

P.2 GRADE tables

P.2.1 Dementia versus no dementia

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Apolinario 2015)	Prospective	230	0.69 (0.59, 0.77)	0.94 (0.88, 0.97)	LR+	10.67 (5.40, 21.12)	Serious	n/a	Serious	Not serious	-	LOW
					LR-	0.33 (0.25, 0.44)	Serious	n/a	Serious	Not serious		LOW
<p>Notes on risk of bias Apolinario 2015: Optimised thresholds were calculated and people with moderate to severe dementia were excluded from the study.</p> <p>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>												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Apolinario 2015)	Prospective	230	0.94 (0.88, 0.97)	0.60 (0.51, 0.68)		LR+	2.34 (1.88, 2.91)	Serious	n/a	Serious	Serious	-	VERY LOW
						LR-	0.09 (0.04, 0.21)	Serious	n/a	Serious	Not serious		LOW
<p>Notes on risk of bias Apolinario 2015: Optimised thresholds were calculated and people with moderate to severe dementia were excluded from the study.</p> <p>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>													

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Apolinario 2015)	Prospective	230	0.97 (0.92, 0.99)	0.40 (0.32, 0.49)		LR+	1.63 (1.40, 1.89)	Serious	n/a	Serious	Not serious	-	LOW
						LR-	0.07 (0.02, 0.22)	Serious	n/a	Serious	Not serious		LOW
<p>Notes on risk of bias Apolinario 2015: Optimised thresholds were calculated and people with moderate to severe dementia were excluded from the study.</p> <p>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>													

P.2.1.4 6 item screener (≥0)

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

P.2.1.5 6 item screener (≥1)

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

P.2.1.6 6 item screener (≥2)

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

P.2.1.7 6 item screener (≥3)

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

P.2.1.8 6 item screener (≥4)

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

P.2.1.9 6 item screener (≥5)

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

P.2.1.10 6 item screener (≥6)

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

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

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

P.2.1.12 99mTc-HMPAO SPECT

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

P.2.1.24 AD8 (≥2)

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Flicker 1997)	Prospective	299	0.97 (0.94, 0.99)	0.28 (0.19, 0.38)	LR+	1.34 (1.17, 1.54)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.10 (0.04, 0.24)	V. serious	n/a	Not serious	Not serious		LOW
Notes on risk of bias												
Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Flicker 1997)	Prospective	299	0.58 (0.52, 0.65)	0.87 (0.78, 0.93)	LR+	4.40 (2.51, 7.72)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.48 (0.40, 0.57)	V. serious	n/a	Not serious	Serious		VERY LOW
Notes on risk of bias Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Flicker 1997)	Prospective	299	0.73 (0.66, 0.78)	0.71 (0.60, 0.80)	LR+	2.51 (1.78, 3.56)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.38 (0.30, 0.50)	V. serious	n/a	Not serious	Not serious		LOW
Notes on risk of bias Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Flicker 1997)	Prospective	299	0.88 (0.82, 0.91)	0.53 (0.42, 0.63)	LR+	1.86 (1.47, 2.35)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.24 (0.16, 0.35)	V. serious	n/a	Not serious	Not serious		LOW
Notes on risk of bias												
Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.												

P.2.1.29 Amyloid Beta 1-42 and total tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Frisoni 2009)	Prospective	94	0.42 (0.31, 0.55)	0.79 (0.60, 0.90)	LR+	1.98 (0.92, 4.25)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.73 (0.55, 0.97)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias												
Frisoni 2009: Patients whose cognitive deficit reverted (regarded as primarily depressed with secondary cognitive impairment) were excluded from the study; unclear whether reference test was interpreted without knowledge of index test and unclear whether results of index test interpreted without knowledge of reference test.												

P.2.1.30 Applause sign (<3)

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.39 (0.28, 0.52)	0.93 (0.88, 0.96)	LR+	5.94 (3.12, 11.33)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.65 (0.53, 0.79)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias												
Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.												

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

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

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

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

P.2.1.34 Brief Neuropsychological Test Battery

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Beinhoff 2005)	Prospective	232	0.86 (0.76, 0.93)	0.52 (0.45, 0.60)		LR+	1.81 (1.51, 2.19)	Serious	n/a	Not serious	Serious	-	LOW
						LR-	0.26 (0.14, 0.49)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias													
Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.													

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

P.2.1.45 CERAD battery

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

P.2.1.46 Computed Tomography, CT

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

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

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

P.2.1.48 FDG-PET

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

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

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
2 studies (Garcia 2002; Knaefelc 2003)	2 × prospective	436	0.93 (0.90, 0.96)	0.65 (0.27, 0.91)		LR+	2.80 (0.97, 8.10)	Serious	Serious	Not serious	Serious	-	VERY LOW
						LR-	0.12 (0.07, 0.18)	Serious	Not serious	Not serious	Not serious		MODERATE
Notes on risk of bias													
Garcia 2002: Inappropriate exclusions at patient selection stage.													
Knaefelc 2003: Unclear whether all patients were included in the analysis; unclear interval between index and reference tests; lack of a pre-specified threshold.													

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Goncalves 2011)	Prospective	204	0.72 (0.64, 0.78)	0.67 (0.54, 0.79)		LR+	2.19 (1.47, 3.28)	Serious	n/a	Not serious	Serious	-	LOW
						LR-	0.42 (0.31, 0.58)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias													
Goncalves 2011: The reference diagnosis was not independent of the index tests; optimised test thresholds were used.													

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Flicker 1997; Hancock 2009)	2 × prospective	443	0.87 (0.82, 0.90)	0.49 (0.31, 0.67)	LR+	1.69 (1.16, 2.47)	V. serious	Serious	Not serious	Serious	-	VERY LOW
					LR-	0.27 (0.17, 0.42)	V. serious	Not serious	Not serious	Not serious		LOW
Notes on risk of bias Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test. Hancock 2009: An optimised test threshold was used.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Cruz-Orduna 2012)	Prospective	160	0.80 (0.53, 0.93)	0.77 (0.69, 0.83)	LR+	3.14 (2.31, 5.03)	Serious	n/a	Not serious	Not serious		MODERATE
					LR-	0.26 (0.09, 0.72)	Serious	n/a	Not serious	Serious		LOW
SECONDARY CARE												
1 study (Flicker 1997)	Prospective	299	0.81 (0.76, 0.86)	0.61 (0.51, 0.71)	LR+	2.11 (1.60, 2.79)	V. serious	n/a	Not serious	Serious		VERY LOW
					LR-	0.30 (0.22, 0.42)	V. serious	n/a	Not serious	Not serious		LOW
ALL EVIDENCE POOLED V. serious												
2 studies (Cruz-Orduna 2012; Flicker 1997)	2x prospective	459	0.81 (0.76, 0.86)	0.70 (0.53, 0.82)	LR+	2.63 (1.65, 4.20)	V. serious	Serious	Not serious	Serious	-	VERY LOW
					LR-	0.30 (0.22, 0.41)	V. serious	Not serious	Not serious	Not serious		LOW
Notes on risk of bias												
Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.												
Cruz-Orduna 2012: Thresholds were not pre-specified but were calculated to give optimum sensitivity and specificity												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Flicker 1997)	Prospective	299	0.78 (0.72, 0.83)	0.65 (0.54, 0.75)	LR+	2.23 (1.65, 3.01)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.34 (0.25, 0.46)	V. serious	n/a	Not serious	Not serious		LOW
Notes on risk of bias												
Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Flicker 1997)	Prospective	299	0.75 (0.68, 0.80)	0.71 (0.60, 0.80)	LR+	2.58 (1.82, 3.64)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.36 (0.27, 0.47)	V. serious	n/a	Not serious	Not serious		LOW
Notes on risk of bias												
Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Flicker 1997)	Prospective	299	0.70 (0.64, 0.76)	0.75 (0.64, 0.83)	LR+	2.78 (1.90, 4.07)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.40 (0.31, 0.50)	V. serious	n/a	Not serious	Serious		VERY LOW
Notes on risk of bias												
Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Flicker 1997)	Prospective	299	0.65 (0.58, 0.71)	0.80 (0.69, 0.87)	LR+	3.16 (2.05, 4.89)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.44 (0.36, 0.55)	V. serious	n/a	Not serious	Serious		VERY LOW
Notes on risk of bias												
Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Flicker 1997)	Prospective	299	0.58 (0.52, 0.65)	0.83 (0.74, 0.90)	LR+	3.46 (2.12, 5.65)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.50 (0.42, 0.60)	V. serious	n/a	Not serious	Serious		VERY LOW
Notes on risk of bias												
Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.12 (0.06, 0.22)	0.99 (0.95, 1.00)	LR+	10.06 (2.19, 46.14)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.89 (0.81, 0.97)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias												
Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.												

