LR-	0.45 (0.38, 0.53)	Serious	n/a	Not serious	Serious	-	LOW

Notes on risk of bias

Chohan 2010: Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.

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P.2.14.10 EEG

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	E											
2 studies	0				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

P.2.14.11 European criteria for CJD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Prandal 2000)	Detroppositive	226	0.04 (0.96, 0.05)	0.28 (0.16, 0.43)	LR+	1.26 (1.04, 1.53)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Brandel 2000)	Retrospective	236	0.91 (0.86, 0.95)	0.28 (0.16, 0.43)	LR-	0.32 (0.16, 0.62)	Not serious	n/a	Not serious	Serious	-	MODERATE

P.2.14.12 French criteria for CJD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Prandal 2000)	Detroopediye	226	0.00 (0.03 0.03)	0.50 (0.35, 0.65)	LR+	1.77 (1.29, 2.42)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Brandel 2000)	Retrospective	236	0.88 (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

P.2.14.13 Master's criteria for CJD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Prandal 2000)	Detroppositive	226	0.00 (0.05 4.00)		LR+	1.09 (0.99, 1.21)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Brandel 2000)	Retrospective	236	0.98 (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

P.2.14.14 MRI

IVIIXI													
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
4 studies (Schroter	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 Van Everbroeck 2004:	EVERDIOECK 2004)												

P.2.14.15 MRI, DWI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Tagliapietra	Detroppositive	24	0.72 (0.44, 0.04)		LR+	14.55 (2.08, 101.66)	Not serious	n/a	Not serious	Not serious		HIGH
2013)	Retrospective	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

P.2.14.16 Neuron-specific enolase

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
2 studies (Bahl	2 ×	005	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	295	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

P.2.14.17 New criteria for sporadic CJD

Studies SECONDARY (Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY C	ARE											
1 study (Zerr	Detroopediye	spective 74 0.98 (0.87, 1.00) 0.71 (0.50, 0.8	0.74 (0.50, 0.95)	LR+	3.36 (1.80, 6.28)	V. serious	n/a	Not serious	Serious		VERY LOW	
2009)	Retrospective	74	0.96 (0.67, 1.00)	0.71 (0.50, 0.85)	LR-	0.03 (0.00, 0.20)	V. serious	n/a	Not serious	Not serious	-	LOW

Notes on risk of bias

Zerr 2009: Unclear whether patients were selected randomly or consecutively or whether inappropriate exclusions were avoided; the optimal index test thresholds were determined during the study and a subgroup analysis was used to determine test sensitivity and specificity.

p-tau 181/total tau P.2.14.18

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	lΕ											
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.

P.2.14.19 RT-QuIC

iti-Quic												
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY	CARE											
2 studies (Foutz 2017; Lattanzio 2017)	1 × prospective; 1 × retrospective	779	0.89 (0.69, 0.97)	0.99 (0.96, 1.00)	LR+	99.38 (26.52, 372.49)	Not serious	Not serious	Not serious	Not serious	-	HIGH

P.2.14.20 S100B, 1.0ng/ml

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	RE											
1 study (Chohan	Retrospective	410	0.65 (0.50, 0.71)	0.90 (0.84, 0.94)	LR+	6.46 (4.08, 10.24)	Serious	n/a	Not serious	Not serious		MODERATE
2010)	Retrospective	412	0.65 (0.59, 0.71)		LR-	0.39 (0.33, 0.47)	Serious	n/a	Not serious	Not serious	-	MODERATE

Notes on risk of bias

Chohan 2010: Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.

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P.2.14.21 S100B, 2.5ng/ml

,	ARY CARE					bias	ency	ess	ion	ations		
Studies	Design			Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of b	Inconsistency	Indirectn	Imprecision	Other considera	Quality
SECONDARY CARE												
2 studies (Beudry	2 ×	1,053	0.87 (0.82,	0.87 (0.84,	LR+	6.65 (5.52, 8.00)	Serious	Not serious	Not serious	Not serious		MODERAT E
1998; Coulthart 2011)	prospective	1,055	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.

P.2.14.22 S100B, 4.2ng/ml

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

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P.2.14.23 Total Tau

Studies SECONDARY CARE	Design	Tot al N	Sens (95%CI)	Spec (95%CI)	Mea sure	Summar y of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Qua lity
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
Lattanzio 2017; Leitao 2016; Rohan 2015; Tagliapietra 2013; Van Everbroeck 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.

P.2.14.24 Total Tau and S100B

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	RE											
1 study (Chohan	Detropportive	251	0.50 (0.52, 0.65)	0.95 (0.90, 0.98)	LR+	11.34 (5.46, 23.53)	Serious	n/a	Not serious	Not serious		MODERATE
2010)	Retrospective	351	0.59 (0.52, 0.65)	0.95 (0.90, 0.98)	LR-	0.43 (0.37, 0.51)	Serious	n/a	Not serious	Serious	-	LOW

Notes on risk of bias

Chohan 2010: Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.

P.2.14.25 WHO CJD criteria

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE	.				•							
2 studies (Heath	2 ×	200	0.90 (0.85,	0.71 (0.61,	LR+	3.14 (2.29, 4.30)	V. serious	Not serious	Serious	Not serious		VERY LOW
2010; Zerr 2009)	retrospective	306	0.94)	0.79)	LR-	0.14 (0.09, 0.21)	V. serious	Not serious	Serious	Not serious	-	VERY LOW

Notes on risk of bias

Zerr 2009: Unclear whether patients were selected randomly or consecutively or whether inappropriate exclusions were avoided; the optimal index test thresholds were determined during the study and a subgroup analysis was used to determine test sensitivity and specificity.

Heath 2010: It was unclear whether the index test was interpreted without knowledge of the results of the reference test; whether a consecutive or random sample of patients was enrolled or inappropriate exclusions were avoided.

Notes on indirectness

Heath 2010: Mean age at onset< 40 years old

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P.2.15 DLB versus AD

P.2.15.1 Lewy body composite risk score, LBCRS, ≥ 3

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Calvin 2015)	Dragnostiva	153	0.04 (0.94, 0.09)	0.79 (0.60, 0.95)	LR+	4.29 (2.95, 6.24)	Serious	n/a	Not serious	Not serious		MODERATE
1 study (Galvin 2015)	Prospective	155	0.94 (0.84, 0.98)	0.78 (0.69, 0.85)	LR-	0.07 (0.02, 0.22)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of bias												

Galvin 2015: Subgroup analysis was carried out excluding >30% study population.

P.2.15.2 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Droopootivo	270	0.42 (0.20, 0.57)	, 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	210	0.43 (0.29, 0.57)		LR-	0.81 (0.62, 1.04)	Serious	n/a	Not serious	Not serious	-	MODERATE

Notes on risk of bias

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

P.2.16 DLB versus FTD

P.2.16.1 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Prognostivo	139	0.43 (0.20, 0.57)	0.96 (0.77, 0.02)	LR+	3.01 (1.65, 5.51)	Serious	n/a	Not serious	Serious		LOW
(Koikkalainen 2016)	Prospective	139	0.43 (0.29, 0.57)	0.86 (0.77, 0.92)	LR-	0.67 (0.52, 0.87)	Serious	n/a	Not serious	Not serious		MODERATE

Notes on risk of bias

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

P.2.17 DLB versus non-DLB

P.2.17.1 123I-FP-CIT SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAME	RA											
1 study	Retrospective	23	0.95 (0.55, 1.00)	0.89 (0.61, 0.98)	LR+	8.91 (1.95, 40.64)	Serious	n/a	Not serious	Serious		LOW
(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 CAI	MERA											
2 studies (Kemp 2011;	1x				LR+	15.40 (6.24, 38.01)	Serious	Not serious	Not serious	Not serious		MODERATE
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	POOLED											
3 studies	1x				LR+	13.34 (6.14, 29.01)	Serious	Not serious	Not serious	Not serious		MODERATE
(Kemp 2011; O'Brien 2009; Walker 2009; Thomas 2017)	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

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

P.2.17.2 123I-IMP SPECT

1231-IIVII OI LOI												
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
MULTIPLE CAMERA												
1 study (Sakamoto	Detroopediye	101	0.62 (0.42, 0.79)	0.75 (0.64, 0.93)	LR+	2.43 (1.48, 3.98)	Serious	n/a	Not serious	Serious		LOW
2014)	Retrospective 101 0.62 (0.42, 0.78) 0.75 (0.64, 0.83	0.75 (0.64, 0.83)	LR-	0.52 (0.31, 0.85)	Serious	n/a	Not serious	Serious	-	LOW		
Notes on risk of hige												

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.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	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)	е	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.

P.2.17.4 123I-MIBG cardiac scintigraphy

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
5 studies (Estorch 2008; Manabe 2017;	4 × prospective;		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.

P.2.17.5 EEG

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	nconsistency	ndirectness	Imprecision	Other considerations	Quality
SECONDARY CARE	233.9.1		(55,651)	(55,651)		(557601)	LE CONTRACTOR DE				0 3	Lamity
1 study (Engodal 2015)	Droopoetiyo	207	0.87 (0.50, 0.07)	0.88 (0.84, 0.01)	LR+	7.01 (5.01, 9.80)	Not serious	n/a	Not serious	Not serious		HIGH
i study (Engedai 2015)	dy (Engedal 2015) Prospective 387 0.87 (0.59, 0.97	0.67 (0.59, 0.97)	0.88 (0.84, 0.91)	LR-	0.15 (0.04, 0.55)	Not serious	n/a	Not serious	Serious	-	MODERATE	

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P.2.17.6 FDG-PET

Studies SECONDARY CARE	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
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	255	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.

MRI P.2.17.7

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen	Prospective	504	0.43 (0.20, 0.57)	0.76 (0.72, 0.80)	LR+	1.80 (1.24, 2.61)	Not serious	n/a	Not serious	Serious		MODERATE
2016)	Fiospective	504	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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Forman 2011)	Prophostivo	234	0.00 (0.82, 0.04)	0.72 (0.65, 0.90)	LR+	3.30 (2.49, 4.38)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Ferman 2011)	Prospective	234	0.90 (0.82, 0.94)	0.73 (0.65, 0.80)	LR-	0.14 (0.08, 0.25)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Forman 2011)	Dragnastiva	224	0.05 (0.76, 0.04)	0.72 (0.65, 0.90)	LR+	3.11 (2.34, 4.15)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Ferman 2011)	Prospective	234	0.85 (0.76, 0.91)	0.73 (0.65, 0.80)	LR-	0.21 (0.13, 0.34)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Forman 2011)	Dragnactive	224	0.02 (0.74, 0.00)	0.05 (0.77, 0.00)	LR+	5.35 (3.58, 8.01)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Ferman 2011)	Prospective	234	0.83 (0.74, 0.89)	0.85 (0.77, 0.90)	LR-	0.21 (0.13, 0.32)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Forman 2011)	Droopoetivo	234	0.00 (0.00 0.03)	0.72 (0.65, 0.90)	LR+	3.23 (2.43, 4.29)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Ferman 2011)	Prospective	234	0.88 (0.80, 0.93)	0.73 (0.65, 0.80)	LR-	0.17 (0.10, 0.29)	Not serious	n/a	Not serious	Not serious	-	HIGH

P.2.18 DLB versus other dementias

P.2.18.1 123I-FP-CIT SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAME	RA											
1 study	Prospective	31	0.90 (0.68, 0.97)	0.91 (0.56, 0.99)	LR+	9.90 (1.52, 64.52)	Not serious	n/a	Not serious	Serious		MODERATE
(Treglia 2012)	Frospective	31	0.90 (0.08, 0.97)	0.91 (0.30, 0.99)	LR-	0.11 (0.03, 0.42)	Not serious	n/a	Not serious	Not serious	-	HIGH
MULTIPLE CAN	MERA											
1 study	Detroopeding	20	0.02 (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	E 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 of Treglia 2012: Sp		ed as the	e reference standard	not reported								

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P.2.18.2 123I-MIBG cardiac scintigraphy

1201-WIBO cardi	ao comagi	шрпу										
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Tradia 2012)	Droopoetiyo	24	0.00 (0.69, 0.07)	0.04 (0.56, 0.00)	LR+	9.90 (1.52, 64.52)	Not serious	n/a	Not serious	Serious		MODERATE
1 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 c	riteria used as t	he refere	nce standard not rep	ported								

P.2.18.3 DLB consensus criteria

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skogseth	Droopoetiyo	EE	0.90 (0.57, 0.03)	0.89 (0.74, 0.96)	LR+	7.20 (2.79, 18.61)	Serious	n/a	Not serious	Not serious		HIGH
2017)	Prospective	55	0.80 (0.57, 0.92)	0.89 (0.74, 0.96)	LR-	0.23 (0.09, 0.54)	Serious	n/a	Not serious	Serious	-	LOW

P.2.18.4 FDG-PET

150121	1	1	1							1		
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ossenkoppele	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.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 atualy (Calvin 2045)	Dunamantina	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	analysis was ca	urried out	evoludina >30% etua	ly nonulation								

Galvin 2015: Subgroup analysis was carried out excluding >30% study population.

P.2.18.6 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Drooppotive	206	0.43 (0.29,	0.76 (0.72,	LR+	1.80 (1.23, 2.65)	Serious	n/a	Not serious	Serious		LOW
(Koikkalainen 2016)	Prospective	386	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.

P.2.19 DLB versus VaD

P.2.19.1 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Dragnostivo	71	0.42 (0.20, 0.57)	0.88 (0.68, 0.96)	LR+	3.40 (1.12, 10.32)	Serious	n/a	Not serious	Serious		LOW
(Koikkalainen 2016)	Prospective	71	0.43 (0.29, 0.57)	0.66 (0.66, 0.96)	LR-	0.66 (0.49, 0.88)	Serious	n/a	Not serious	Serious	-	LOW

Notes on risk of bias

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

P.2.20 FTD versus AD

P.2.20.1 99mTc-HMPAO SPECT

Studies	Design	Tota I N	Sens (95%CI)	Spec (95%CI)	Measu re	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA								1				
	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

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Dementia

Appendix P: Diagnosis evidence tables & GRADE

		Tota I	Sens	Spec	Measu	Summary of findings	Risk of bias	consistency	directness	precision	Other considerations	
Studies	Design	N	(95%CI)	(95%CI)	re	(95%CI)	涩	Ĕ	Ĕ	트	58	Quality

Notes on risk of bias

Launes 1991: Subgroup analysis used with >10% study population excluded.

Read 1995: Subgroup analysis used with >10% study population excluded; unclear whether random or consecutive patient enrolment was used; unclear if inappropriate exclusions avoided. Velakoulis 1997: Subgroup analysis where >10% study population excluded and it was unclear whether: the index test results were interpreted without knowledge of the results of the reference standard; the index test threshold was pre-specified or the reference standard results interpreted without knowledge of the results of the index test.

Talbot 1998: Unclear if avoided inappropriate exclusions; unclear whether the reference standard results were interpreted without knowledge of the index test and whether the index test was carried out without knowledge of reference test result; no pre-specified index test threshold; subgroup analysis used with >10% study population excluded.

Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.

Rollin-Sillaire 2012: Subgroup analysis where >10% study population excluded

P.2.20.2 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE	SECONDARY CARE											
1 study	Prospective	315	0.50 (0.40, 0.60)	0.72 (0.66, 0.78)	LR+	1.80 (1.34, 2.41)	Serious	n/a	Not serious	Serious		LOW
(Koikkalainen 2016)					LR-	0.69 (0.56, 0.86)	Serious	n/a	Not serious	Not serious	-	MODERATE

Notes on risk of bias

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

P.2.20.3 FTD versus DLB

P.2.20.4 FDG-PET

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

Notes on risk of bias

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

Notes on indirectness

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

P.2.20.5 MRI

IALLZI												
Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	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
(Koikkalainen 2016)					LR-	0.53 (0.43, 0.66)	Serious	n/a	Not serious	Serious		LOW

Notes on risk of bias

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

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P.2.21 FTD versus non-FTD dementia plus unclassifiable

P.2.21.1 99mTc-HMPAO SPECT

Studies MULTIPLE CAMERA	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
WULTIPLE CAWERA												
1 study (Boutoleau-	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
Bretonniere 2012)					LR-	0.35 (0.13, 0.93)	Serious	n/a	Not serious	Serious	-	LOW

Notes on risk of bias

Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used but <10% study population discarded

P.2.22 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Boutoleau-	Prospective	56	0.18 (0.05, 0.51)	0.62 (0.47, 0.75)	LR+	0.48 (0.13, 1.78)	Serious	n/a	Not serious	Serious		LOW
Bretonniere 2012)					LR-	1.31 (0.92, 1.88)	Serious	n/a	Not serious	Not serious	-	MODERATE

Notes on risk of bias

Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases.

P.2.23 FTD versus non-FTD

P.2.23.1 99mTc-ECD SPECT, visual assessment

Studies MULTIPLE CAMERA	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
1 study (Tripathi	Dragnactive	117	0.06 (0.79, 0.00)	0.00 (0.03, 1.00)	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-	0.04 (0.01, 0.26)	Serious	n/a	Not serious	Not serious	-	MODERATE

Notes on risk of bias

Tripathi 2010: 14% of participants were lost to follow up and did not receive a reference standard; it is unclear whether the index test was interpreted without knowledge of the reference standard.

P.2.23.2 99mTc-HMPAO SPECT

SITTC-TIMIT AC ST LCT													
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	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

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SPECT/PET P.2.23.3

OI LO 1/1 L 1												
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
1 study (Mandaz 2007)	Droopostivo	124	0.00 (0.90, 0.06)	0.75 (0.62, 0.82)	LR+	3.57 (2.38, 5.36)	Not serious	n/a	Serious	Not serious		HIGH
1 study (Mendez 2007)	Prospective	134	0.90 (0.80, 0.96)	0.75 (0.63, 0.83)	LR-	0.13 (0.06, 0.28)	Not serious	n/a	Serious	Not serious	-	HIGH

P.2.23.4 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	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	200	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.

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P.2.23.5 FTD consensus criteria

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Mandaz 2007)	Detroppostive	134	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
1 study (Mendez 2007)	Retrospective	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

P.2.23.6 MRI

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECUNDARY 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

P.2.24 FTD versus other dementias

P.2.24.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
1 study	Propostivo	33	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)	0.96 (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.