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

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

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

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

P.2.1.62 Mini-ACE (<26)

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

P.2.1.63 Mini-Cog (≤2)

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

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

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

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

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnero-Pardo 2011)	Prospective	117	0.97 (0.80, 1.00)	0.71 (0.61, 0.80)	LR+	3.36 (2.40, 4.71)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.05 (0.01, 0.32)	Not serious	n/a	Not serious	Not serious		HIGH
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.82 (0.71, 0.89)	0.81 (0.75, 0.87)	LR+	4.38 (3.13, 6.14)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.22 (0.13, 0.37)	Serious	n/a	Not serious	Not serious		MODERATE
ALL EVIDENCE POOLED												
2 studies (Beinhoff 2005; Carnero-Pardo 2011)	2 × prospective	349	0.90 (0.61, 0.98)	0.77 (0.66, 0.85)	LR+	3.84 (2.96, 4.97)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.14 (0.03, 0.57)	Serious	Serious	Not serious	Serious		VERY LOW
Notes on risk of bias												
Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.												

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

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

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

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

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

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

P.2.1.70 MMSE (<17)

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

P.2.1.71 MMSE (<18)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Cruz-Orduna 2012)	Prospective	360	0.81 (0.70, 0.88)	0.92 (0.88, 0.95)	LR+	9.91 (6.60, 14.88)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.21 (0.13, 0.33)	Serious	n/a	Not serious	Not serious		MODERATE
SECONDARY CARE												
1 study (Flicker 1997)	Prospective	299	0.50, 0.43, 0.57)	0.90 (0.82, 0.95)	LR+	5.19 (2.65, 10.16)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.55 (0.48, 0.64)	V. serious	n/a	Not serious	Serious		VERY LOW
ALL EVIDENCE POOLED V. serious												
2 studies (Cruz-Orduna 2012; Flicker 1997)	2x prospective	659	0.67 (0.33, 0.89)	0.92 (0.88, 0.94)	LR+	7.59 (4.07, 14.17)	V. serious	Serious	Not serious	Not serious	-	VERY LOW
					LR-	0.35 (0.14, 0.90)	V. serious	Serious	Not serious	Serious		VERYLOW
Notes on risk of bias												
Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.												
Cruz-Orduna 2012: Thresholds were not pre-specified but were calculated to give optimum sensitivity and specificity												

P.2.1.72 MMSE (<19)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
2 studies (Carnero-Pardo 2013, Cruz-Orduna 2012)	2x prospective	520	0.87 (0.78, 0.92)	0.87 (0.83, 0.90)	LR+	6.46 (4.97, 8.38)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.16 (0.09, 0.26)	Serious	Not serious	Not serious	Not serious		MODERATE
SECONDARY CARE												
1 study (Flicker 1997)	Prospective	299	0.56 (0.49, 0.62)	0.97 (0.78, 0.93)	LR+	4.19 (2.39, 7.36)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.51 (0.43, 0.61)	V. serious	n/a	Not serious	Serious		VERY LOW
ALL EVIDENCE POOLED V. serious												
2 studies (Carnero-Pardo 2013; Cruz-Orduna 2012; Flicker 1997)	3x prospective	819	0.76 (0.46, 0.93)	0.87 (0.83, 0.89)	LR+	5.95 (4.64, 7.62)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.26 (0.10, 0.70)	V. serious	Serious	Not serious	Serious		VERYLOW
Notes on risk of bias												
Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.												
Cruz-Orduna 2012: Thresholds were not pre-specified but were calculated to give optimum sensitivity and specificity												
Carnero-Pardo 2013: Multiple test thresholds were used												

P.2.1.73 MMSE (<20)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnero-Pardo 2013)	Prospective	360	0.94 (0.85, 0.97)	0.82 (0.77, 0.86)	LR+	5.19 (4.02, 6.70)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.08 (0.03, 0.19)	Serious	n/a	Not serious	Not serious		MODERATE
SECONDARY CARE												
1 study (Flicker 1997)	Prospective	299	0.62 (0.55, 0.68)	0.84 (0.75, 0.91)	LR+	3.96 (2.38, 6.60)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.45 (0.37, 0.55)	V. serious	n/a	Not serious	Serious		VERY LOW
ALL EVIDENCE POOLED V. serious												
2 studies (Carnero-Pardo 2013; Flicker 1997)	2x prospective	659	0.82 (0.36, 0.98)	0.82 (0.78, 0.86)	LR+	4.92 (3.91, 6.18)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.20 (0.04, 1.09)	V. serious	Serious	Not serious	Serious		VERYLOW
Notes on risk of bias												
Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.												
Carnero-Pardo 2013: Multiple test thresholds were used												

P.2.1.74 MMSE (<21)

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

P.2.1.75 MMSE (<22)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnero-Pardo 2013)	Prospective	360	0.96 (0.89, 0.99)	0.67 (0.61, 0.72)	LR+	2.92 (2.46, 3.48)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.06 (0.02, 0.18)	Serious	n/a	Not serious	Serious		MODERATE
3 studies (Callahan 2002; Flicker 1997; Kukull 1994)	3x prospective	1,089	0.69 (0.60, 0.78)	0.94 (0.64, 0.99)	LR+	12.43 (1.75, 88.49)	Very serious	Serious	Not serious	Serious	-	VERY LOW
					LR-	0.35 (0.26, 0.46)	Serious	Serious	Not serious	Serious		LOW
ALL EVIDENCE POOLED												
4 studies (Callahan 2002; Carnero-Pardo 2013; Flicker 1997; Kukull 1994)	4 × prospective	1,443	0.76 (0.64, 0.85)	0.89 (0.67, 0.97)	LR+	6.54 (2.67, 16.01)	Serious	Serious	Not serious	Not serious	-	LOW
					LR-	0.30 (0.21, 0.43)	Serious	Serious	Not serious	Not serious		LOW
Notes on risk of bias												
Kukull 1994: It is unclear whether the index test results were interpreted without knowledge of the results of the reference standard; multiple pre-specified cut offs were used to determine the optimal cut off; the index test result was known during the reference standard diagnosis.												
Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.												
Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.												
Carnero-Pardo 2013: Multiple test thresholds were used												

P.2.1.76 MMSE (<23)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnero-Pardo 2013)	1 × prospective	360	0.99 (0.91, 1.00)	0.57 (0.51, 0.63)	LR+	2.29 (2.00, 2.62)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.02 (0.00, 0.16)	Serious	n/a	Not serious	Not serious		MODERATE
SECONDARY CARE												
5 studies (Abdel-Aziz 2015; Callahan 2002; Flicker 1997; Kukull 1994; Nielsen 2013)	5 × prospective	1,364	0.67 (0.55, 0.77)	0.89 (0.75, 0.96)	LR+	6.79 (2.70, 15.00)	Very serious	Serious	Not serious	Not serious	-	VERY LOW
					LR-	0.38 (0.26, 0.52)	Very serious	Serious	Not serious	Serious		VERY LOW
ALL EVIDENCE POOLED												
6 studies (Abdel-Aziz 2015; Callahan 2002; Carnero-Pardo 2013; Flicker 1997; Kukull 1994; Nielsen 2013)	6 × prospective	1,724	0.75 (0.54, 0.88)	0.85 (0.69, 0.94)	LR+	5.47 (2.60, 10.80)	V. serious	Serious	Not serious	Not serious	-	VERY LOW
					LR-	0.31 (0.15, 0.51)	V. serious	Serious	Not serious	Serious		VERY LOW
Notes on risk of bias												
Kukull 1994: It is unclear whether the index test results were interpreted without knowledge of the results of the reference standard; multiple pre-specified cut offs were used to determine the optimal cut off; the index test result was known during the reference standard diagnosis.												
Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.												
Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.												
Carnero-Pardo 2013: Multiple test thresholds were used												
Nielsen 2013: The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; the test threshold was not pre-specified.												
Abdel-Aziz 2015: Subgroup of 6 CIT tested patients were tested with MMSE as well; MMSE cut off was not pre-specified as chosen for comparison to 6CIT test.												

P.2.1.77 MMSE (<24)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnero-Pardo 2013)	Prospective	360	0.99 (0.91, 1.00)	0.46 (0.40, 0.52)	LR+	1.84 (1.65, 2.05)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.08 (0.01, 1.32)	Serious	n/a	Not serious	Not serious		MODERATE
SECONDARY CARE												
11 studies (Bastide 2012; Callahan 2002; Goncalves 2011; Flicker 1997; Hancock 2011; Knaefelc 2003; Kukull 1994; Mathuranath 2000; Nielsen 2013; Postel-Vinay 2014; Sager 2006)	11 × prospective	2,975	0.73 (0.63, 0.81)	0.91 (0.83, 0.96)	LR+	8.43 (4.47, 14.80)	Serious	Serious	Not serious	Not serious	-	LOW
					LR-	0.31 (0.23, 0.40)	Serious	Serious	Not serious	Not serious		LOW
ALL EVIDENCE POOLED												
12 studies (Bastide 2012; Callahan 2002; Carnero-Pardo 2013; Flicker 1997; Goncalves 2011; Hancock 2011; Knaefelc 2003; Kukull 1994; Mathuranath 2000; Nielsen 2013; Postel-Vinay 2014; Sager 2006)	12 × prospective	3,355	0.75 (0.65, 0.84)	0.88 (0.78, 0.94)	LR+	6.65 (3.70, 11.00)	Serious	Serious	Not serious	Not serious	-	LOW
					LR-	0.29 (0.20, 0.38)	Serious	Serious	Not serious	Not serious		LOW

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
<p>Notes on risk of bias</p> <p>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.</p> <p>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> <p>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> <p>Knaefelc 2003: Unclear whether all patients were included in the analysis; unclear interval between index and reference tests; lack of a pre-specified threshold.</p> <p>Goncalves 2011: The reference diagnosis was not independent of the index tests; optimised test thresholds were used.</p> <p>Goncalves 2011: The reference diagnosis was not independent of the index tests; optimised test thresholds were used.</p> <p>Hancock 2011: Optimised test threshold.</p> <p>Bastide 2012: Optimised test cut-offs used.</p> <p>Carnero-Pardo 2013: Multiple test thresholds were used</p> <p>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> <p>Postel-Vinay 2014: Optimised cut-off was used; the study was not downgraded for exclusions as <10% population was excluded</p>												

P.2.1.78 MMSE (<25)

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
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Notes on risk of bias

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

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

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

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

Carnero-Pardo 2013: Multiple test thresholds were used

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

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

P.2.1.79 MMSE (<26)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 studies (Callahan 2002; Flicker 1997; Milian 2012; Nielsen 2013)	3 × prospective; 1 × retrospective	1,583	0.85 (0.77, 0.91)	0.78 (0.53, 0.92)	LR+	3.84 (1.68, 8.76)	V. serious	Serious	Not serious	Serious	-	VERY LOW
					LR-	0.19 (0.14, 0.28)	V. serious	Serious	Not serious	Not serious		VERY LOW
Notes on risk of bias												
Flicker 1997: Due to non-pre-specification of test thresholds; large number of patients excluded from study; lack of clarity about patient groups included in the analysis and whether the reference standard results were interpreted without knowledge of the results of the index test.												
Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.												
Milian 2012: Unclear whether inappropriate exclusions were avoided; whether the patients were a random or consecutive sample and whether the reference standard result was interpreted without knowledge of the results of the index test.												
Nielsen 2013: The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; the test threshold was not pre-specified.												

P.2.1.80 MMSE (<27)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 studies (Bastide 2012; Callahan 2002; Mathuranath 2000; Nielsen 2013)	4 × prospective	1,241	0.86 (0.73, 0.94)	0.75 (0.66, 0.82)	LR+	3.43 (2.43, 4.85)	Serious	Serious	Not serious	Not serious	-	LOW
					LR-	0.17 (0.09, 0.33)	Serious	Serious	Not serious	Not serious		LOW
Notes on risk of bias Mathuranath 2000: Optimised test-threshold used and it was unclear whether the index test results were interpreted without knowledge of the results of the reference standard. Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified. Bastide 2012: Optimised test cut-offs used. Nielsen 2013: The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; the test threshold was not pre-specified.												

P.2.1.81 MMSE (<28)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Callahan 2002; Mormont 2012)	2 × prospective	796	0.96 (0.87, 0.99)	0.70 (0.57, 0.81)	LR+	3.13 (2.22, 4.41)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.05 (0.02, 0.16)	V. serious	Serious	Not serious	Not serious		VERY LOW
Notes on risk of bias												
Callahan 2002: It was unclear whether a consecutive or random sample of patients was enrolled in the study; whether the index and reference tests were independent of each other and the test threshold was not pre-specified.												
Mormont 2012: Exclusion of >35% population at analysis and use of optimised test thresholds.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Chen 2011; Yeung 2014)	2 × prospective	495	0.93 (0.90, 0.96)	0.81 (0.44, 0.96)	LR+	5.18 (1.32, 20.41)	V. serious	Serious	Not serious	Serious	-	VERY LOW
					LR-	0.09 (0.06, 0.13)	V. serious	Not serious	Not serious	Not serious		LOW
Notes on risk of bias												
Chen 2011: Unclear whether inappropriate exclusions were avoided or if a pre-specified test threshold was used; unclear whether index and reference tests were interpreted without knowledge of each other and whether all participants were included in the analysis.												
Yeung 2014: Unclear whether patients were selected randomly or consecutively or whether inappropriate exclusions were avoided; the optimal index test thresholds were determined during the study; it is unclear whether the index test results and reference test results were assessed independently of each other: subgroup analysis was carried out with >10% population (MCI) being excluded.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Yeung 2014)	Prospective	272	1.00 (0.94, 1.00)	0.37 (0.29, 0.45)	LR+	1.57 (1.39, 1.78)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.01 (0.00, 0.17)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias												
Yeung 2014: Unclear whether patients were selected randomly or consecutively or whether inappropriate exclusions were avoided; the optimal index test thresholds were determined during the study; it is unclear whether the index test results and reference test results were assessed independently of each other.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Goldstein 2014)	Prospective	81	0.96 (0.78, 0.99)	0.31 (0.21, 0.45)	LR+	1.41 (1.16, 1.71)	Not serious	n/a	Serious	Not serious	-	MODERATE
					LR-	0.12 (0.02, 0.84)	Not serious	n/a	Serious	Serious		LOW
Notes on indirectness												
Goldstein 2014: Study only recruited African Americans ≥ 50 years old.												