P.2.24.2 FDG-PET

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE					·		•	·	•	·		
2 studies (Arslan 2015;	1 × prospective;	440	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	146	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.

P.2.24.3 FTD scale (≥6)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Custofoon 2010)	Droopoetiyo	100	0.02 (0.94, 0.07)	0.02 (0.96.0.06)	LR+	11.58 (6.53, 20.52)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Gustafson 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 downg	raded for	subgroup analysis	as <10% population	was exclude	d.						

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P.2.24.4 MRI

1											
Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
Prognactiva	206	0.50 (0.40, 0.60)	0.79 (0.72, 0.92)	LR+	2.23 (1.66, 2.99)	Serious	n/a	Not serious	Serious		LOW
Frospective	300	0.50 (0.40, 0.60)	0.76 (0.72, 0.62)	LR-	0.64 (0.52, 0.80)	Serious	n/a	Not serious	Not serious	_	MODERATE
		Design N	Design N (95%CI)	Design N (95%CI) (95%CI)	Design N (95%CI) (95%CI) Measure Prospective 386 0.50 (0.40, 0.60) 0.78 (0.72, 0.82) LR+	Design Total N Sens (95%CI) Spec (95%CI) Measure of findings (95%CI) Prospective 386 0.50 (0.40, 0.60) 0.78 (0.72, 0.82) LR+ 2.23 (1.66, 2.99)	Design Total Sens (95%CI) Spec (95%CI) Measure Summary of findings (95%CI) Serious	Design Total Sens (95%CI) Spec (95%CI) Measure Summary of findings (95%CI) Serious N/a	Total N Sens (95%Cl) Spec (95%Cl) Measure Summary of findings (95%Cl) Serious Not serious	Design Total Sens (95%CI) Spec (95%CI) Measure Summary of findings (95%CI) Serious Design Serious Design Total Sens (95%CI) Spec (95%CI) Measure Summary of findings (95%CI) Serious	
Notes on risk of bias

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

P.2.25 FTD versus VaD

P.2.25.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
2 studies (Launes 1991; Talbot	2 ×	196	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	Dunnanativa	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
Bretonniere 2012; Launes 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.

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P.2.25.2 MRI

Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
Droopoetivo	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
Fiospective	110	0.50 (0.40, 0.60)	0.90 (0.76, 0.99)	LR-	0.52 (0.42, 0.65)	Serious	n/a	Not serious	Serious	-	LOW
	Design Prospective	Design N	Design N (95%CI)	Design N (95%CI) (95 [*] %CI)	Design N (95%CI) (95%CI) Measure Prospective 116 0.50 (0.40, 0.60) 0.96 (0.76, 0.99) LR+	Design Total N Sens (95%CI) Spec (95%CI) Measure of findings (95%CI) Prospective 116 0.50 (0.40, 0.60) 0.96 (0.76, 0.99) LR+ 12.00 (1.74, 82.64)	Total N Sens (95%CI) Spec (95%CI) Measure Summary of findings (95%CI) Serious	Design Total Sens (95%CI) Spec (95%CI) Measure Of findings (95%CI) Serious Design Total N (95%CI) Serious N (95%CI) Design N (95%CI) N (95%CI) Design N (95%CI) De	Design Total N Sens (95%CI) Spec (95%CI) Measure Of findings (95%CI) Of fi	Total N Sens (95%CI) Spec (95%CI) Measure Of findings (95%CI) Measure Of findings (95%CI) Measure Of findings (95%CI) Measure Of findings (95%CI) Of fin	Prospective 116 0.50 (0.40, 0.60) 0.96 (0.76, 0.99) LR+ 12.00 (1.74, 82.64) Serious n/a Not serious Serious -

Notes on risk of bias

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

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

P.2.26.1 HIV dementia scale (<10)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Clannor 2000)	tudy (Skinner 2009) Prospective	33	0.46 (0.22, 0.72)	0.90 (0.57, 0.03)	LR+	2.31 (0.80, 6.63)	Not serious	n/a	Not serious	Serious		MODERATE
i study (Skirinei 2009)	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

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P.2.26.2 HIV dementia scale (<11)

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Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Chinner 2000)	Dragnostiva	22	0.62 (0.24, 0.92)	0.90 (0.57, 0.02)	LR+	3.08 (1.16, 8.17)	Serious	n/a	Not serious	Serious		LOW
1 study (Skinner 2009)	Prospective	33	0.62 (0.34, 0.83)	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 o	ptimised thresho	ıld.										

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skinner 2000)	Droopoetiyo	33	0.77 (0.49, 0.02)	0.65 (0.42, 0.92)	LR+	2.20 (1.13, 4.28)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Skinner 2009)	Prospective	33	0.77 (0.48, 0.92)	0.65 (0.43, 0.82)	LR-	0.36 (0.13, 1.01)	Not serious	n/a	Not serious	Serious	-	MODERATE

P.2.26.4 Grooved pegboard test

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Davia 2002)		0.74 (0.62, 0.79)	0.46 (0.44, 0.52)	LR+	1.31 (1.13, 1.52)	Serious	n/a	Serious	Not serious		LOW	
i study (Davis 2002)	riospective	400	0.71 (0.63, 0.78)	0.46 (0.41, 0.52)	LR-	0.63 (0.48, 0.84)	Serious	n/a	Serious	Serious	-	VERY LOW

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Davis 2002)	Dragnostiva	AEE	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)	Prospective	455	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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Davia 2002)		0.77 (0.70, 0.93)	0.40 (0.35, 0.45)	LR+	1.28 (1.13, 1.46)	Serious	n/a	Serious	Not serious		LOW	
1 study (Davis 2002) F	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

P.2.27 Neurosyphilis versus not neurosyphilis

P.2.27.1 CSF EIA

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
1 atudy (Chan 2011)	Dragnactive	4E	0.07 (0.69, 4.00)	0.47 (0.20, 0.64)	LR+	1.82 (1.28, 2.58)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Chan 2014) F	Prospective	45	0.97 (0.68, 1.00)	0.47 (0.30, 0.64)	LR-	0.06 (0.00, 0.94)	Not serious	n/a	Not serious	Serious	-	MODERATE

P.2.27.2 FTA-ABS

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
4 at the (Duraness 2010)	Datasasastina	400	0.07 (0.05, 4.00)	0.44 (0.00, 0.00)	LR+	1.09 (0.97, 1.22)	Not serious	n/a	Serious	Not serious		MODERATE	
1 study (Dumaresq 2013)	Retrospective	100	0.97 (0.65, 1.00)	0.11 (0.06, 0.20)	LR-	0.28 (0.02, 4.62)	Not serious	n/a	Serious	V. serious	-	VERY LOW	
Notes on indirectness Dumaresq 2013: >99% men	Notes on indirectness Dumaresq 2013: >99% men who have sex with men												

P.2.27.3 INNO-LIA

ININO-LIA				1								
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE							•					
4 -tudy (Dumanaa 2012)	Detreseestive	00	0.00 (0.00 4.00)	0.42 (0.00 0.24)	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												
Dumaresq 2013: >99% me	n who have sex w	ith men										

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Dumarasa 2012)	Detroopediye	100	0.40 (0.10, 0.65)	0.64 (0.54, 0.74)	LR+	1.03 (0.53, 2.02)	Not serious	n/a	Serious	Serious		LOW
1 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 Dumaresq 2013: >99% me	n who have sex w	rith men										

P.2.27.5 TPPA

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 atd. (Dumanaa 2042)	Detrees estive	100	0.07 (0.44, 0.05)	0.47 (0.07, 0.50)	LR+	1.26 (0.84, 1.90)	Not serious	n/a	Serious	Not serious		MODERATE
1 study (Dumaresq 2013)	Retrospective	100	0.67 (0.41, 0.85)	0.47 (0.37, 0.58)	LR-	0.71 (0.33, 1.50)	Not serious	n/a	Serious	Serious	-	LOW
Notes on indirectness Dumaresq 2013: >99% me	n who have sex w	ith men										

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P.2.28 PDD and DLB versus other dementias

P.2.28.1 123I-MIBG cardiac scintigraphy

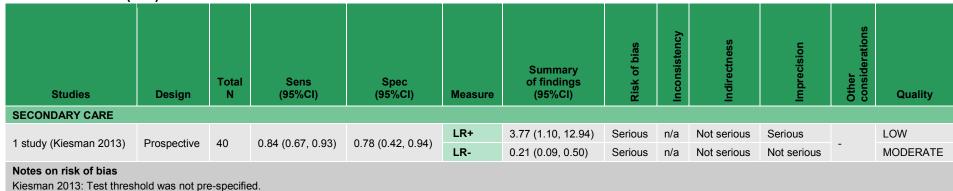
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
1 study (Hanyu	Dragnostiva	96	0.05 (0.93, 0.00)	0.07 (0.76, 0.04)	LR+	7.47 (3.73, 14.98)	Serious	n/a	Not serious	Not serious		MODERATE
2006)		90	0.95 (0.82, 0.99)	0.87 (0.76, 0.94)	LR-	0.06 (0.01, 0.22)	Serious	n/a	Not serious	Not serious	-	MODERATE

Notes on risk of bias

Hanyu 2006: It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard and whether the reference standard results were interpreted without knowledge of the results of the index test.

P.2.29 PDD versus non-PDD

P.2.29.1 FCSRT-IR 3- FR (≤22)



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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
4 atudu (Kiaaman 2042)	Description	40	0.00 (0.00, 0.00)	0.05 (0.52, 4.00)	LR+	15.94 (1.06, 238.88)	Serious	n/a	Not serious	Serious		LOW	
1 study (Kiesman 2013)	Prospective	40	0.80 (0.62, 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													

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE					•		•					
4 - 1 - 1 - (16 0040)	Description	40	0.04 (0.70, 0.00)	0.70 (0.40, 0.04)	LR+	4.21 (1.24, 14.34)	Serious	n/a	Not serious	Serious		LOW
1 study (Kiesman 2013)	Prospective	40	0.94 (0.78, 0.98)	0.78 (0.42, 0.94)	LR-	0.08 (0.02, 0.33)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of bias Kiesman 2013: Test thres	hold was not pro	e-specifie	ed.									

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Kissman 2012)	Droopostivo	40	0.09 (0.70, 4.00)	0.45 (0.40, 0.74)	LR+	1.79 (1.02, 3.14)	Serious	n/a	Not serious	Serious		LOW
1 study (Kiesman 2013)	Prospective	40	0.98 (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 thresh	old was not pre-s	pecified.										

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Kisaman 2012)	Droopostiyo	40	0.00 (0.74, 0.07)	0.79 (0.42, 0.04)	LR+	4.06 (1.19, 13.87)	Serious	n/a	Not serious	Serious		LOW	
1 study (Kiesman 2013)	Prospective	40	0.90 (0.74, 0.97)	0.78 (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 thres	Notes on risk of bias Kiesman 2013: Test threshold was not pre-specified.												

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P.2.30 PPA versus non-PPA

P.2.30.1 FDG-PET

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
	D "	100	0.50 (0.40.0.04)	0.00 (0.00 4.00)	LR+	97.00 (5.54, 1697.47)	Not serious	n/a	Serious	Not serious		MODERATE
1 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
Notes on indirectness												

Panegyres 2009: The study only recruited people with early onset dementia (<65 years old).

P.2.31 VaD and mixed dementias versus AD

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
1 study (Siritho	Dunnanastiva	24.4	0.00 (0.77, 0.00)	0.72 (0.05, 0.00)	LR+	3.17 (2.36, 4.25)	V. serious	n/a	Not serious	Not serious		LOW
2006)		0.00 (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.

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

P.2.32.1 ADDTC (possible)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Cold 2002)	Detropportive	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
1 Study (G010 2002)	study (Gold 2002) Retrospective 89	09	0.70 (0.47, 0.86)	0.78 (0.67, 0.86)	LR-	0.38 (0.19, 0.76)	Not serious	n/a	Not serious	Serious	-	MODERATE

P.2.32.2 ADDTC (probable)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Cald 2002)	Potropoetivo	89	0.25 (0.11, 0.49)	0.01 (0.92, 0.06)	LR+	2.88 (0.98, 8.44)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Gold 2002) Ret	Retrospective	09	0.25 (0.11, 0.48)	0.91 (0.82, 0.96)	LR-	0.82 (0.63, 1.07)	Not serious	n/a	Not serious	Not serious	-	HIGH

P.2.32.3 ADDTC criteria

ABB 10 criteria			1									
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 -tudy (Db-tt- 2007)	Detuces estive	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
1 study (Bachetta 2007)	Retrospective	110	0.58 (0.42, 0.73)	0.74 (0.63, 0.83)	LR-	0.56 (0.37, 0.84)	Not serious	n/a	Serious	Serious	-	LOW
Notes on indirectness												
Bachetta 2007: Participant	s were selected to	be >90 ye	ears old									

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Bashetta 2007)	Detroppostive	110	0.56 (0.30, 0.71)	0.66 (0.55, 0.76)	LR+	1.64 (1.07, 2.53)	Not serious	n/a	Serious	Serious		LOW
1 study (Bachetta 2007)	Retrospective	110	0.56 (0.39, 0.71)	0.66 (0.55, 0.76)	LR-	0.67 (0.45, 1.00)	Not serious	n/a	Serious	Serious	-	LOW
Notes on indirectness Bachetta 2007: Participants	s were selected to	be >90 ye	ears old									

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P.2.32.5 NINDS-AIREN (possible)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Cold 2002)	Detropportivo	89	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
1 study (Gold 2002)	Retrospective	09	0.55 (0.34, 0.75)	0.84 (0.73, 0.91)	LR-	0.54 (0.33, 0.88)	Not serious	n/a	Not serious	Serious	-	MODERATE

P.2.32.6 NINDS-AIREN (probable)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Cald 2002)	Detroppostive	90	0.20 (0.09, 0.42)	0.03 (0.04, 0.07)	LR+	2.76 (0.82, 9.32)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Gold 2002)	Retrospective	89	0.20 (0.08, 0.43)	0.93 (0.84, 0.97)	LR-	0.86 (0.69, 1.08)	Not serious	n/a	Not serious	Not serious	-	HIGH

P.2.32.7 NINDS-AIREN criteria

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Bashetta 2007)	Detroppostive	110	0.56 (0.39, 0.71)	0.72 (0.62, 0.92)	LR+	2.06 (1.28, 3.31)	Not serious	n/a	Serious	Serious		LOW
1 study (Bachetta 2007)	Retrospective	110	0.56 (0.59, 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: Participant	s were selected to	be >90 ye	ears old									

P.2.33 VaD versus AD

P.2.33.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
2 studies (Launes 1991;	2 ×	97	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 (0.64, 0.86)	LR-	0.33 (0.18, 0.60)	Serious	Not serious	Not serious	Serious	-	LOW
Notes on risk of bias Launes 1991: Subgroup analys McMurdo 1994: Subgroup anal												

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P.2.33.2 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Prospective	247	0.71 (0.50,	0.97 (0.94,	LR+	22.57 (10.42, 48.88)	Serious	n/a	Not serious	Not serious	-	MODERATE
(Koikkalainen 2016)	,		0.85)	0.98)	LR-	0.30 (0.16, 0.56)	Serious	n/a	Not serious	Serious		LOW

Notes on risk of bias

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

P.2.34 VaD versus DLB

P.2.34.1 MRI

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

P.2.35 VaD versus FTD

P.2.35.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
atudy (Lauras 1001)	Dragnastiva	38	0.76 (0.59, 0.97)	0.60 (0.30, 0.00)	LR+	1.89 (0.64, 5.64)	Serious	n/a	Not serious	Serious		LOW
1 study (Launes 1991)	Prospective	30	0.76 (0.58, 0.87)	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 analysis used with >10% study population excluded.

P.2.35.2 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Prospective	116	0.71 (0.50,	0.96 (0.89,	LR+	16.29 (6.04, 43.94)	Serious	n/a	Not serious	Not serious	_	MODERATE
(Koikkalainen 2016)	,		0.85)	0.98)	LR-	0.30 (0.16, 0.57)	Serious	n/a	Not serious	Serious		LOW

Notes on risk of bias

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

P.2.36 VaD versus non-VaD dementia plus unclassifiable

P.2.36.1 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Boutoleau-	Prospective	56	0.88 (0.46, 0.98)	0.75 (0.61, 0.95)	LR+	3.50 (2.01, 6.10)	Serious	n/a	Not serious	Not serious		MODERATE
Bretonniere 2012)	Prospective	50	0.66 (0.46, 0.96)	0.75 (0.61, 0.85)	LR-	0.17 (0.03, 1.05)	Serious	n/a	Not serious	Serious	-	LOW

Notes on risk of bias

Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases.