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

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

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

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

P.2.1.87 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Frisoni 2009; Hentschel 2005)	2 × prospective	234	0.83 (0.49, 0.96)	0.57 (0.47, 0.66)	LR+	1.87 (1.45, 2.37)	V. serious	Not serious	Not serious	Serious	-	VERY LOW
					LR-	0.30 (0.09, 1.04)	V. serious	Serious	Not serious	Serious		VERY LOW
Notes on risk of bias												
Hentschel 2005: The index tests were carried out with knowledge of the primary care diagnosis and it is unclear whether pre-specified thresholds were used; the reference standard diagnosis used all available data including the index test results.												

P.2.1.88 Orientation, OR (<7)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.39 (0.28, 0.52)	0.99 (0.95, 1.00)	LR+	32.70 (7.99, 133.88)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.61 (0.50, 0.75)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias												
Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.												

P.2.1.89 Orientation, OR (<8)

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

P.2.1.90 Palmo-Mental Reflex

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Streit 2015)	Retrospective	154	0.71 (0.46, 0.87)	0.64 (0.55, 0.71)	LR+	1.93 (1.33, 2.82)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.46 (0.22, 0.98)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Streit 2015: Patients had to have cognitive complaints, but normal MMSE and CDT tests at baseline..												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Streit 2015)	Retrospective	154	0.24 (0.09, 0.49)	0.93 (0.88, 0.97)	LR+	3.58 (1.24, 10.38)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.82 (0.63, 1.07)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Streit 2015: Patients had to have cognitive complaints, but normal MMSE and CDT tests at baseline.												
Notes on indirectness Streit 2015: Patients had to have cognitive complaints, but score as normal on the MMSE and CDT tests.												

P.2.1.93 Phototest (<27)

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

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

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

Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Nielsen 2013)	Prospective	137	0.49 (0.37, 0.60)	0.91 (0.81, 0.96)	LR+	5.27 (2.37, 11.70)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.57 (0.45, 0.72)	V. serious	n/a	Not serious	Serious		VERY LOW
Notes on risk of bias												
Nielsen 2013: The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; a variety of test thresholds are reported.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Nielsen 2013)	Prospective	137	0.64 (0.52, 0.74)	0.83 (0.72, 0.90)	LR+	3.78 (2.14, 6.65)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.43 (0.31, 0.60)	V. serious	n/a	Not serious	Serious		VERY LOW
Notes on risk of bias												
Nielsen 2013: The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; a variety of test thresholds are reported.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Nielsen 2013)	Prospective	137	0.69 (0.58, 0.79)	0.80 (0.69, 0.88)	LR+	3.47 (2.09, 5.78)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.38 (0.26, 0.55)	V. serious	n/a	Not serious	Serious		VERY LOW
Notes on risk of bias												
Nielsen 2013: The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; a variety of test thresholds are reported.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Nielsen 2013)	Prospective	137	0.76 (0.65, 0.85)	0.66 (0.54, 0.77)	LR+	2.26 (1.57, 3.25)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.36 (0.23, 0.56)	V. serious	n/a	Not serious	Serious		VERY LOW
Notes on risk of bias												
Nielsen 2013: The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; the test threshold was not pre-specified.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Nielsen 2013)	Prospective	137	0.82 (0.71, 0.89)	0.65 (0.52, 0.75)		LR+	2.32 (1.64, 3.27)	V. serious	n/a	Not serious	Serious	-	VERY LOW
						LR-	0.28 (0.17, 0.47)	V. serious	n/a	Not serious	Not serious		LOW
Notes on risk of bias													
Nielsen 2013: The study selected some participants on the basis of immigrant background and excluded non-immigrants during this time period; the people with immigrant backgrounds were significantly younger than Danish-born participants; the test threshold was not pre-specified.													

P.2.1.100 Seven Minute Screen (P>0.6)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Skjerve 2008)	Prospective	95	0.72 (0.61, 0.82)	0.65 (0.46, 0.81)		LR+	2.09 (1.21, 3.62)	Serious	n/a	Not serious	Serious	-	LOW
						LR-	0.42 (0.26, 0.68)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias													
Skjerve 2008: Use of an alternative threshold to the standard one and that was not pre-specified.													

P.2.1.101 Seven Minute Screen (P>0.7)

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

P.2.1.102 Seven Minute Screen (P>0.8)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skjerve 2008)	Prospective	95	0.71 (0.59, 0.80)	0.73 (0.53, 0.87)	LR+	2.64 (1.38, 5.06)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.40 (0.26, 0.61)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias												
Skjerve 2008: Use of an alternative threshold to the standard one and that was not pre-specified.												

P.2.1.103 Short smell test

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Streit 2015)	Retrospective	154	0.53 (0.30, 0.74)	0.75 (0.67, 0.82)	LR+	2.13 (1.25, 3.64)	Serious	n/a	Serious	Serious	-	VERY LOW
					LR-	0.63 (0.37, 1.05)	Serious	n/a	Serious	Serious		VERY LOW
<p>Notes on risk of bias Streit 2015: Patients had to have cognitive complaints, but normal MMSE and CDT tests at baseline.</p> <p>Notes on indirectness Streit 2015: Patients had to have cognitive complaints, but score as normal on the MMSE and CDT tests.</p>												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Malhotra 2013)	Prospective	127	0.79 (0.70, 0.86)	0.75 (0.54, 0.88)	LR+	3.15 (1.56, 6.34)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.28 (0.18, 0.44)	V. serious	n/a	Not serious	Not serious		LOW
<p>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).</p> <p>Notes on indirectness Malhotra 2013: Participants had ≥ 6 years education</p>												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Malhotra 2013)	Prospective	127	0.78 (0.69, 0.85)	0.75 (0.54, 0.88)	LR+	3.11 (1.54, 6.26)	Serious	n/a	Serious	Serious	-	VERY LOW
					LR-	0.30 (0.19, 0.46)	Serious	n/a	Serious	Not serious		LOW
<p>Notes on risk of bias Malhotra 2013: It was unclear whether the study avoided inappropriate exclusions and optimised test cut-offs were used.</p> <p>Notes on indirectness Malhotra 2013: 60% participants had < 6 years education</p>												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Malhotra 2013)	Prospective	127	0.72 (0.62, 0.80)	0.42 (0.24, 0.62)	LR+	1.23 (0.86, 1.76)	V. serious	n/a	Serious	Not serious	-	VERY LOW
					LR-	0.68 (0.38, 1.19)	V. serious	n/a	Serious	Serious		VERY LOW
<p>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).</p> <p>Notes on indirectness Malhotra 2013: Participants had < 6 years education</p>												

P.2.1.107 Syndrom Kurztest (≥7)

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

P.2.1.108 Syndrom Kurztest (≥8)

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

P.2.1.109 Syndrom Kurztest (≥9)

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

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

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

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

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

P.2.1.112 Test Your Memory, TYM (≤30)

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

P.2.1.113 Test Your Memory, TYM (≤42)

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

P.2.1.114 Test Your Memory (≤39)

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

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

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Beinhoff 2005)	Prospective	232	0.85 (0.74, 0.92)	0.63 (0.56, 0.70)	LR+	2.31 (1.85, 2.89)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.24 (0.13, 0.43)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias												
Beinhoff 2005: Use of multiple non-pre-specified thresholds; interval between tests was unclear and it was unclear whether the index and reference tests were interpreted independently of each other.												

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

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

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

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

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

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

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

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

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

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

P.2.2 AD versus DLB

P.2.2.1 Amyloid Beta 1-42

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

P.2.2.2 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ossenkoppele 2013)	Prospective	70	0.58 (0.46, 0.70)	0.20 (0.03, 0.69)	LR+	0.73 (0.45, 1.19)	V. serious	n/a	Serious	Serious	-	VERY LOW
					LR-	2.08 (0.35, 12.27)	V. serious	n/a	Serious	V. serious		VERY LOW
<p>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.</p> <p>Notes on indirectness Ossenkoppele 2013: It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.</p>												

P.2.2.3 MRI

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

P.2.3 AD versus FTD

P.2.3.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
2 studies (Launes 1991; Velakoulis 1997)	2 × prospective	59	0.73 (0.42, 0.91)	0.71 (0.43, 0.89)	LR+	2.78 (1.20, 6.42)	V. serious	Not serious	Not serious	Serious	-	VERY LOW
					LR-	0.41 (0.23, 0.74)	Serious	Not serious	Not serious	Serious		LOW
MULTIPLE CAMERA												
1 study (Boutoleau-Bretonniere 2012)	Prospective	29	0.78 (0.54, 0.91)	0.73 (0.41, 0.91)	LR+	2.85 (1.05, 7.72)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.31 (0.12, 0.78)	V. serious	n/a	Not serious	Serious		VERY LOW
ALL EVIDENCE POOLED												
3 studies (Boutoleau-Bretonniere 2012; Launes 1991; Velakoulis 1997)	3 × prospective	88	0.72 (0.56, 0.83)	0.72 (0.51, 0.86)	LR+	2.81 (1.48, 5.33)	V. serious	Not serious	Not serious	Serious	-	VERY LOW
					LR-	0.38 (0.23, 0.62)	V. serious	Not serious	Not serious	Serious		VERY LOW
Notes on risk of bias												
Launes 1991: Subgroup analysis used with >10% study population excluded.												
Velakoulis 1997: Subgroup analysis where >10% study population excluded and it was unclear whether: the index test results were interpreted without knowledge of the results of the reference standard; the index test threshold was pre-specified or the reference standard results interpreted without knowledge of the results of the index test.												
Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded												

P.2.3.2 Amyloid Beta 1-42 and Total Tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Toledo 2012)	Retrospective	100	0.90 (0.81, 0.95)	0.83 (0.65, 0.93)	LR+	5.23 (2.35, 11.65)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.12 (0.06, 0.25)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of bias												
Toledo 2012: >10% population excluded from analysis; the index test thresholds used are not stated and it is unclear if they were pre-specified												

P.2.3.3 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ossenkoppele 2013)	Prospective	83	0.58 (0.46, 0.70)	0.78 (0.54, 0.91)	LR+	2.63 (1.08, 6.39)	V. serious	n/a	Serious	Serious	-	VERY LOW
					LR-	0.53 (0.37, 0.78)	V. serious	n/a	Serious	Serious	-	VERY LOW
Notes on risk of bias												
Ossenkoppele 2013: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the index test was interpreted with knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.												
Notes on indirectness												
Ossenkoppele 2013: It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.												

P.2.3.4 MRI

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

P.2.3.5 p-tau 181

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

P.2.4 AD versus no dementia

P.2.4.1 Amyloid Beta 1-42

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

P.2.4.2 FDG-PET

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

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

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

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

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

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

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

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

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Sikkes 2010)	Prospective	269	0.89 (0.84, 0.93)	0.69 (0.58, 0.77)	LR+	2.84 (2.08, 3.88)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.15 (0.10, 0.24)	V. serious	n/a	Not serious	Not serious		LOW
Notes on risk of bias												
Sikkes 2010: Use of subgroup analysis where >10% study population excluded (MCI group); lack of a pre-specified test threshold; unclear that index and reference tests are interpreted without knowledge of each other.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Sikkes 2010)	Prospective	269	0.86 (0.80, 0.90)	0.74 (0.64, 0.82)	LR+	3.31 (2.32, 4.73)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.19 (0.13, 0.28)	V. serious	n/a	Not serious	Not serious		LOW
Notes on risk of bias												
Sikkes 2010: Use of subgroup analysis where >10% study population excluded (MCI group); lack of a pre-specified test threshold; unclear that index and reference tests were interpreted without knowledge of each other.												

P.2.5.6 MMSE (<28)

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

P.2.5.7 p-tau 181

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

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

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

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

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

P.2.5.10 Total Tau

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

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

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

P.2.6 AD versus non-AD dementia plus unclassifiable

P.2.6.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA												
1 study (Boutoleau-Brettonniere 2012)	Prospective	56	0.78 (0.54, 0.91)	0.66 (0.50, 0.79)	LR+	2.27 (1.37, 3.77)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.34 (0.14, 0.83)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias												
Boutoleau-Brettonniere 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-Brettonniere 2012)	Prospective	56	0.33 (0.16, 0.57)	0.66 (0.50, 0.79)	LR+	0.97 (0.44, 2.14)	Serious	n/a	Not serious	V. serious	-	VERY LOW
					LR-	1.01 (0.68, 1.51)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias												
Boutoleau-Brettonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases												

P.2.7 AD versus non-AD

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

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

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

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

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

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

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

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA												
1 study (Kaneta 2016)	Prospective	89	0.71 (0.57, 0.82)	0.68 (0.53, 0.81)	LR+	2.31 (1.38, 3.63)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.43 (0.26, 0.7)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias												
Kaneta 2016: The SMH was defined based on the data and it was unclear whether the index test results were interpreted without knowledge of the results of the reference standard or whether the reference standard results were interpreted without knowledge of the results of the index test.												

P.2.7.6 99mTc-ECD SPECT, automated method

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

P.2.7.7 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
5 studies (Bergman 1997; Holman 1992; Launes 1991; Masterman 1997; McMurdo 1994)	5 × prospective	505	0.70 (0.55, 0.81)	0.62 (0.30, 0.86)	LR+	2.07 (1.08, 4.47)	Not serious	Serious	Not serious	Serious	-	LOW
					LR-	0.52 (0.37, 0.84)	Not serious	Serious	Not serious	Serious		LOW
MULTIPLE CAMERA												
2 studies (Dobert 2005; Rollin-Sillaire 2012)	1x prospective 1x retrospective	72	0.45 (0.24, 0.69)	0.93 (0.77, 0.98)	LR+	6.80 (1.98, 23.36)	Not serious	Not serious	Not serious	Serious	-	MODERATE
					LR-	0.60 (0.40, 0.90)	Serious	Not serious	Not serious	Serious		LOW
ALL EVIDENCE POOLED												
7 studies (Bergman 1997; Dobert 2005; Holman 1992; Launes 1991; Masterman 1997; McMurdo 1994; Rollin-Sillaire 2012)	6 × prospective; 1 × retrospective	577	0.63 (0.49, 0.75)	0.74 (0.45, 0.90)	LR+	2.10 (1.29, 3.43)	Not serious	Serious	Not serious	Serious	-	LOW
					LR-	0.56 (0.43, 0.73)	Not serious	Not serious	Not serious	Serious		MODERATE
Notes on risk of bias												
Holman 1992: People with uncertain clinical diagnoses (> 10% population) were excluded from analysis												
Dobert 2005: It is unclear whether a consecutive or random sample of patients was enrolled or whether inappropriate exclusions were avoided.												