P.2.37 VaD versus non-VaD

P.2.37.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
2 studies (Launes	2 ×	004	0.70 (0.00 0.07)	0.04 (0.40, 0.00)	LR+	2.16 (1.05, 4.45)	Not serious	Serious	Not serious	Serious		LOW
1991; McMurdo 1994)	prospective	204	0.76 (0.60, 0.87)	0.64 (0.40, 0.83)	LR-	0.44 (0.24, 0.81)	Not serious	Not serious	Not serious	Serious	-	MODERATE

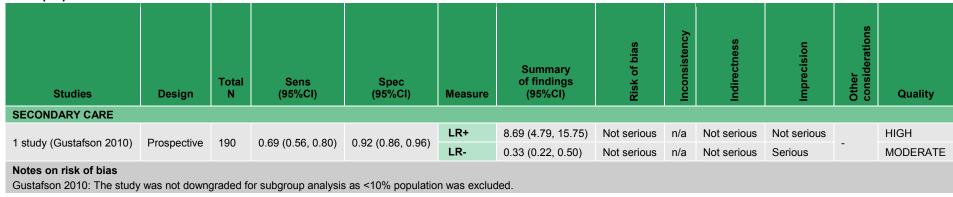
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P.2.38 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen	D	504	0.74 (0.50, 0.05)	0.00 (0.04, 0.00)	LR+	18.89 (11.22, 31.80)	Not serious	n/a	Not serious	Not serious		HIGH
2016)	Prospective	504	0.71 (0.50, 0.85)	0.96 (0.94, 0.98)	LR-	0.30 (0.16, 0.57)	Not serious	n/a	Not serious	Serious	-	MODERATE

P.2.39 VaD versus other dementias

P.2.39.1 HIS (≥7)



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P.2.39.2 MRI

1411 X1												
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Prospective	386	0.71 (0.50,	0.96 (0.94,	LR+	19.72 (10.91, 35.66)	Serious	n/a	Not serious	Not serious	_	MODERATE
(Koikkalainen 2016)	·		0.85)	0.98)	LR-	0.30 (0.16, 0.56)	Serious	n/a	Not serious	Serious		LOW

Notes on risk of bias

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

P.3 Meta-analyses

P.3.1 Dementia versus no dementia

P.3.1.1 ACE (<83)

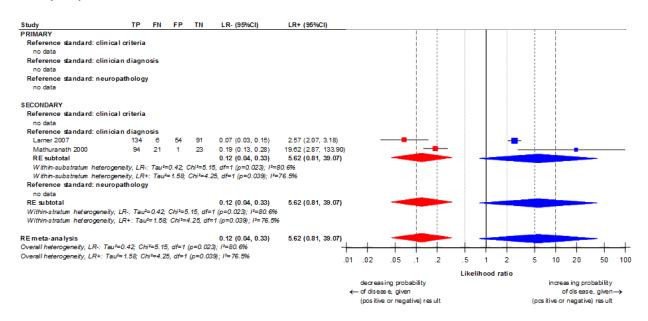


Figure 1 Dementia versus no dementia: ACE (<83) – forest plot: likelihood ratios

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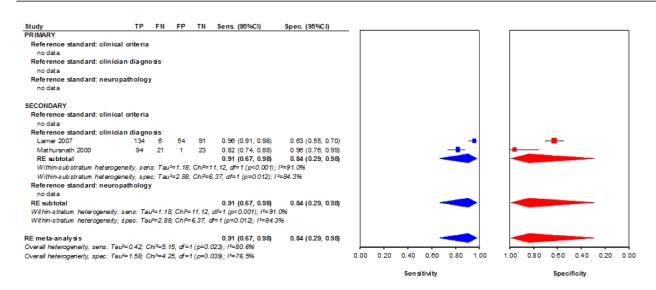


Figure 2 Dementia versus no dementia: ACE (<83) – forest plot: sensitivity and specificity

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P.3.1.2 ACE (<88)

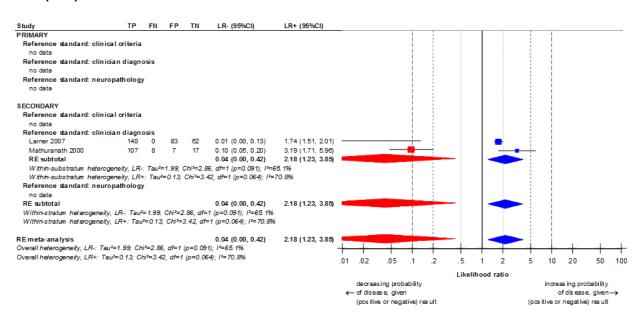


Figure 3 Dementia versus no dementia: ACE (<88) – forest plot: likelihood ratios

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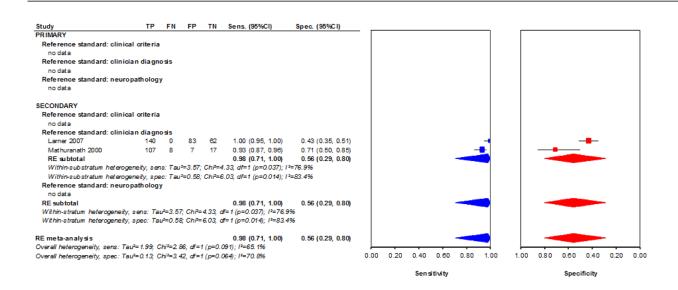


Figure 4 Dementia versus no dementia: ACE (<88) – forest plot: sensitivity and specificity

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P.3.1.3 ACE-R (<83)

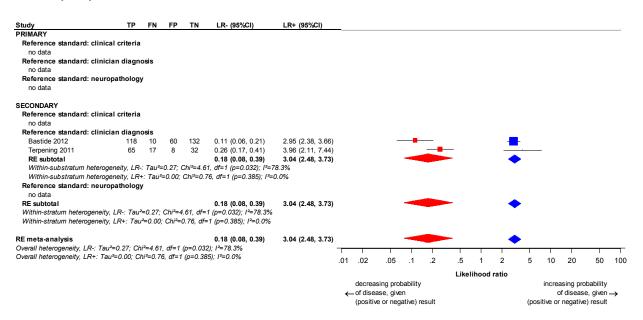


Figure 5 Dementia versus no dementia: ACE-R (<83) – forest plot: likelihood ratios

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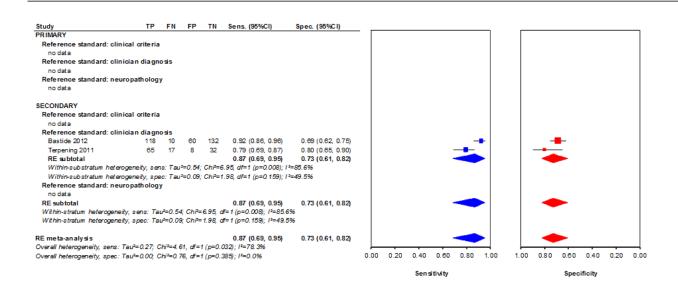


Figure 6 Dementia versus no dementia: ACE-R (<83) – forest plot: sensitivity and specificity

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P.3.1.4 Clock Drawing Test, CDT, Shulman scoring method (>2)

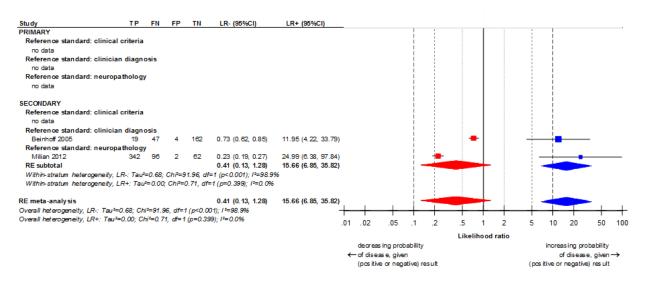


Figure 7 Dementia versus no dementia: CDT (>2) - forest plot: likelihood ratios

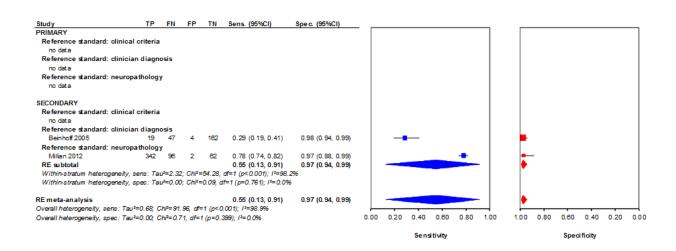


Figure 8 Dementia versus no dementia: CDT (>2) – forest plot: sensitivity and specificity

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P.3.1.5 FDG-PET

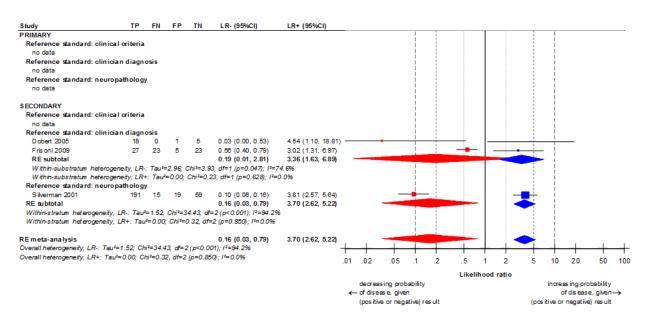


Figure 9 Dementia versus no dementia: FDG-PET – forest plot: likelihood ratios

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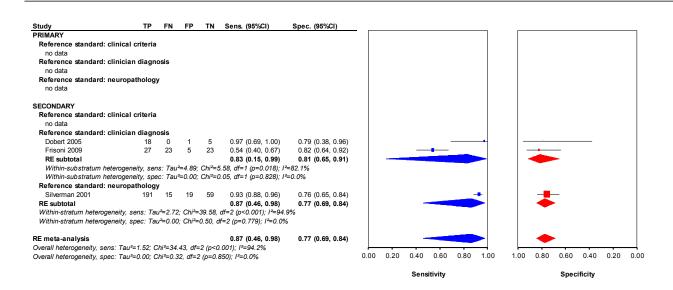


Figure 10Dementia versus no dementia: FDG-PET – forest plot: sensitivity and specificity

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P.3.1.6 IQCODE (16 item, >3.5)

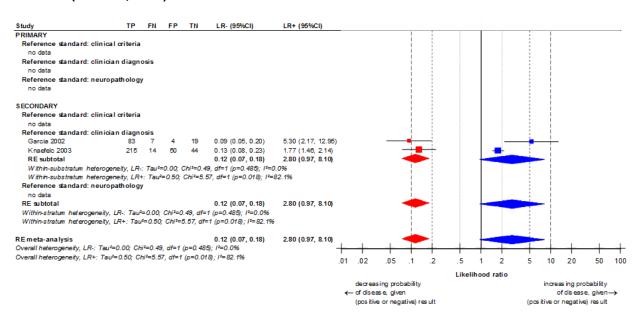


Figure 11Dementia versus no dementia: IQCODE (16 item, >3.5) – forest plot: likelihood ratios

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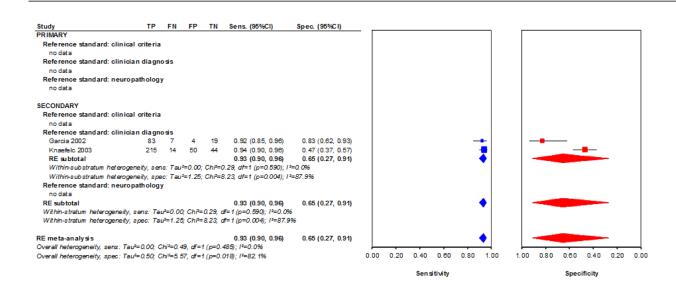


Figure 12Dementia versus no dementia: IQCODE (16 item, >3.5) – forest plot: sensitivity and specificity

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P.3.1.7 IQCODE (26 item, >3.5)

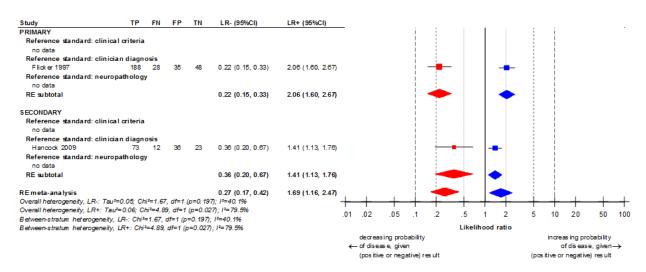


Figure 13Dementia versus no dementia: IQCODE (26 item, >3.5) – forest plot: likelihood ratios

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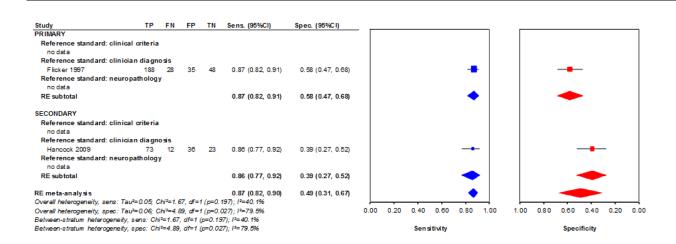


Figure 14Dementia versus no dementia: IQCODE (26 item, >3.5) – forest plot: sensitivity and specificity

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P.3.1.8 IQCODE (26 item, >3.6)

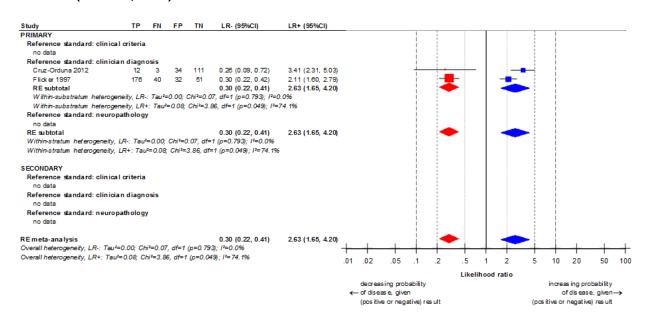


Figure 15Dementia versus no dementia: IQCODE (26 item, >3.6) – forest plot: likelihood ratios

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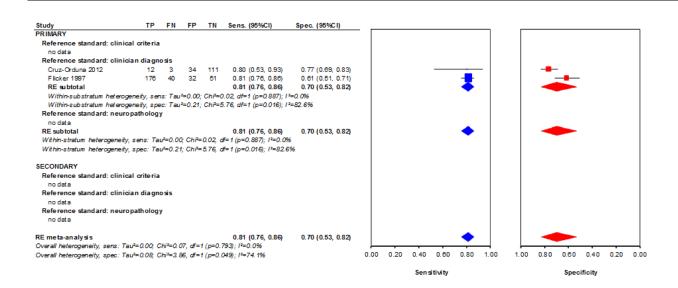


Figure 16Dementia versus no dementia: IQCODE (26 item, >3.6) – forest plot: sensitivity and specificity

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P.3.1.9 MIS (<5)

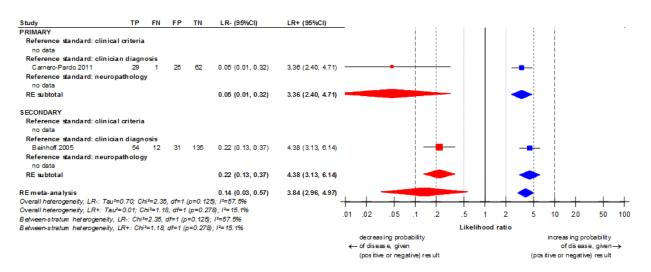


Figure 17 Dementia versus no dementia: MIS (<5) – forest plot: likelihood ratios

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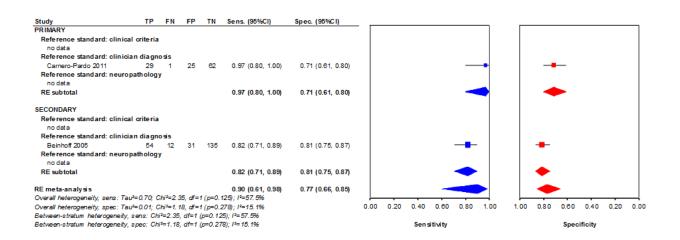


Figure 18Dementia versus no dementia: MIS (<5) – forest plot: sensitivity and specificity

P.3.1.10 MMSE (<18)

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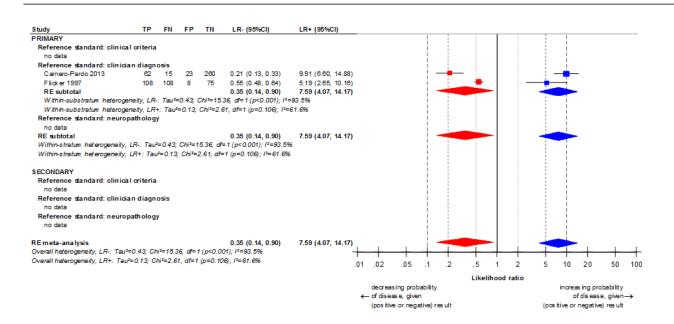


Figure 19Dementia versus no dementia: MMSE (<18) – forest plot: likelihood ratios

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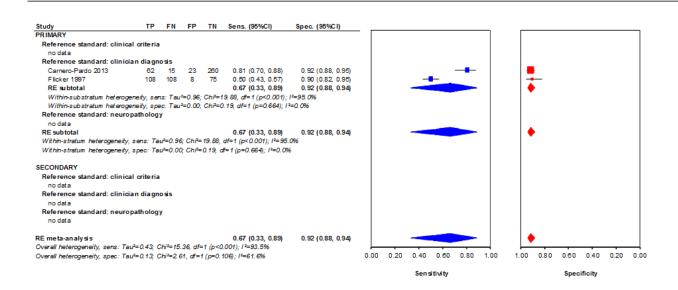


Figure 20Dementia versus no dementia: MMSE (<18) – forest plot: sensitivity and specificity

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P.3.1.11 MMSE (<19)

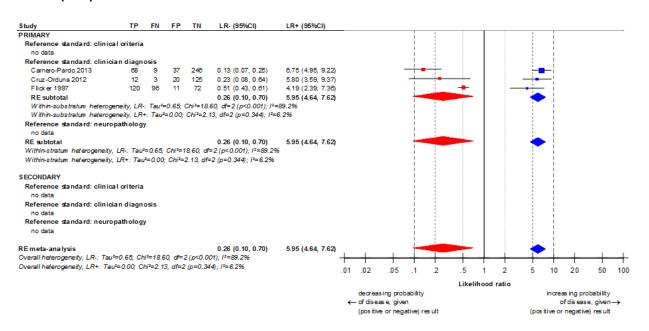


Figure 21 Dementia versus no dementia: MMSE (<19) – forest plot: likelihood ratios

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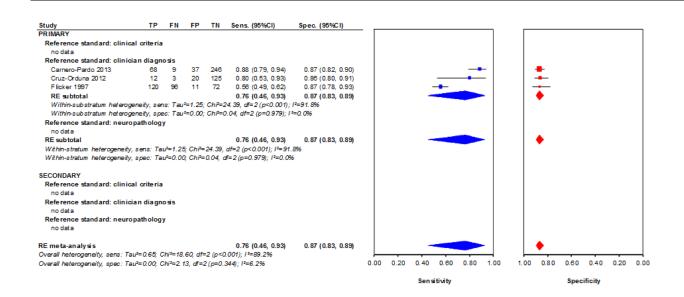


Figure 22Dementia versus no dementia: MMSE (<19) – forest plot: sensitivity and specificity

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P.3.1.12 MMSE (<20)