P.2.7.8 Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
ALL EVIDENCE POOLED												
10 studies (Andreasen 2001; Brandt 2008; Duits 2014; Dumurgier 2015 (Lille); Dumurgier 2015 (Paris); Dumurgier 2015 (Montpellier); Gabelle 2012 (Lille and Paris); Gabelle 2012 (Montpellier); Knapskogog 2016; Mulder 2010)	8 × prospective; 2 × retrospective	3,685	0.76 (0.67, 0.83)	0.74 (0.68, 0.79)	LR+	2.88 (2.23, 3.67)	Serious	Serious	Not serious	Not serious	-	LOW
					LR-	0.34 (0.23, 0.46)	Serious	Serious	Not serious	Not serious		LOW
Notes on risk of bias												
Mulder 2010: It is unclear whether participants were consecutively or randomly recruited; the test cut offs were not pre-specified but selected to obtain 85% sensitivity; the timing between the reference and index tests is unclear and it is unclear whether the index test was interpreted independently of the reference test results												
Gabelle 2012: Test thresholds were not pre-specified, but optimised based on the data; it was unclear whether the study enrolled random or consecutive people or avoided inappropriate exclusions. A subgroup analysis was carried out but as < 10% population was excluded the study was not downgraded for this.												
Dumurgier 2015: The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study and the timing of the reference and index tests is unclear.												
Additional notes: the Dumurgier study had 3 independent data sets from 3 different clinics; the Gabelle study had 2 independent data sets from 2 clinics.												

P.2.7.9 Amyloid Beta 1-42 and total tau

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

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

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

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

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

P.2.7.12 Amyloid Beta 1-42/Total Tau

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

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

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

P.2.7.14 EEG

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

P.2.7.15 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
6 studies (Dobert 2005; Frisoni 2009; Ossenkoppele 2013; Panegyres 2009; Silverman 2001; Yakushev 2010)	6 × prospective	544	0.72 (0.53, 0.86)	0.77 (0.70, 0.83)	LR+	3.19 (2.05, 4.60)	Serious	Serious	Serious	Not serious	-	VERY LOW
					LR-	0.37 (0.18, 0.62)	Serious	Serious	Serious	Serious		VERY LOW
<p>Notes on risk of bias</p> <p>Dobert 2005: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided.</p> <p>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> <p>Yakushev 2010: Subgroup analysis with >10% population excluded</p> <p>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.</p> <p>Notes on indirectness</p> <p>Panegyres 2009: The study only recruited people with early onset dementia (<65 years old).</p> <p>Ossenkoppele 2013: It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.</p>												

P.2.7.16 FDG-PET/CT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Motara 2017)	Retrospective	98	0.87 (0.74, 0.94)	0.96 (0.86, 0.99)	LR+	22.61 (5.78, 88.40)	Serious	n/a	Serious	Not serious	-	LOW
					LR-	0.14 (0.06, 0.29)	Serious	n/a	Serious	Not serious		LOW
<p>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.</p> <p>Notes on indirectness Motara 2017: There were 22 unstated reasons for exclusion</p>												

P.2.7.17 [18F] flutemetamol PET

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

P.2.7.18 Formula Hulstaert (biomarkers)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Duits 2014)	Prospective	1,149	0.93 (0.91,0.95)	0.74 (0.70, 0.77)	LR+	3.54 (3.06, 4.10)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.09 (0.07, 0.13)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.7.19 Formula Mattson (biomarkers)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Duits 2014)	Prospective	1,149	0.80 (0.77, 0.83)	0.85 (0.81, 0.88)	LR+	5.26 (4.28,6.47)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.24 (0.20, 0.28)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.7.20 Formula Mulder (biomarkers)

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

P.2.7.21 Formula Schoonenboom (biomarkers)

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

P.2.7.22 Mass Spectrometry

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Jahn 2011)	Prospective	86	0.87 (0.77, 0.94)	0.83 (0.62, 0.93)	LR+	5.02 (2.05, 12.29)	Serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.15 (0.08, 0.30)	Serious	n/a	Not serious	Serious		MODERATE

P.2.7.23 MRI

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Suppa 2015)	Retrospective	100	0.61 (0.46, 0.74)	0.86 (0.74, 0.93)		LR+	4.30 (2.17, 8.50)	Serious	n/a	Not serious	Not serious	-	MODERATE
						LR-	0.45 (0.31, 0.66)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias													
Suppa 2015: It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; assay cut-offs were determined using ROC analysis.													

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Suppa 2015)	Retrospective	100	0.70 (0.56, 0.82)	0.71 (0.58, 0.82)		LR+	2.47 (1.56, 3.89)	Serious	n/a	Not serious	Serious	-	LOW
						LR-	0.41 (0.25, 0.67)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias													
Suppa 2015: It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; assay cut-offs were determined using ROC analysis.													

P.2.7.26 MRI Hippocampal grey matter volume left/ total grey matter volume (HVL/GMV). Cut-off 4.69 per mille.

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Suppa 2015)	Retrospective	100	0.80 (0.65, 0.89)	0.66 (0.53, 0.77)	LR+	2.34 (1.58, 3.48)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.31 (0.17, 0.57)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias												
Suppa 2015: It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; assay cut-offs were determined using ROC analysis.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Suppa 2015)	Retrospective	100	0.75 (0.60, 0.86)	0.77 (0.64, 0.86)	LR+	3.23 (1.95, 5.36)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.33 (0.19, 0.55)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias												
Suppa 2015: It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; assay cut-offs were determined using ROC analysis.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Suppa 2015)	Retrospective	100	0.80 (0.65, 0.89)	0.80 (0.68, 0.89)	LR+	4.05 (2.34, 7.02)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.25 (0.14, 0.46)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias												
Suppa 2015: It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; assay cut-offs were determined using ROC analysis.												

P.2.7.29 MRI Total hippocampal grey matter volume/total grey matter volume (HV/GMV). Cut-off 8.36 per mille.

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Suppa 2015)	Retrospective	100	0.66 (0.51, 0.78)	0.88 (0.76, 0.94)	LR+	5.27 (2.55, 10.88)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.39 (0.26, 0.59)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias												
Suppa 2015: It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; assay cut-offs were determined using ROC analysis.												

P.2.7.30 Olfactory Test \geq 3 errors

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

P.2.7.31 Olfactory Test \geq 4 errors

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Christensen 2017)	Prospective	50	0.50 (0.31, 0.69)	0.73 (0.53, 0.87)	LR+	1.86 (0.88, 3.93)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.68 (0.43, 1.09)	Not serious	n/a	Not serious	Serious		MODERATE
Notes on risk of bias Christensen 2017: Although the threshold was not pre-specified, data was presented for all possible cut offs.												

P.2.7.32 Olfactory Test ≥ 5 errors

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

P.2.7.33 p-tau 181

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
ALL EVIDENCE POOLED												
9 studies (Brandt 2008; Duits 2014; Dumurgier 2015 (Lille); Dumurgier 2015 (Paris); Dumurgier 2015 (Montpellier); Gabelle 2012 (Lille and Paris); Gabelle 2012 (Montpellier); Knapskog 2016; Mulder 2010)	7 × prospective; 2 × retrospective	3,448	0.75 (0.62, 0.84)	0.84 (0.76, 0.90)	LR+	4.87 (3.37, 6.92)	V. serious	Serious	Not serious	Not serious	-	VERY LOW
						0.30 (0.20, 0.43)	V. serious	Serious	Not serious	Not serious		VERY LOW
Notes on risk of bias Mulder 2010: It is unclear whether participants were consecutively or randomly recruited; the test cut offs were not pre-specified but selected to obtain 85% sensitivity; the timing between the reference and index tests is unclear and it is unclear whether the index test was interpreted independently of the reference test results Gabelle 2012: Test thresholds were not pre-specified, but optimised based on the data; it was unclear whether the study enrolled random or consecutive people or avoided inappropriate exclusions. A subgroup analysis was carried out but as < 10% population was excluded the study was not downgraded for this. Dumurgier 2015: The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study and the timing of the reference and index tests is unclear. Additional notes: the Dumurgier study had 3 independent data sets from 3 different clinics; the Gabelle study had 2 independent data sets from 2 clinics.												

P.2.7.34 p-tau and Amyloid Beta 1-42 combined then in case of discrepancy between p-tau and Amyloid Beta 1-42 the Amyloid Beta 42/40 ratio was used in place of Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Dumurgier 2015)	Prospective	329	0.88 (0.82, 0.92)	0.91 (0.86, 0.95)	LR+	10.29 (6.41, 16.50)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.13 (0.08, 0.20)	V. serious	n/a	Not serious	Not serious		LOW
Notes on risk of bias												
Dumurgier 2015: The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study; the timing of the reference and index tests is unclear and a subgroup analysis was carried out that excluded >10% population (with indeterminate results).												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Dumurgier 2015)	Prospective	303	0.87 (0.81, 0.92)	0.91 (0.86, 0.95)	LR+	9.79 (6.01, 15.93)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.14 (0.09, 0.22)	V. serious	n/a	Not serious	Not serious		LOW
Notes on risk of bias												
Dumurgier 2015: The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study; the timing of the reference and index tests is unclear and a subgroup analysis was carried out that excluded >10% population (with indeterminate results).												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Duits 2014; Dumurgier 2015)	2 × prospective	1,434	0.87 (0.81, 0.92)	0.90 (0.74, 0.97)	LR+	8.77 (2.95, 26.08)	V. serious	Serious	Not serious	Not serious	-	VERY LOW
					LR-	0.14 (0.08, 0.25)	V. serious	Serious	Not serious	Not serious		VERY LOW
Notes on risk of bias												
Dumurgier 2015: The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study; the timing of the reference and index tests is unclear and a subgroup analysis was carried out that excluded >10% population (with indeterminate results).												

P.2.7.37 Total Tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
ALL EVIDENCE POOLED												
9 studies (Brandt 2008; Duits 2014; Dumurgier (Lille) 2015; Dumurgier 2015 (Paris); Dumurgier 2015 (Montpellier); Gabelle 2012 (Lille and Paris); Gabelle 2012 (Montpellier); Knapskog 2016; Mulder 2010)	7 × prospective; 2 × retrospective	3,447	0.78 (0.71, 0.84)	0.78 (0.74, 0.82)	LR+	3.62 (3.14, 4.17)	Serious	Serious	Not serious	Not serious	-	LOW
					LR-	0.28 (0.21, 0.36)	V. serious	Serious	Not serious	Not serious		VERY LOW
Notes on risk of bias												
Mulder 2010: It is unclear whether participants were consecutively or randomly recruited; the test cut offs were not pre-specified but selected to obtain 85% sensitivity; the timing between the reference and index tests is unclear and it is unclear whether the index test was interpreted independently of the reference test results												
Gabelle 2012: Test thresholds were not pre-specified, but optimised based on the data; it was unclear whether the study enrolled random or consecutive people or avoided inappropriate exclusions. A subgroup analysis was carried out but as < 10% population was excluded the study was not downgraded for this.												
Dumurgier 2015: The reference standard diagnosis included consideration of the CSF results; the test cut-offs were optimised; patients with unknown clinical diagnoses or MCI were excluded from the study and the timing of the reference and index tests is unclear and it is unclear whether a consecutive or random sample of patients was enrolled.												
Additional notes: the Dumurgier study had 3 independent data sets from 3 different clinics; the Gabelle study had 2 independent data sets from 2 clinics.												

P.2.7.38 Total Tau/Amyloid Beta 1-42

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Goodman 2007)	Retrospective	168	0.59 (0.49, 0.69)	0.73 (0.62, 0.81)	LR+	2.15 (1.45, 3.19)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.56 (0.42, 0.75)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.8 AD versus other dementias

P.2.8.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
1 study (Velakoulis 1997)	Prospective	33	0.89 (0.50, 0.98)	0.71 (0.50, 0.85)	LR+	3.05 (1.57, 5.93)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.16 (0.02, 1.01)	V. serious	n/a	Not serious	Serious		VERY LOW

Notes on risk of bias

Velakoulis 1997: Subgroup analysis where >10% study population excluded and it was unclear whether: the index test results were interpreted without knowledge of the results of the reference standard; the index test threshold was pre-specified or the reference standard results interpreted without knowledge of the results of the index test.

P.2.8.2 AD scale (≥6)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Gustafson 2010)	Prospective	190	0.80 (0.71, 0.87)	0.87 (0.78, 0.93)	LR+	6.18 (3.53, 10.82)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.23 (0.16, 0.34)	Not serious	n/a	Not serious	Not serious		HIGH
Notes on risk of bias												
Gustafson 2010: The study was not downgraded for subgroup analysis as <10% population was excluded.												

P.2.8.3 Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
3 studies (Boutoleau-Brettonniere 2012; Ibach 2006; Maddalena 2003)	3 × prospective	249	0.74 (0.67, 0.81)	0.62 (0.53, 0.71)	LR+	1.96 (1.46, 2.62)	V. serious	Not serious	Not serious	Serious	-	VERY LOW
					LR-	0.41 (0.29, 0.58)	V. serious	Not serious	Not serious	Serious		VERY LOW
Notes on risk of bias												
Maddalena 2003: It was unclear whether inappropriate exclusions had been made; an optimised threshold was used for each test and within each test for different analyses; it was unclear whether the index and reference tests were interpreted independently of each other.												
Ibach 2006: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the test thresholds were not pre-specified and it is unclear whether the index test was interpreted without knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.												
Boutoleau-Brettonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.												

P.2.8.4 Amyloid Beta 1-42 and total tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Frisoni 2009)	Prospective	66	0.71 (0.55, 0.83)	0.96 (0.79, 0.99)	LR+	19.89 (2.87, 137.80)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.30 (0.18, 0.50)	V. serious	n/a	Not serious	Not serious		LOW
Notes on risk of bias												
Frisoni 2009: Subgroup analysis with >10% population excluded; patients whose cognitive deficit reverted (regarded as primarily depressed with secondary cognitive impairment) were excluded from the study; unclear whether reference test was interpreted without knowledge of index test and unclear whether results of index test interpreted without knowledge of reference test.												

P.2.8.5 Apo E (≥1 allele)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Mayeux 1998)	Retrospective	2,188	0.65 (0.62, 0.67)	0.68 (0.64, 0.72)	LR+	2.03 (1.75, 2.34)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.52 (0.48, 0.57)	Not serious	n/a	Not serious	Serious		MODERATE

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Boutoleau-Brettonniere 2012)	Prospective	44	0.97 (0.69, 1.00)	0.69 (0.49, 0.83)	LR+	3.09 (1.76, 5.42)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.04 (0.00, 0.60)	V. serious	n/a	Not serious	Serious		VERY LOW
Notes on risk of bias												
Boutoleau-Brettonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.												

P.2.8.7 Computed Tomography, CT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (O'Brien 2000)	Prospective	103	0.51 (0.39, 0.62)	0.38 (0.24, 0.55)	LR+	0.82 (0.58, 1.17)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	1.29 (0.79, 2.10)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias												
O'Brien 2000: Subgroup analysis with >10% population excluded												

P.2.8.8 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
6 studies (Arslan 2015; Frisoni 2009; Hoffman 2000; Jagust 2007; Ossenkoppele 2013; Yakushev 2010)	4 × prospective; 2 × retrospective	300	0.71 (0.60, 0.80)	0.66 (0.57, 0.74)	LR+	2.07 (1.52, 2.78)	Serious	Not serious	Not serious	Serious	-	LOW
					LR-	0.46 (0.30, 0.64)	Serious	Serious	Not serious	Serious		VERY LOW
<p>Notes on risk of bias</p> <p>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> <p>Yakushev 2010: Subgroup analysis with >10% population excluded</p> <p>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.</p> <p>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.</p> <p>Notes on indirectness</p> <p>Ossenkoppele 2013: It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.</p>												

P.2.8.9 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Frisoni 2009; Koikkalainen 2016)	2 × prospective	471	0.62 (0.09, 0.96)	0.67 (0.40, 0.86)	LR+	1.54 (1.08, 2.19)	Serious	Serious	Not serious	Serious	-	VERY LOW
					LR-	0.50 (0.14, 1.84)	Serious	Serious	Not serious	Serious		VERY LOW
Notes on risk of bias												
Frisoni 2009: Subgroup analysis with >10% population excluded; patients whose cognitive deficit reverted (regarded as primarily depressed with secondary cognitive impairment) were excluded from the study; unclear whether reference test was interpreted without knowledge of index test.												
Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.												