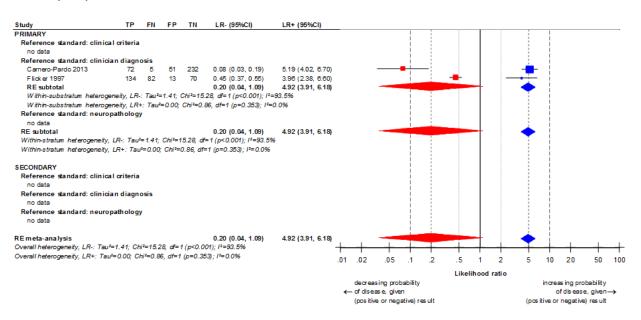


Figure 23Dementia versus no dementia: MMSE (<20) – forest plot: likelihood ratios

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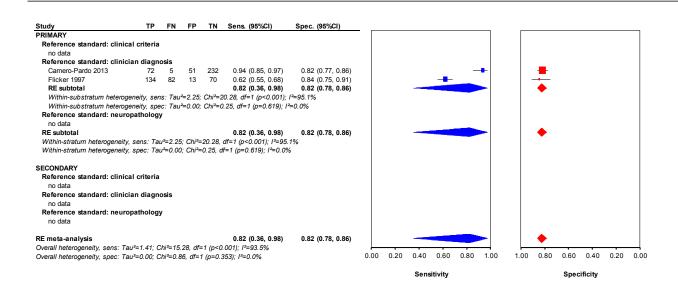


Figure 24Dementia versus no dementia: MMSE (<20) – forest plot: sensitivity and specificity

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P.3.1.13 MMSE (<21)

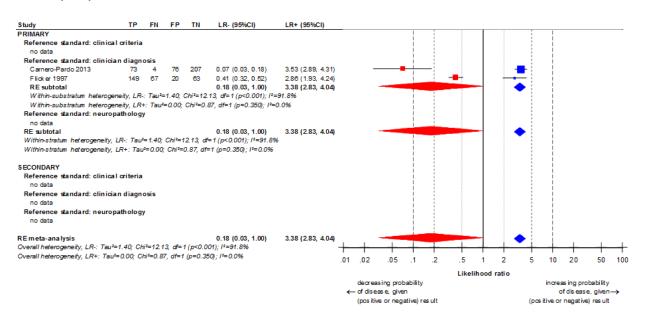


Figure 25Dementia versus no dementia: MMSE (<21) – forest plot: likelihood ratios

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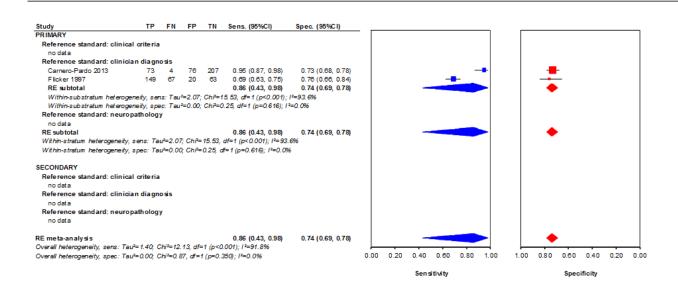


Figure 26Dementia versus no dementia: MMSE (<21) – forest plot: sensitivity and specificity

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P.3.1.14 MMSE (<22)

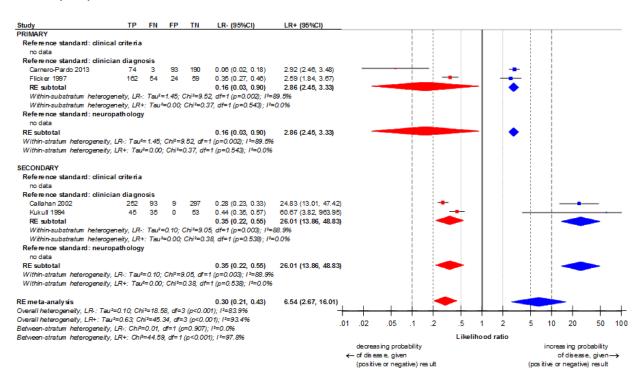


Figure 27Dementia versus no dementia: MMSE (<22) – forest plot: likelihood ratios

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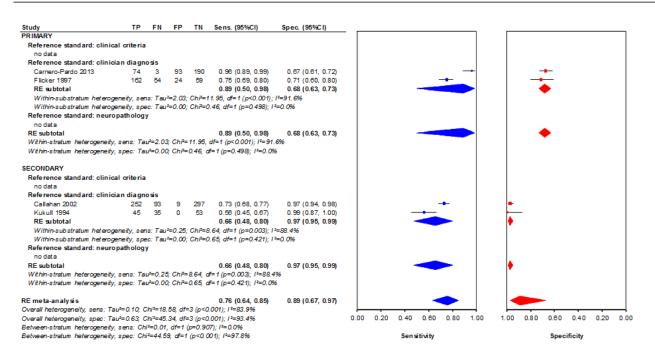


Figure 28Dementia versus no dementia: MMSE (<22) – forest plot: sensitivity and specificity

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P.3.1.15 MMSE (<23)

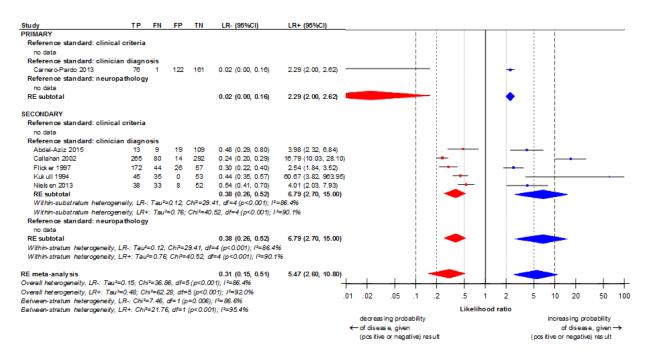


Figure 29Dementia versus no dementia: MMSE (<23) – forest plot: likelihood ratios

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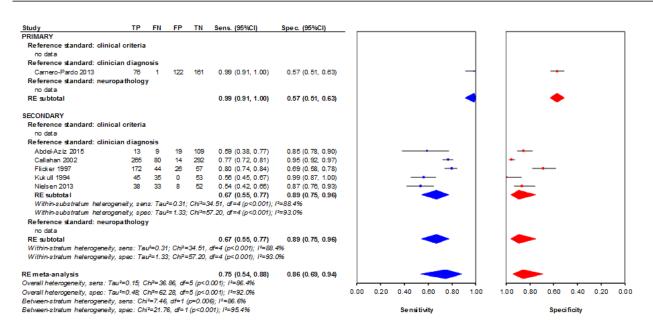


Figure 30Dementia versus no dementia: MMSE (<23) – forest plot: sensitivity and specificity

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P.3.1.16 MMSE (<24)

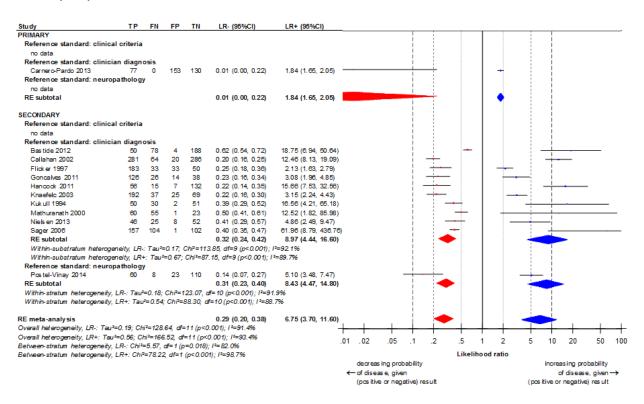


Figure 31 Dementia versus no dementia: MMSE (<24) – forest plot: likelihood ratios

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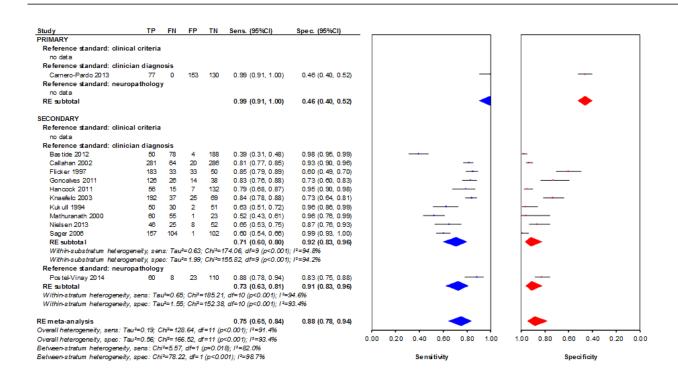


Figure 32Dementia versus no dementia: MMSE (<24) - forest plot: sensitivity and specificity

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P.3.1.17 MMSE (<25)

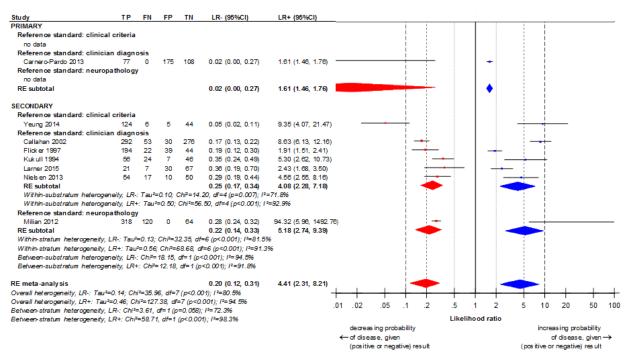


Figure 33Dementia versus no dementia: MMSE (<25) – forest plot: likelihood ratios

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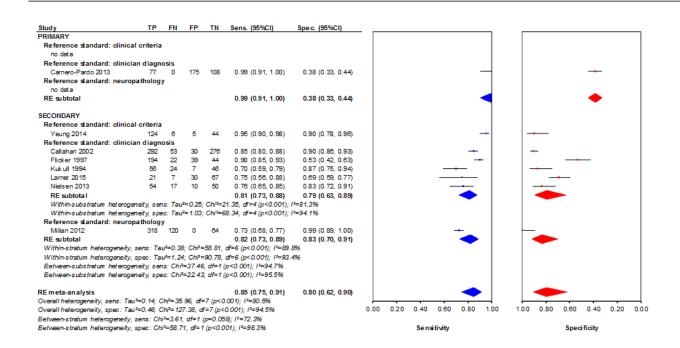


Figure 34Dementia versus no dementia: MMSE (<25) – forest plot: sensitivity and specificity

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P.3.1.18 MMSE (<26)

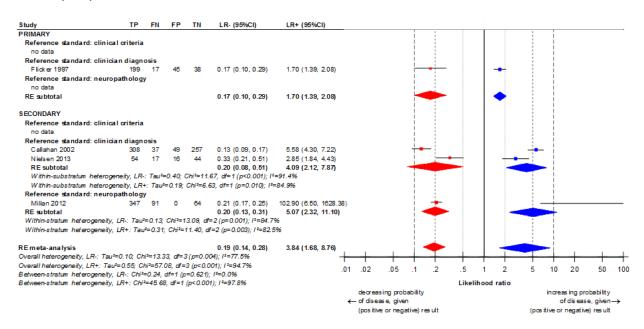


Figure 35Dementia versus no dementia: MMSE (<26) – forest plot: likelihood ratios

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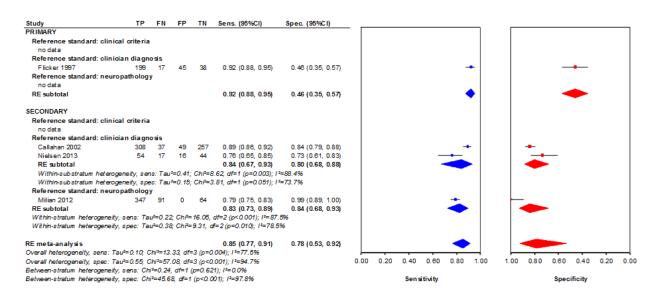


Figure 36Dementia versus no dementia: MMSE (<26) – forest plot: sensitivity and specificity

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P.3.1.19 MMSE (<27)

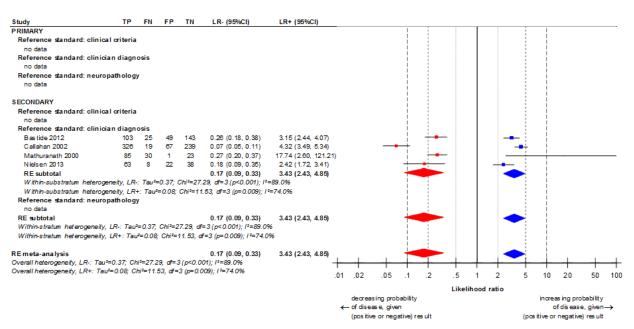


Figure 37Dementia versus no dementia: MMSE (<27) – forest plot: likelihood ratios

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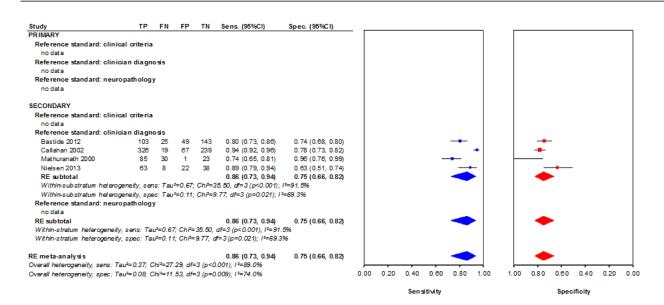


Figure 38Dementia versus no dementia: MMSE (<27) – forest plot: sensitivity and specificity

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P.3.1.20 MMSE (<28)

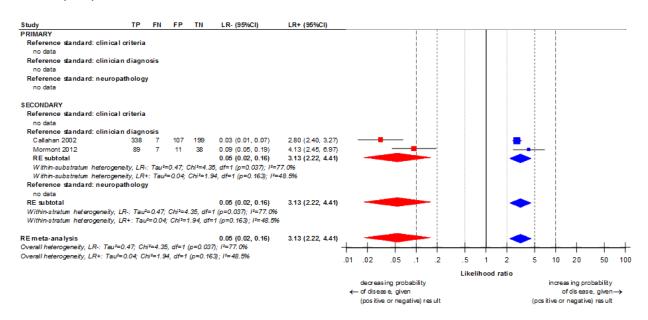


Figure 39Dementia versus no dementia: MMSE (<28) – forest plot: likelihood ratios

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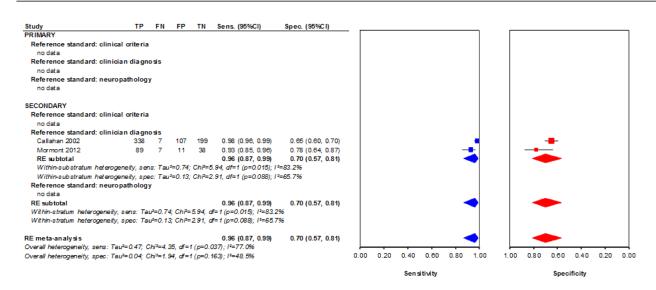


Figure 40Dementia versus no dementia: MMSE (<28) – forest plot: sensitivity and specificity

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P.3.1.21 MoCA (<19)

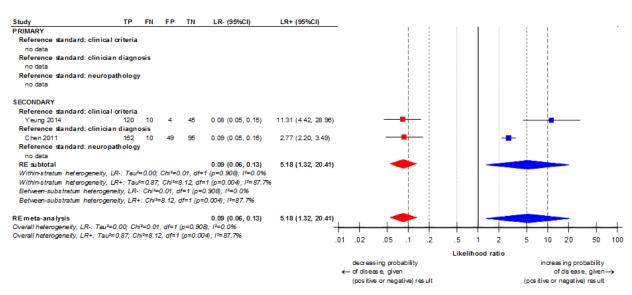


Figure 41 Dementia versus no dementia: MoCA (<19) – forest plot: likelihood ratios

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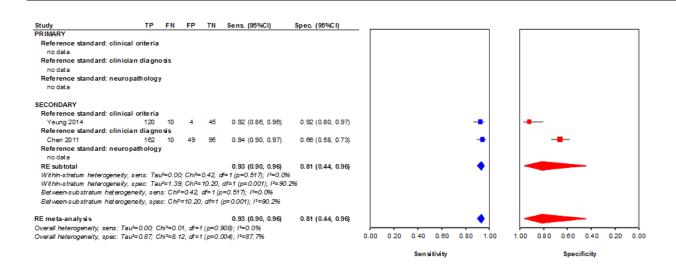


Figure 42Dementia versus no dementia: MoCA (<19) - forest plot: sensitivity and specificity

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P.3.1.22 MRI

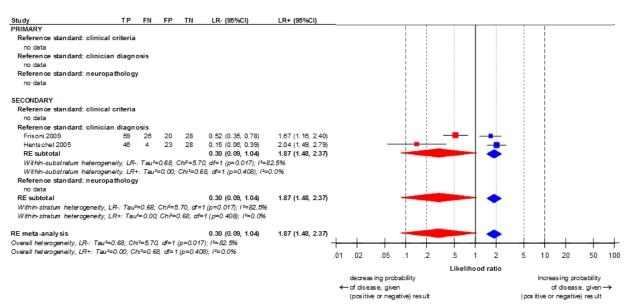


Figure 43 Dementia versus no dementia: MRI - forest plot: likelihood ratios

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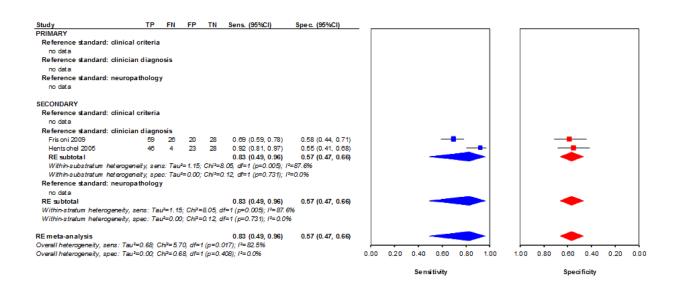


Figure 44 Dementia versus no dementia: MRI – forest plot: sensitivity and specificity

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P.3.2 AD versus FTD

P.3.2.1 99mTc-HMPAO SPECT

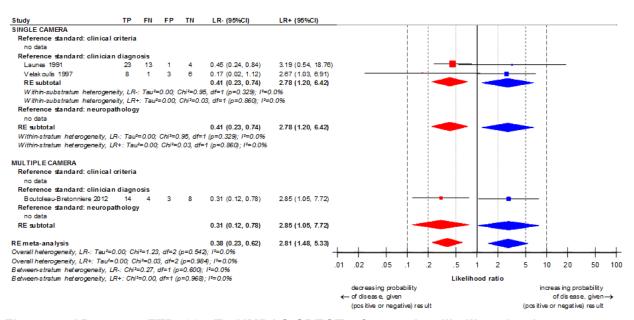


Figure 45AD versus FTD: 99mTc-HMPAO SPECT – forest plot: likelihood ratios

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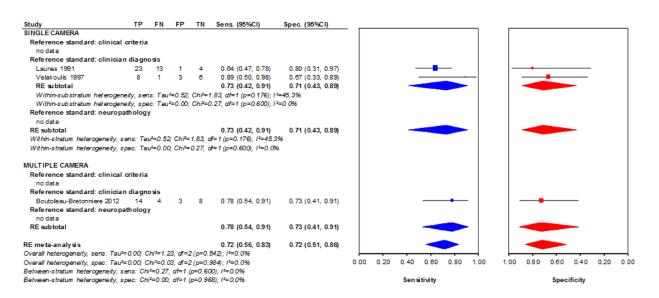


Figure 46AD versus FTD: 99mTc-HMPAO SPECT – forest plot: sensitivity and specificity

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P.3.3 AD versus non-AD

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

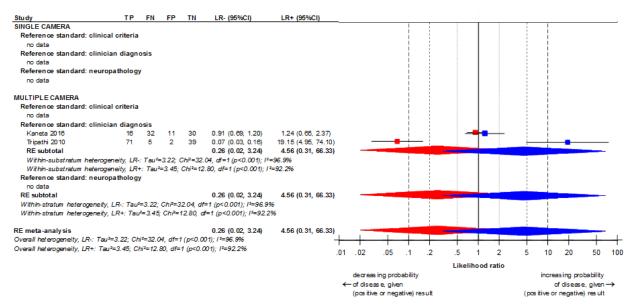


Figure 47AD versus non-AD: 99mTc-ECD SPECT, visual assessment method – forest plot: likelihood ratios

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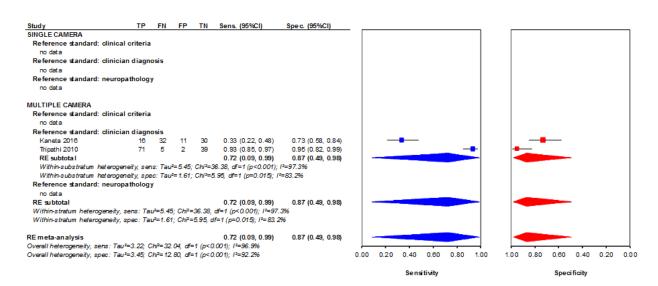


Figure 48AD versus non-AD: 99mTc-ECD SPECT, visual assessment method – forest plot: sensitivity and specificity

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P.3.3.2 99mTc-HMPAO SPECT

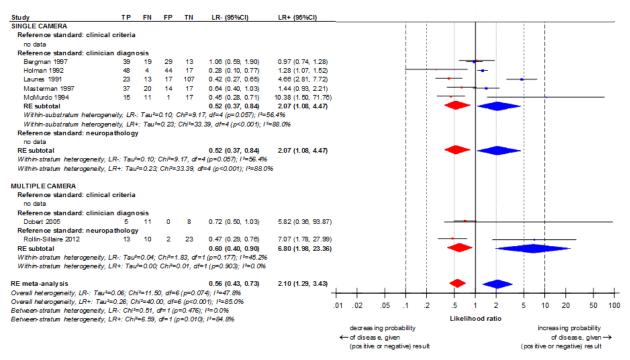


Figure 49AD versus non-AD: 99mTc-HMPAO SPECT – forest plot: likelihood ratios

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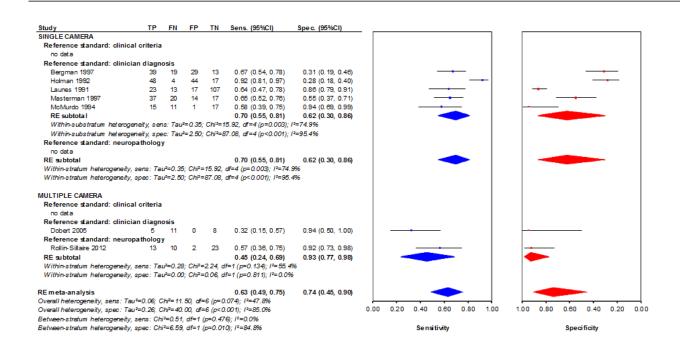


Figure 50AD versus non-AD: 99mTc-HMPAO SPECT – forest plot: sensitivity and specificity

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P.3.3.3 Amyloid Beta 1-42

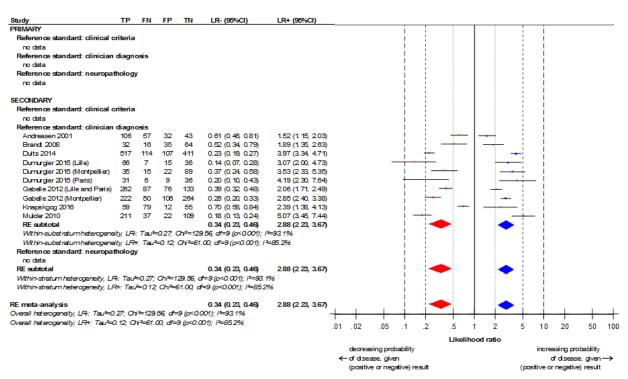


Figure 51AD versus non-AD: Amyloid Beta 1-42 - forest plot: likelihood ratios

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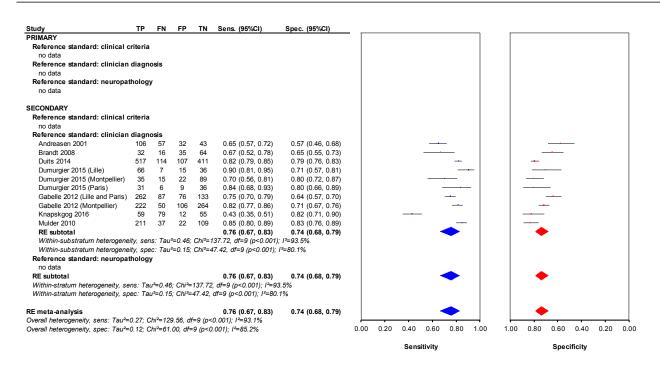


Figure 52 AD versus non-AD: Amyloid Beta 1-42 – forest plot: sensitivity and specificity

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

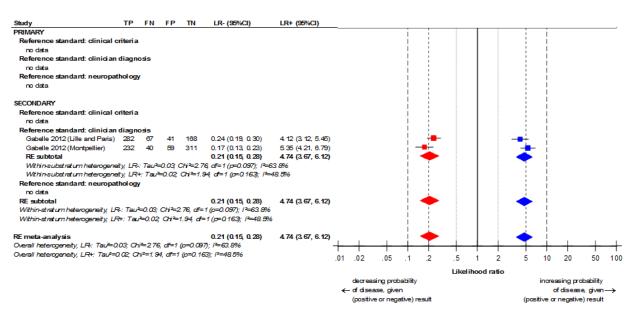


Figure 53AD versus non-AD: Amyloid Beta 1-42/p-tau – forest plot: likelihood ratios

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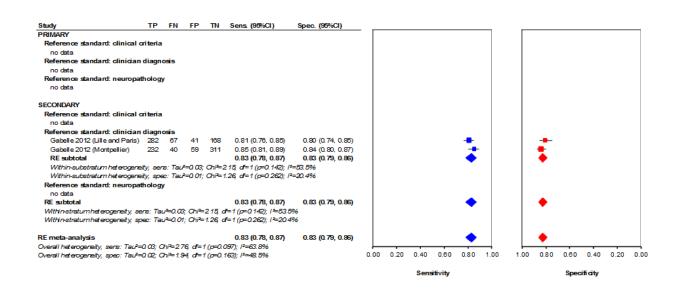


Figure 54AD versus non-AD: Amyloid Beta 1-42/p-tau – forest plot: sensitivity and specificity

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P.3.3.5 Amyloid Beta 1-42/Total Tau

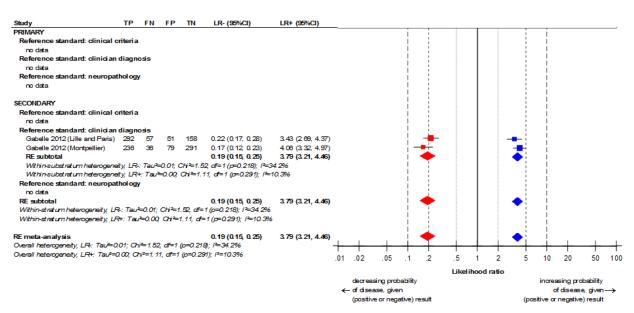


Figure 55AD versus non-AD: Amyloid Beta 1-42/Total Tau – forest plot: likelihood ratios

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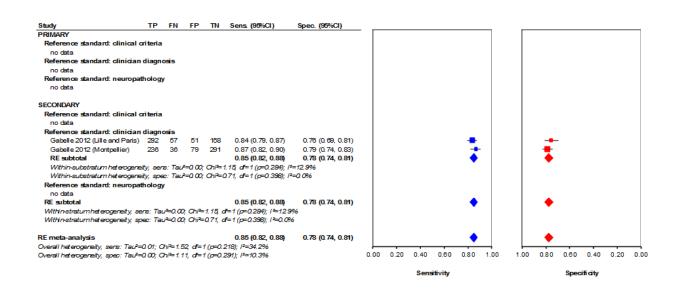


Figure 56AD versus non-AD: Amyloid Beta 1-42/Total Tau – forest plot: sensitivity and specificity

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P.3.3.6 Amyloid Beta 42/40

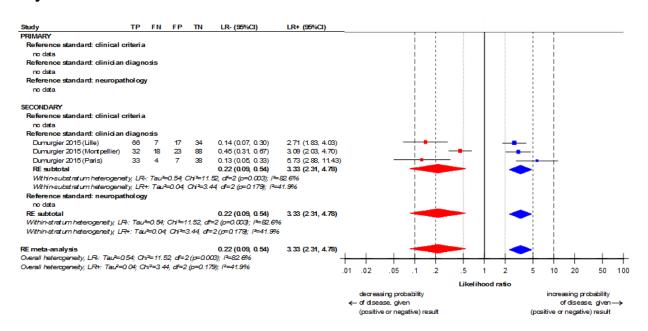


Figure 57AD versus non-AD: Amyloid Beta 42/40 – forest plot: likelihood ratios

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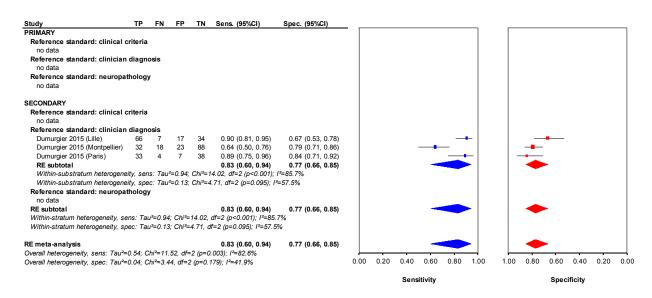


Figure 58AD versus non-AD: Amyloid Beta 42/40 - forest plot: sensitivity and specificity

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

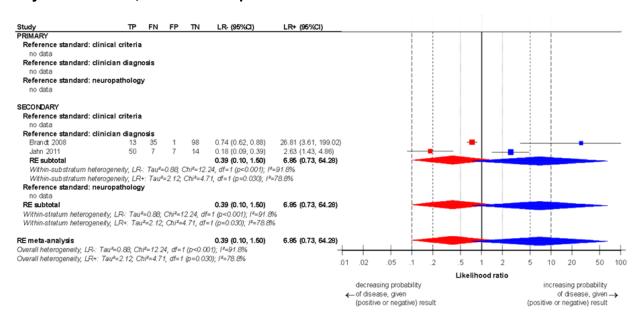


Figure 59: AD versus non-AD: Amyloid Beta 1-42, total tau and p-tau 181- forest plot- likelihood ratios

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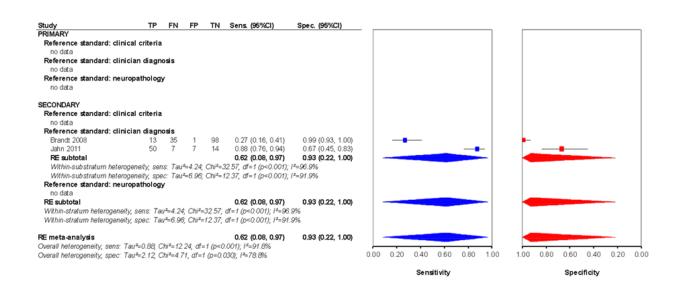


Figure 60 AD versus non-AD: Amyloid Beta 1-42, total tau and p-tau 181- forest plot- sensitivity and specificity

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P.3.3.8 FDG-PET

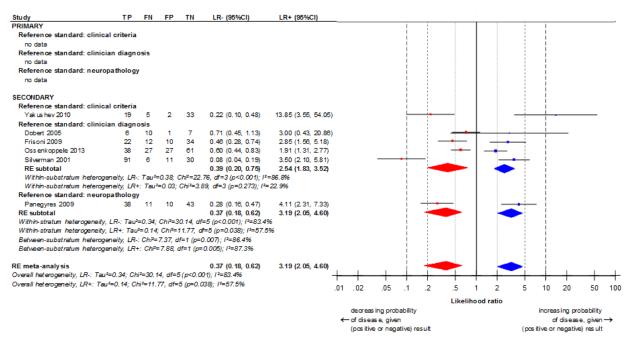


Figure 61AD versus non-AD: FDG-PET - forest plot: likelihood ratios

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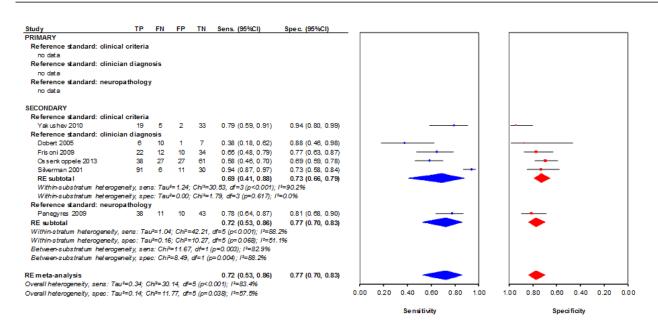


Figure 62AD versus non-AD: FDG-PET – forest plot: sensitivity and specificity

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P.3.3.9 MRI

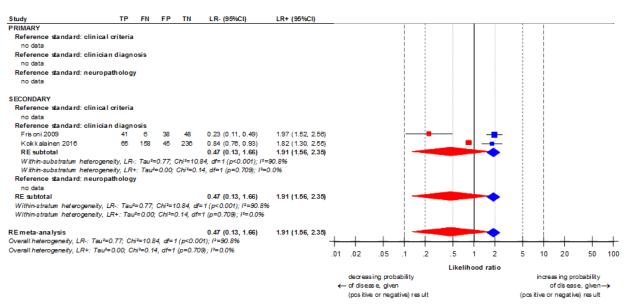


Figure 63AD versus non-AD: MRI - forest plot: likelihood ratios

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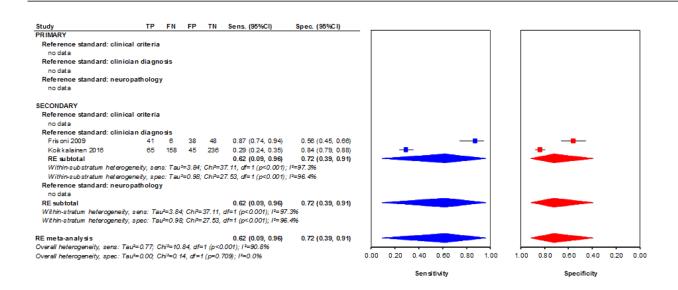


Figure 64AD versus non-AD: MRI – forest plot: sensitivity and specificity

P.3.3.10 p-tau 181

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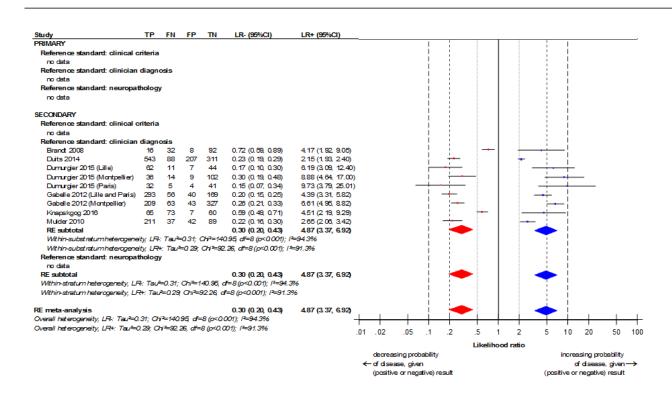


Figure 65AD versus non-AD: p-tau 181 – forest plot: likelihood ratios

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

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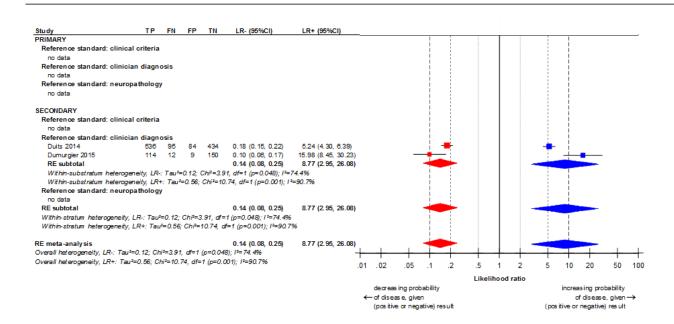


Figure 66AD versus non-AD: p-tau/Amyloid Beta 1-42 – forest plot: likelihood ratios

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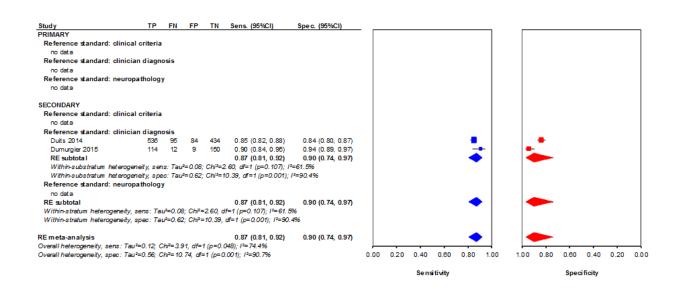
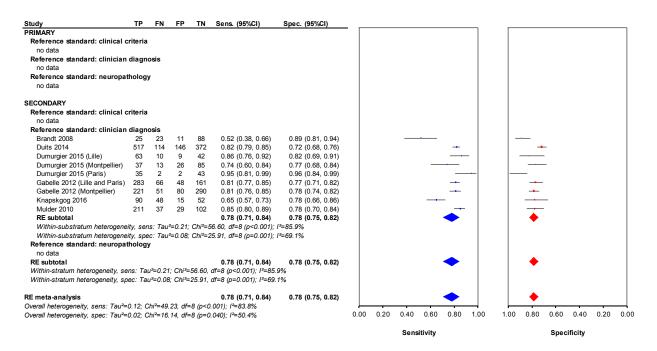


Figure 67AD versus non-AD: p-tau/Amyloid Beta 1-42 – forest plot: sensitivity and specificity

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P.3.3.12 Total Tau



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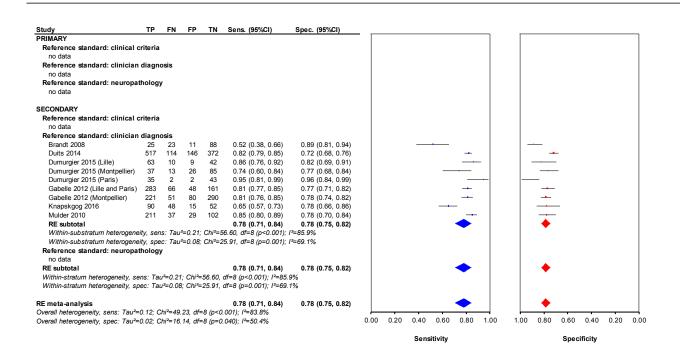


Figure 68AD versus non-AD: Total Tau – forest plot: sensitivity and specificity

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P.3.4 AD versus other dementias

P.3.4.1 Amyloid Beta 1-42

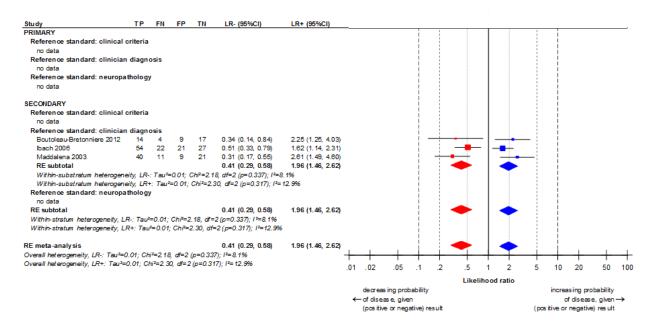


Figure 69AD versus other dementias: Amyloid Beta 1-42 – forest plot: likelihood ratios

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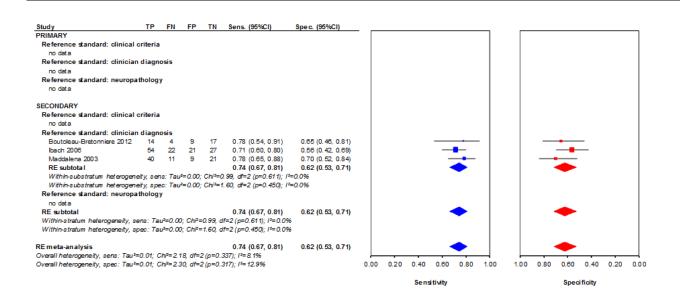


Figure 70AD versus other dementias: Amyloid Beta 1-42 – forest plot: sensitivity and specificity

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P.3.4.2 FDG-PET

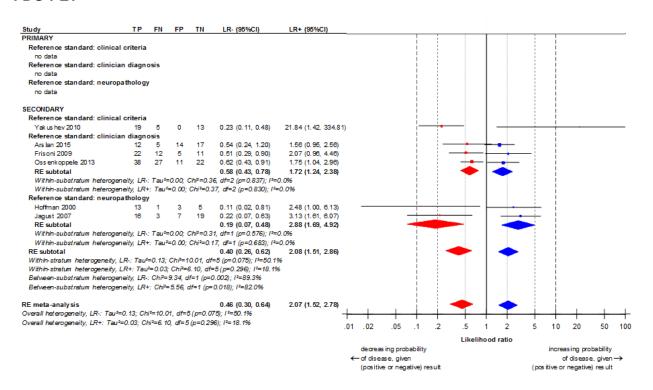


Figure 71AD versus other dementias: FDG-PET – forest plot: likelihood ratios

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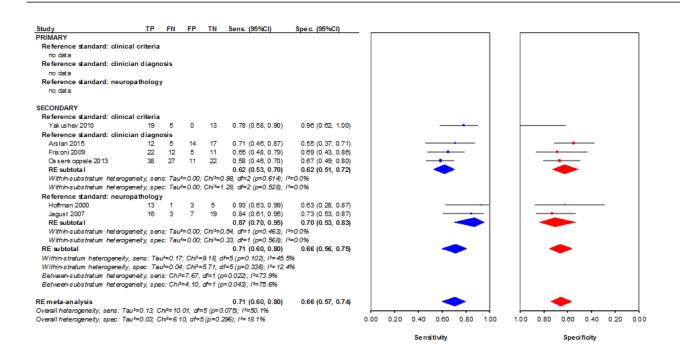


Figure 72AD versus other dementias: FDG-PET – forest plot: sensitivity and specificity

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P.3.4.3 MRI

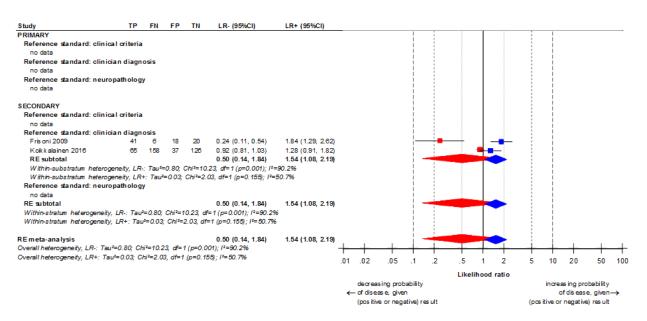


Figure 73AD versus other dementias: MRI – forest plot: likelihood ratios

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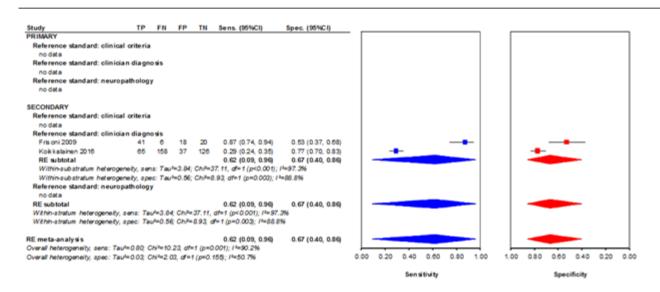


Figure 74AD versus other dementias: MRI – forest plot: sensitivity and specificity

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P.3.4.4 p-tau 181

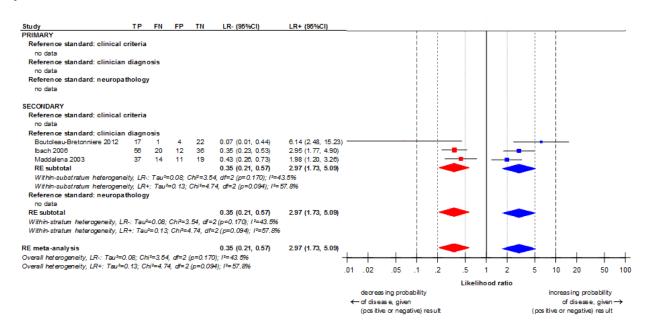


Figure 75AD versus other dementias: p-tau 181 – forest plot: likelihood ratios

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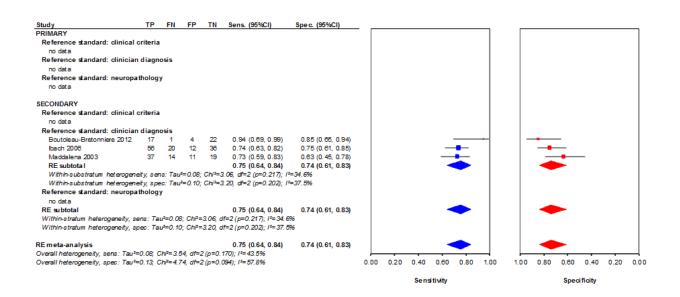
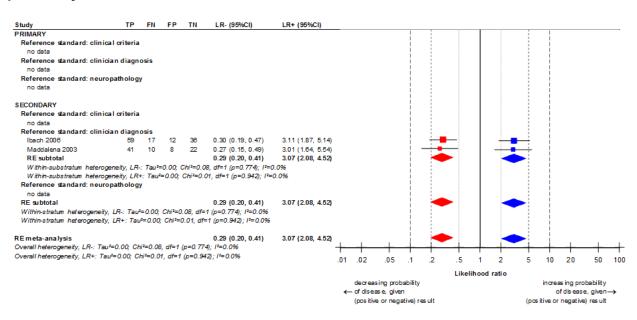
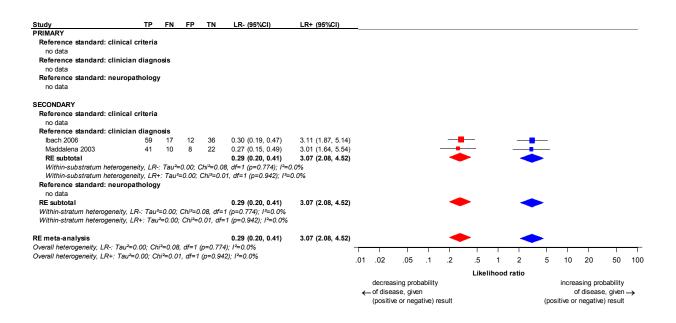


Figure 76AD versus other dementias: p-tau 181 – forest plot: sensitivity and specificity

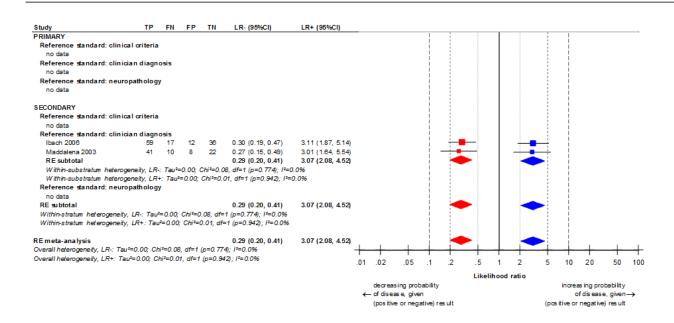
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P.3.4.5 p-tau/Amyloid Beta 1-42





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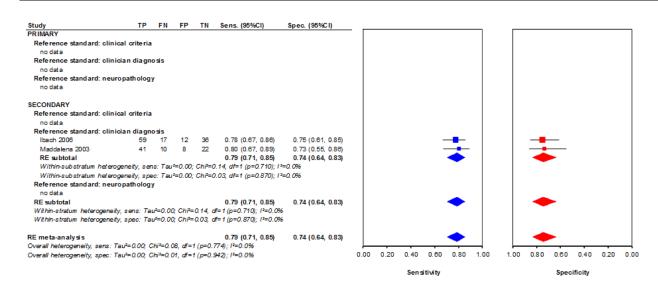


Figure 77AD versus other dementias: p-tau/Amyloid Beta 1-42 – forest plot: sensitivity and specificity

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P.3.4.6 Total tau

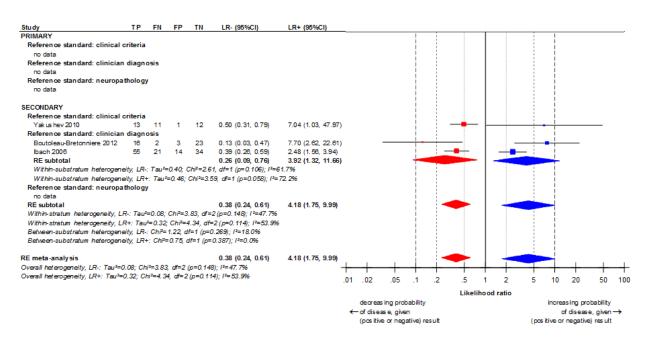


Figure 78AD versus other dementias: Total tau – forest plot: likelihood ratios

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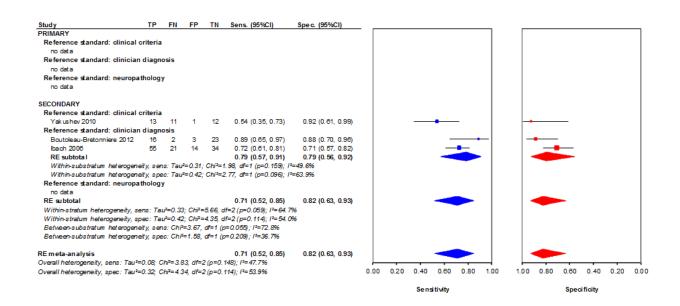


Figure 79AD versus other dementias: Total tau – forest plot: sensitivity and specificity

P.3.5 AD versus VaD

P.3.5.1 99mTc-HMPAO SPECT

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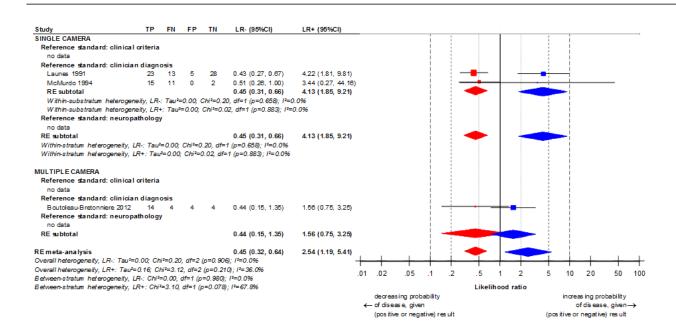


Figure 80AD versus VaD: 99mTc-HMPAO SPECT - forest plot: likelihood ratios

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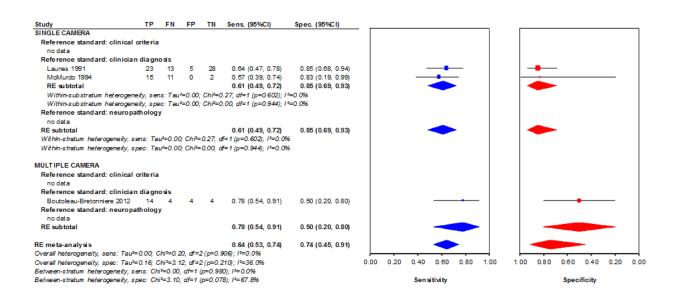


Figure 81AD versus VaD: 99mTc-HMPAO SPECT – forest plot: sensitivity and specificity

P.3.6 CJD versus non-CJD

P.3.6.1 CSF 14-3-3 ELISA

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Appendix P: Diagnosis evidence tables & GRADE

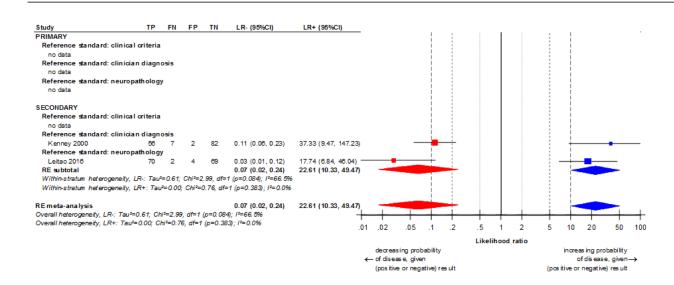


Figure 82CJD versus non-CJD: CSF 14-3-3 ELISA – forest plot: likelihood ratios

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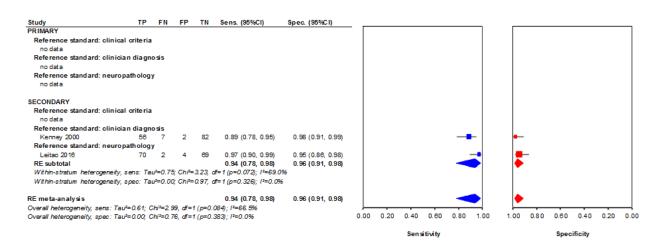


Figure 83CJD versus non-CJD: CSF 14-3-3 ELISA – forest plot: sensitivity and specificity

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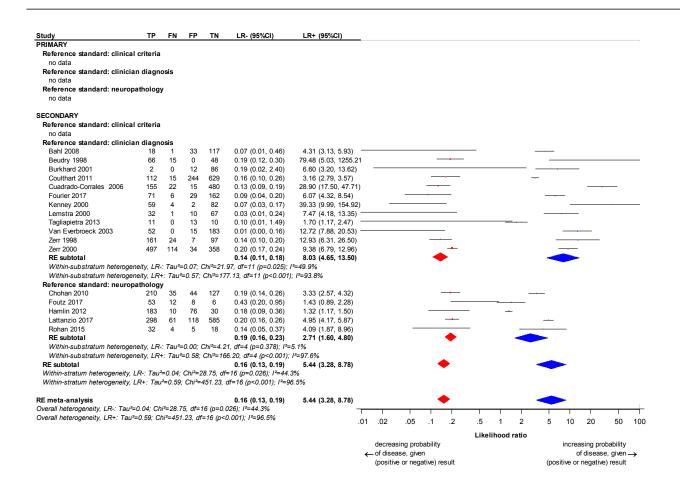


Figure 84CJD versus non-CJD: CSF 14-3-3 ELISA – forest plot: sensitivity and specificity

P.3.6.2 CSF 14-3-3 immunoblotting

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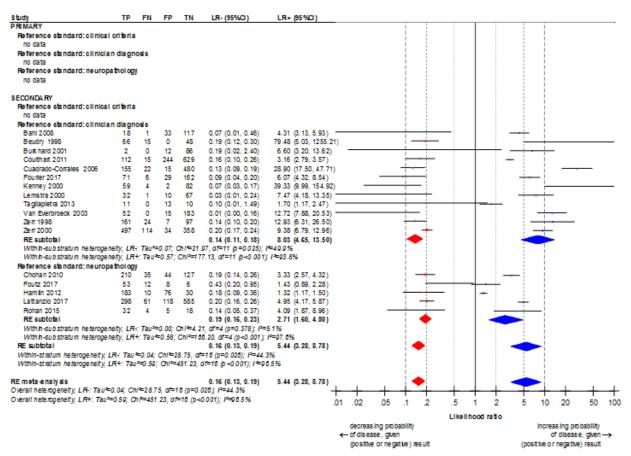


Figure 85CJD versus non-CJD: CSF 14-3-3 immunoblotting – forest plot: likelihood ratios

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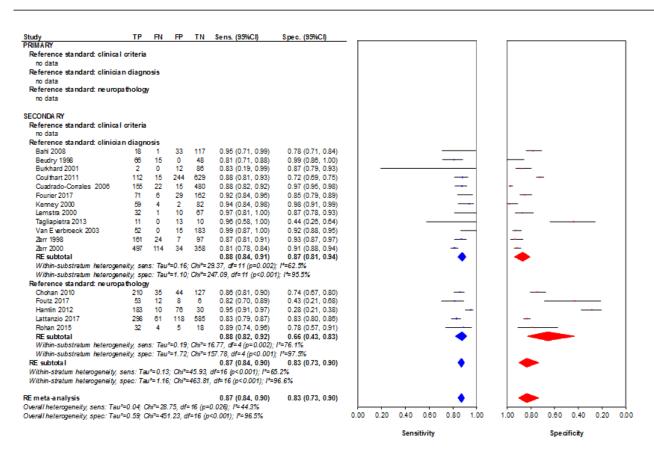


Figure 86CJD versus non-CJD: CSF 14-3-3 immunoblotting – forest plot: sensitivity and specificity

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P.3.6.3 EEG

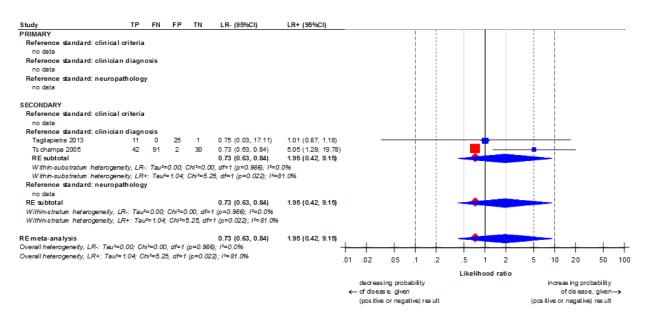


Figure 87CJD versus non-CJD: EEG – forest plot: likelihood ratios

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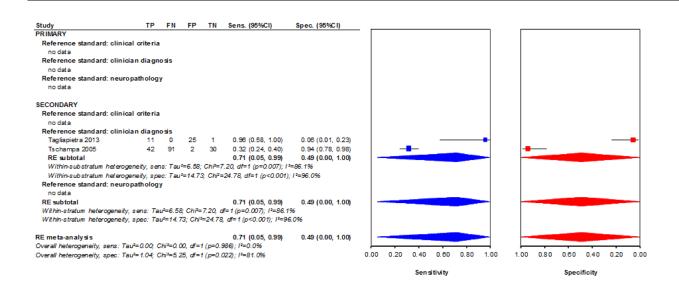


Figure 88CJD versus non-CJD: EEG – forest plot: sensitivity and specificity

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P.3.6.4 MRI

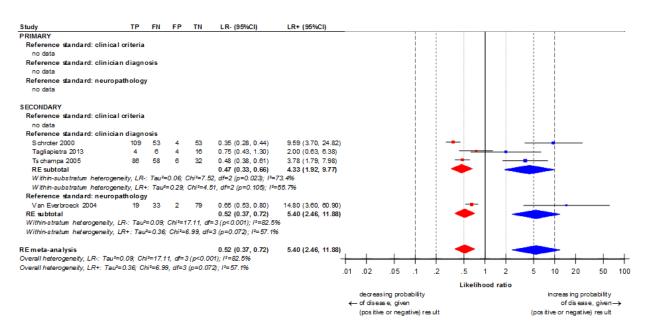


Figure 89CJD versus non-CJD: EEG – forest plot: sensitivity and specificity

P.3.6.5 MRI

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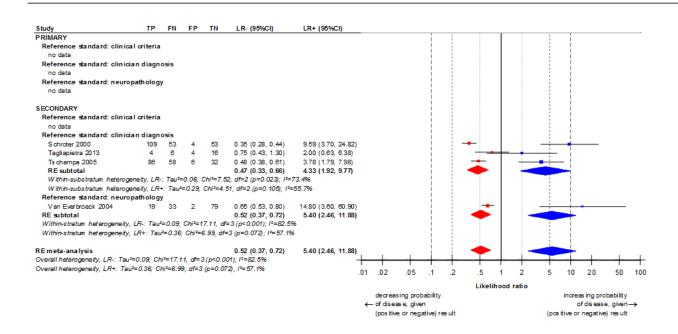


Figure 90CJD versus non-CJD: MRI – forest plot: likelihood ratios

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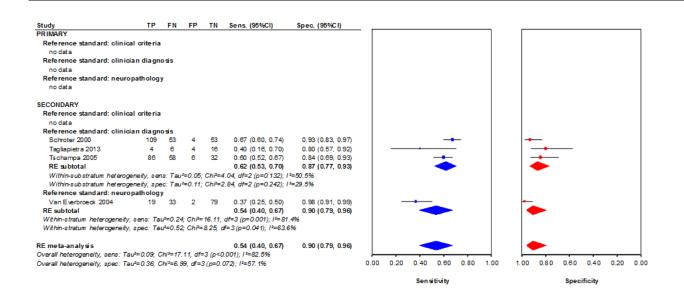


Figure 91CJD versus non-CJD: MRI – forest plot: sensitivity and specificity

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P.3.6.6 Neuron-specific enolase

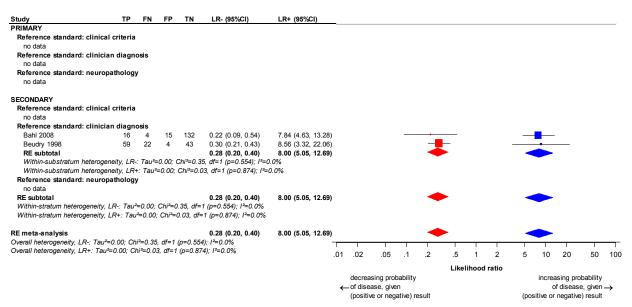


Figure 92CJD versus non-CJD: Neuron-specific enolase – forest plot: likelihood ratios

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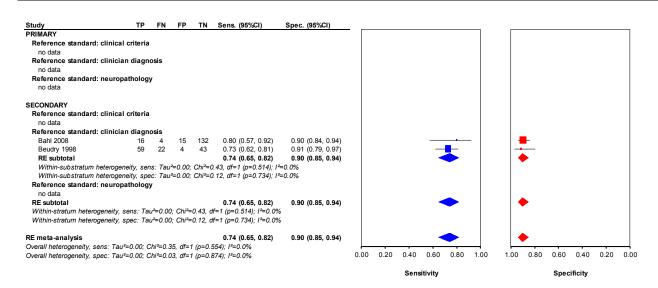


Figure 93CJD versus non-CJD: Neuron-specific enolase – forest plot: sensitivity and specificity

P.3.6.7 p-tau/total tau

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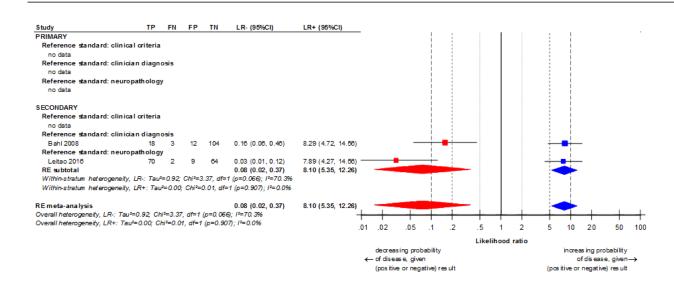


Figure 94CJD versus non-CJD: p-tau/total tau - forest plot: likelihood ratios

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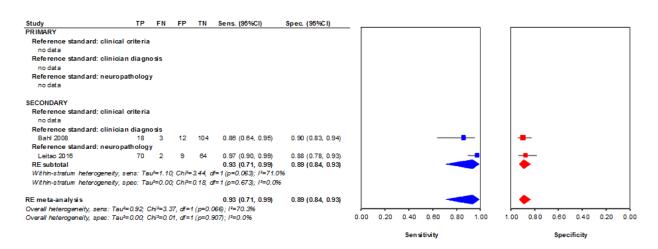


Figure 95CJD versus non-CJD: p-tau/total tau - forest plot: sensitivity and specificity

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P.3.6.8 RT-QuIC

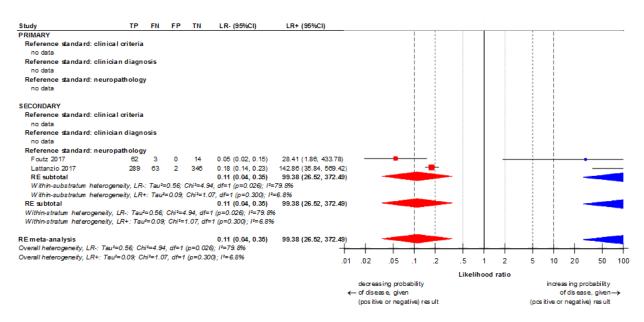


Figure 96CJD versus non-CJD: RT-QuIC – forest plot: likelihood ratios

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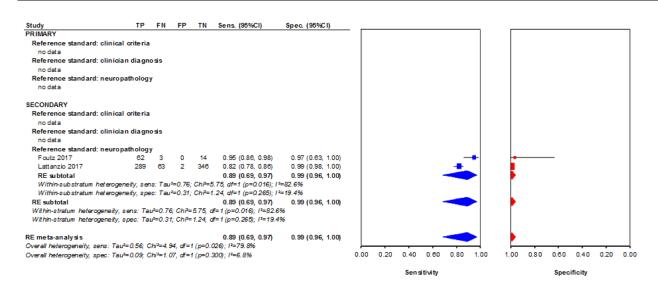


Figure 97CJD versus non-CJD: RT-QuIC – forest plot: sensitivity and specificity

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P.3.6.9 S100B, 2.5ng/ml

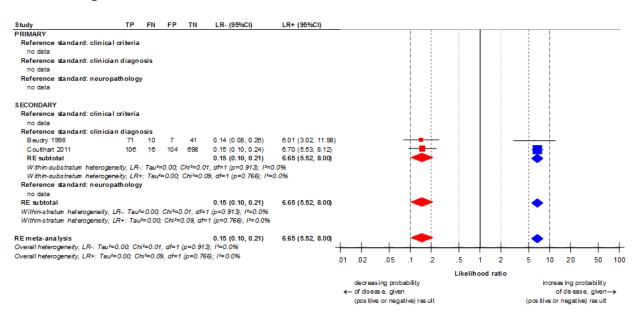


Figure 98CJD versus non-CJD: S100B, 2.5ng/ml – forest plot: likelihood ratios

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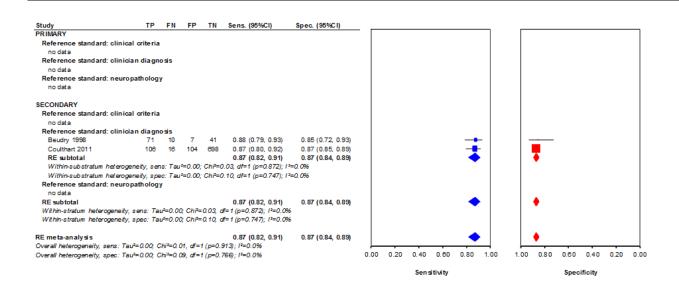


Figure 99CJD versus non-CJD: S100B, 2.5ng/ml – forest plot: sensitivity and specificity

P.3.6.10 Total Tau

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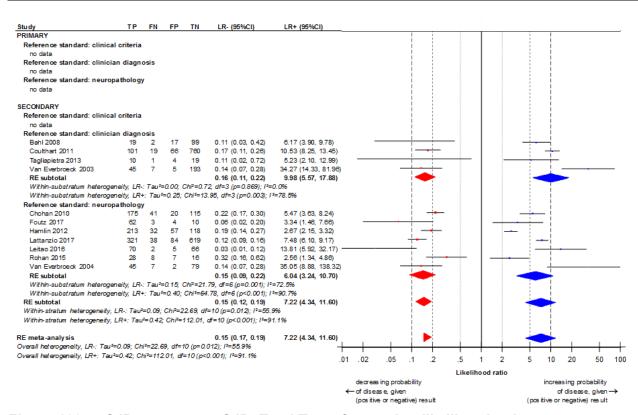


Figure 100 CJD versus non-CJD: Total Tau – forest plot: likelihood ratios

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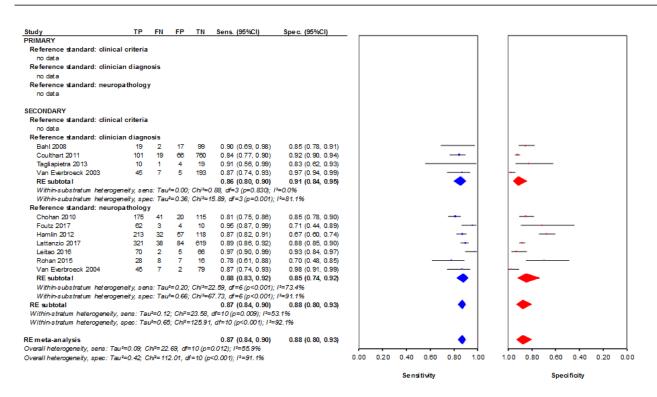


Figure 101 CJD versus non-CJD: Total Tau – forest plot: sensitivity and specificity

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P.3.6.11 WHO CJD criteria

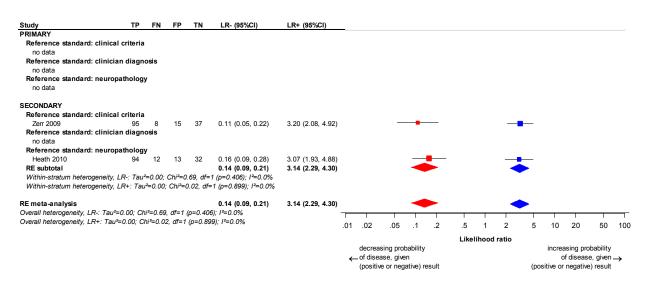


Figure 102 CJD versus non-CJD: WHO CJD criteria – forest plot: likelihood ratios

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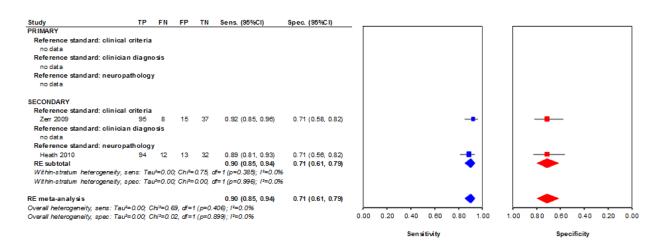


Figure 103 CJD versus non-CJD: WHO CJD criteria – forest plot: sensitivity and specificity

P.3.7 DLB versus non-DLB

P.3.7.1 123I-FP-CIT SPECT

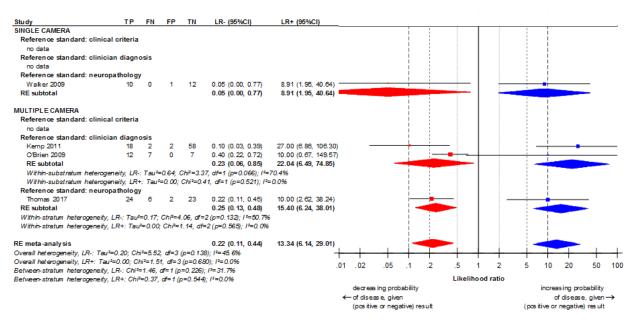


Figure 104 DLB versus non-DLB: 123I-FP-CIT SPECT – forest plot: likelihood ratios

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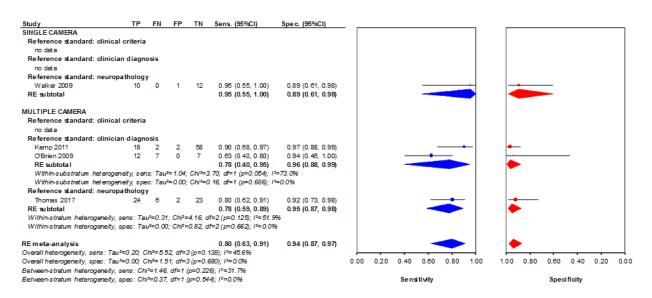


Figure 105 DLB versus non-DLB: 123I-FP-CIT SPECT – forest plot: sensitivity and specificity

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P.3.7.2 123I-MIBG cardiac scintigraphy

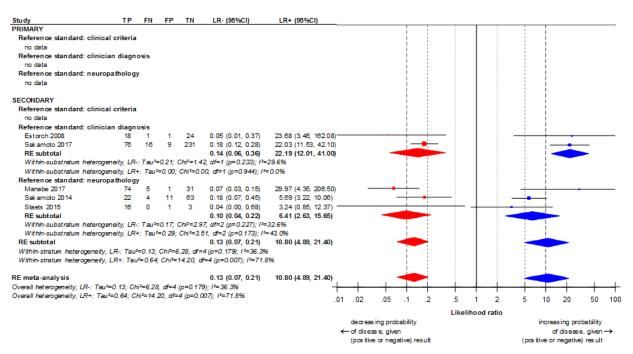


Figure 106 DLB versus non-DLB: 123I-MIBG cardiac scintigraphy – forest plot: likelihood ratios

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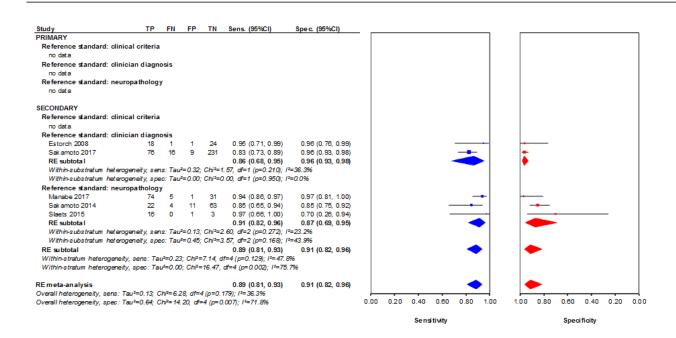


Figure 107 DLB versus non-DLB: 123I-MIBG cardiac scintigraphy – forest plot: sensitivity and specificity

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P.3.7.3 FDG-PET

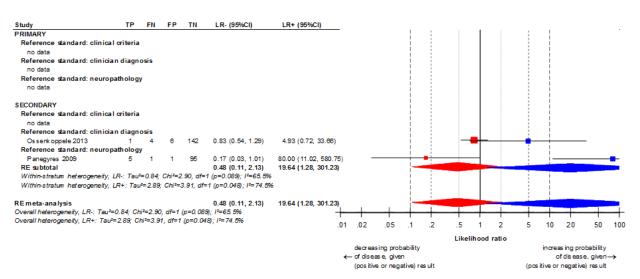


Figure 108 DLB versus non-DLB: FDG-PET – forest plot: likelihood ratios

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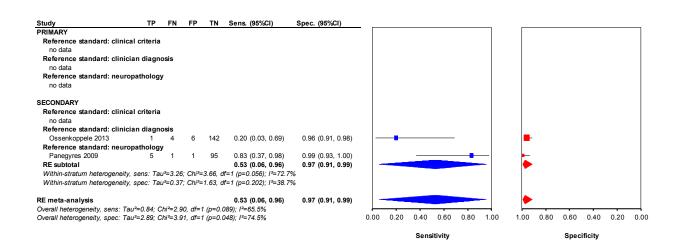


Figure 109 DLB versus non-DLB: FDG-PET – forest plot: sensitivity and specificity

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P.3.8 DLB versus other dementias

P.3.8.1 123I-FP-CIT SPECT

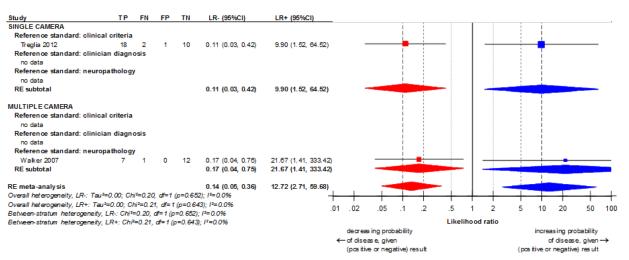


Figure 110 DLB versus other dementias: 123I-FP-CIT SPECT – forest plot: likelihood ratios

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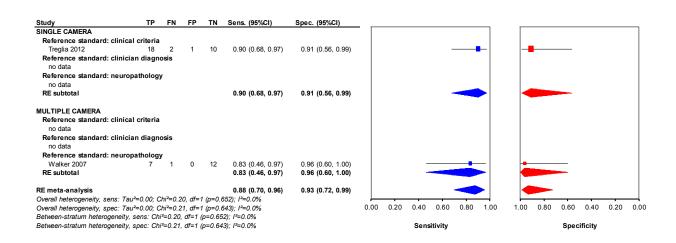


Figure 111 DLB versus other dementias: 123I-FP-CIT SPECT – forest plot: sensitivity and specificity

P.3.9 FTD versus AD

P.3.9.1 99mTc-HMPAO SPECT

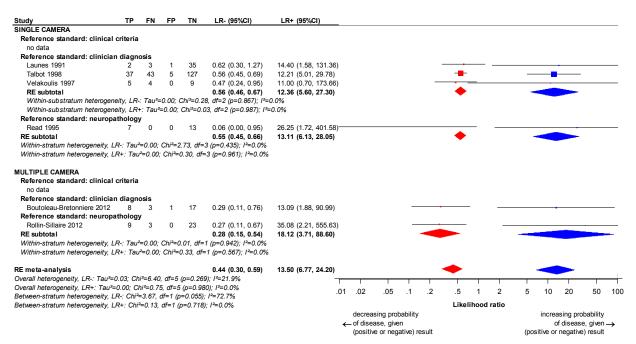


Figure 112 FTD versus AD: 99mTc-HMPAO SPECT – forest plot: likelihood ratios

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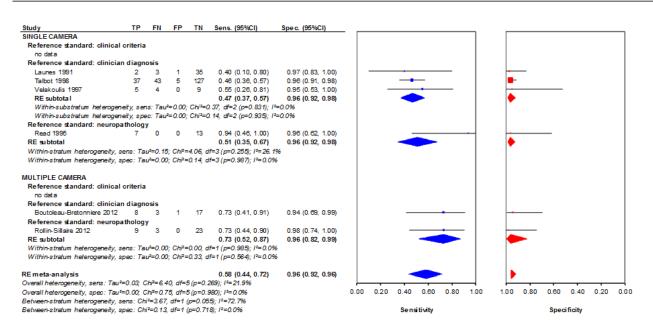


Figure 113 FTD versus AD: 99mTc-HMPAO SPECT – forest plot: sensitivity and specificity

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P.3.10 FTD versus non-FTD

P.3.10.1 99mTc-HMPAO SPECT

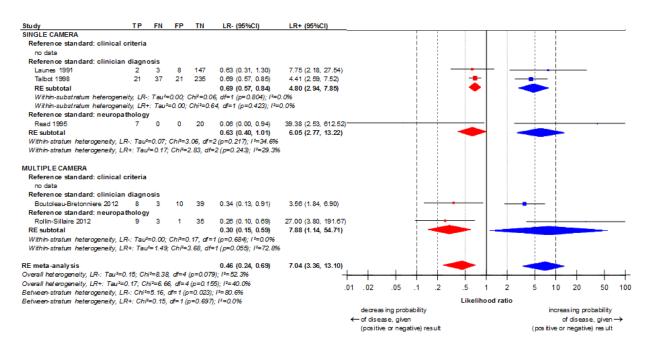


Figure 114 FTD versus non-FTD: 99mTc-HMPAO SPECT – forest plot: likelihood ratios

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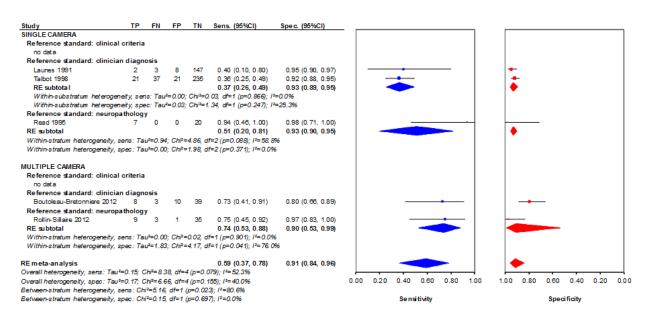


Figure 115 FTD versus non-FTD: 99mTc-HMPAO SPECT – forest plot: sensitivity and specificity

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P.3.10.2 FDG-PET

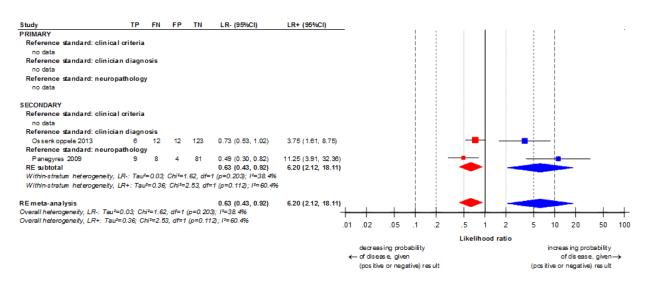


Figure 116 FTD versus non-FTD: FDG-PET – forest plot: likelihood ratios

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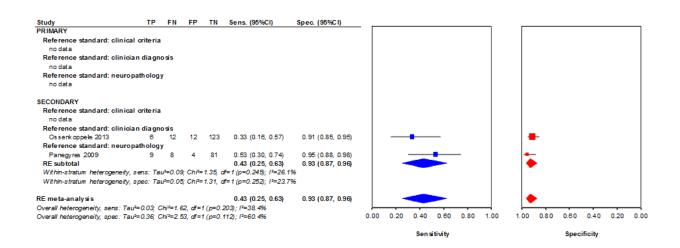


Figure 117 FTD versus non-FTD: FDG-PET – forest plot: sensitivity and specificity

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P.3.10.3 MRI

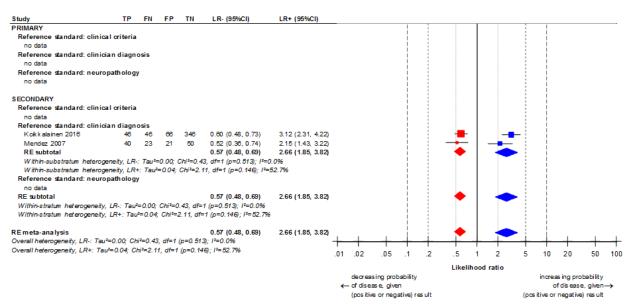


Figure 118 FTD versus non-FTD: MRI – forest plot: likelihood ratios

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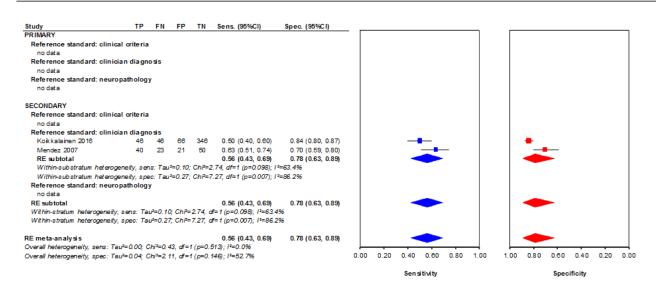


Figure 119 FTD versus non-FTD: MRI – forest plot: sensitivity and specificity

P.3.11 FTD versus other dementias

P.3.11.1 FDG-PET

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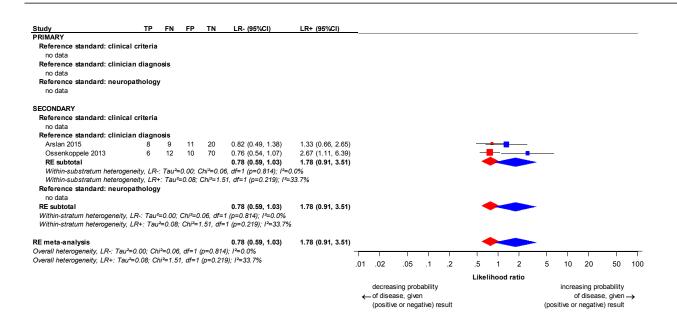


Figure 120 FTD versus other dementias: FDG-PET – forest plot: likelihood ratios

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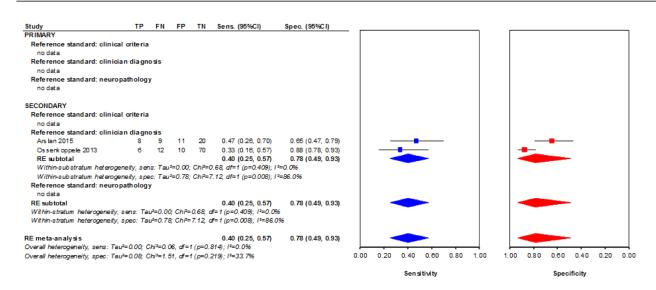


Figure 121 FTD versus other dementias: FDG-PET – forest plot: likelihood ratios

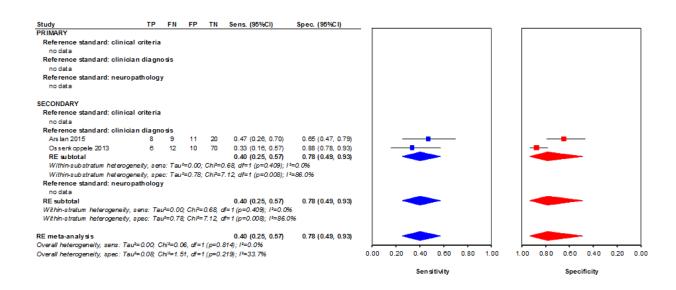


Figure 122 FTD versus other dementias: FDG-PET – forest plot: sensitivity and specificity

P.3.12 FTD versus VaD

P.3.12.1 99mTc-HMPAO SPECT

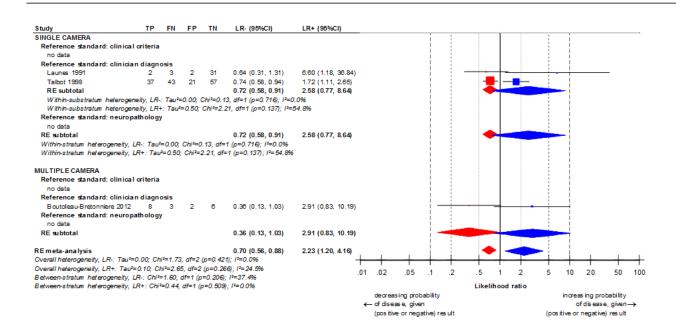


Figure 123 FTD versus VaD: 99mTc-HMPAO SPECT – forest plot: likelihood ratios

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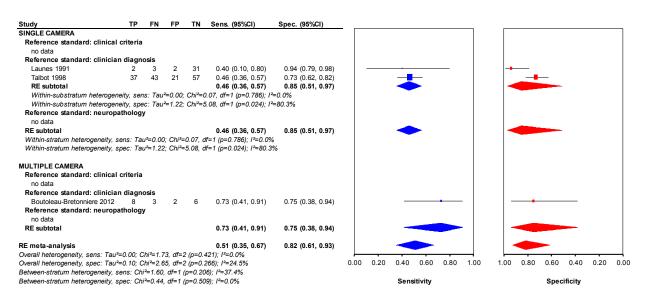


Figure 124 FTD versus VaD: 99mTc-HMPAO SPECT – forest plot: sensitivity and specificity

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P.3.13 VaD versus AD

P.3.13.1 99mTc-HMPAO SPECT

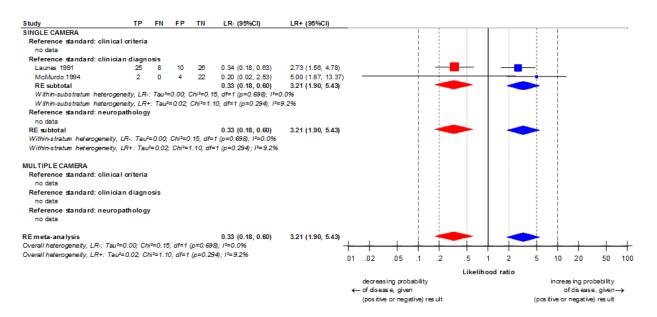


Figure 125 VaD versus AD: 99mTc-HMPAO SPECT – forest plot: likelihood ratios

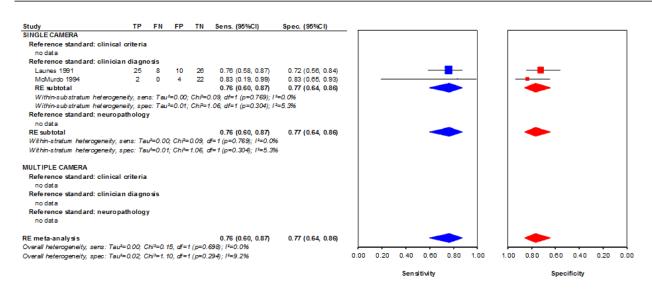


Figure 126 VaD versus AD: 99mTc-HMPAO SPECT – forest plot: sensitivity and specificity

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P.3.14 VaD versus non-VaD

P.3.14.1 99mTc-HMPAO SPECT

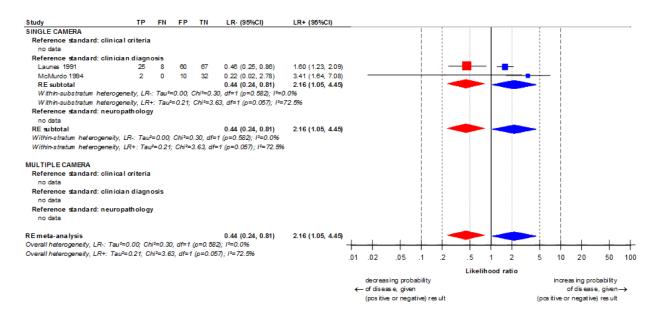


Figure 127 VaD versus non-VaD: 99mTc-HMPAO SPECT – forest plot: likelihood ratios

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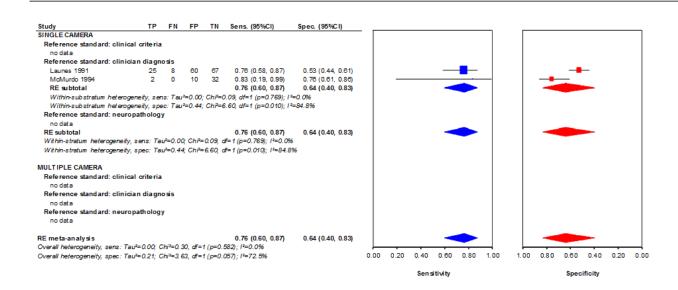


Figure 128 VaD versus non-VaD: 99mTc-HMPAO SPECT – forest plot: sensitivity and specificity

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