P.2.8.10 p-tau 181

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
3 studies (Boutoleau-Bretonniere 2012; Ibach 2006; Maddalena 2003)	3 x prospective	2249	0.75 (0.64, 0.84)	0.74 (0.61, 0.83)	LR+	2.97 (1.73, 5.09)	V. serious	Serious	Not serious	Serious	-	VERY LOW
					LR-	0.35 (0.21, 0.57)	V. serious	Not serious	Not serious	Serious		VERY LOW
Notes on risk of bias												
Maddalena 2003: It was unclear whether inappropriate exclusions had been made; an optimised threshold was used for each test and within each test for different analyses; it was unclear whether the index and reference tests were interpreted independently of each other.												
Ibach 2006: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the test thresholds were not pre-specified and it is unclear whether the index test was interpreted without knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.												
Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Ibach 2006; Maddalena 2003)	2 × prospective	205	0.79 (0.71, 0.85)	0.74 (0.64, 0.83)	LR+	3.07 (2.08, 4.52)	V. serious	Not serious	Not serious	Not serious	-	LOW
					LR-	0.29 (0.20, 0.41)	V. serious	Not serious	Not serious	Not serious		LOW
Notes on risk of bias Maddalena 2003: It was unclear whether inappropriate exclusions had been made; an optimised threshold was used for each test and within each test for different analyses; it was unclear whether the index and reference tests were interpreted independently of each other. Ibach 2006: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the test thresholds were not pre-specified and it is unclear whether the index test was interpreted without knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.												

P.2.8.12 Total tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
3 studies (Boutoleau-Brettonniere 2012; Ibach 2006; Yakushev 2010)	3 × prospective	205	0.71 (0.52, 0.85)	0.82 (0.63, 0.93)	LR+	4.28 (1.75, 9.99)	V. serious	Not serious	Not serious	Not serious	-	LOW
					LR-	0.38 (0.24, 0.61)	V. serious	Serious	Not serious	Serious		VERY LOW
Notes on risk of bias												
Ibach 2006: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the test thresholds were not pre-specified and it is unclear whether the index test was interpreted without knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.												
Yakushev 2010: Subgroup analysis with >10% population excluded; use of optimised thresholds for test												
Boutoleau-Brettonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.												

P.2.8.13 Total Tau/Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ibach 2006)	Prospective	124	0.75 (0.64, 0.83)	0.75 (0.61, 0.85)	LR+	3.00 (1.81, 4.98)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.33 (0.22, 0.51)	V. serious	n/a	Not serious	Serious		VERY LOW
Notes on risk of bias												
Ibach 2006: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the test thresholds were not pre-specified and it is unclear whether the index test was interpreted without knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.												

P.2.9 AD versus VaD

P.2.9.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
2 studies (Launes 1991; McMurdo 1994)	2 × prospective	97	0.61 (0.49, 0.72)	0.85 (0.69, 0.93)	LR+	4.13 (1.85, 9.21)	Serious	Not serious	Not serious	Serious	-	LOW
					LR-	0.45 (0.31, 0.66)	Serious	Not serious	Not serious	Serious		LOW
MULTIPLE CAMERA												
1 study (Boutoleau-Bretonniere 2012)	Prospective	26	0.78 (0.54, 0.91)	0.50 (0.20, 0.80)	LR+	1.56 (0.75, 3.25)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.44 (0.15, 1.35)	V. serious	n/a	Not serious	Serious		VERY LOW
ALL EVIDENCE POOLED												
3 studies (Boutoleau-Bretonniere 2012; Launes 1991; McMurdo 1994)	3 × prospective	123	0.64 (0.53, 0.74)	0.74 (0.45, 0.91)	LR+	2.54 (1.19, 5.41)	V. serious	Not serious	Not serious	Serious	-	VERY LOW
					LR-	0.45 (0.32, 0.64)	Serious	Not serious	Not serious	Serious		LOW
Notes on risk of bias												
Launes 1991: Subgroup analysis used with >10% study population excluded.												
McMurdo 1994: Subgroup analysis used with >10% study population discarded.												
Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded												

P.2.9.2 Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Andreasen 2001)	Prospective	186	0.65 (0.57, 0.72)	0.48 (0.29, 0.68)	LR+	1.25 (0.83, 1.87)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.73 (0.45, 1.18)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.9.3 Computed Tomography, CT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (O'Brien 2000)	Prospective	94	0.51 (0.39, 0.62)	0.32 (0.17, 0.52)	LR+	0.75 (0.52, 1.06)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	1.54 (0.83, 2.86)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias												
O'Brien 2000: Subgroup analysis with >10% population excluded												

P.2.9.4 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	247	0.29 (0.24, 0.35)	0.88 (0.68, 0.96)	LR+	2.33 (0.79, 6.85)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.81 (0.68, 0.96)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias												
Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.												

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

P.2.10.1 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Vijverberg 2016b)	Prospective	111	0.89 (0.71, 0.96)	0.68 (0.57, 0.77)	LR+	2.77 (1.97, 3.88)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.16 (0.06, 0.48)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias												
Vijverberg 2016b: 19% study population was excluded from analysis and it is unclear whether a consecutive or random group of patients was enrolled or whether inappropriate exclusions were avoided; all test results (including the index tests) were used to reach the clinical diagnosis.												

P.2.10.2 FDG-PET and MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Vijverberg 2016b)	Prospective	111	0.96 (0.78, 0.99)	0.73 (0.62, 0.81)	LR+	3.52 (2.46, 5.02)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.05 (0.01, 0.35)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias												
Vijverberg 2016b: 19% study population was excluded from analysis and it is unclear whether a consecutive or random group of patients was enrolled or whether inappropriate exclusions were avoided; all test results (including the index tests) were used to reach the clinical diagnosis.												

P.2.10.3 FTDC criteria for bv FTD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Harris 2013)	Retrospective	147	0.79 (0.69, 0.87)	0.96 (0.88, 0.99)	LR+	18.48 (6.07, 56.26)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.22 (0.14, 0.34)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias												
Harris 2013: Study excludes third of sample at initial screening												

P.2.10.4 FTDC criteria for possible bvFTD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Vijverberg 2016a)	Prospective	116	0.85 (0.67, 0.94)	0.27 (0.19, 0.37)	LR+	1.17 (0.95, 1.43)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.55 (0.21, 1.44)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias												
Vijverberg 2016a: 19% study population was excluded from analysis and it is unclear whether a consecutive or random group of patients was enrolled or whether the reference standard results were interpreted without knowledge of the results of the index test.												

P.2.10.5 FTDC criteria for probable bvFTD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Vijverberg 2016a)	Prospective	116	0.85 (0.67, 0.94)	0.82 (0.73, 0.89)	LR+	4.74 (2.96, 7.59)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.18 (0.07, 0.45)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias												
Vijverberg 2016a: 19% study population was excluded from analysis and it is unclear whether a consecutive or random group of patients was enrolled or whether the reference standard results were interpreted without knowledge of the results of the index test.												

P.2.10.6 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Vijverberg 2016b)	Prospective	111	0.70 (0.51, 0.84)	0.93 (0.85, 0.97)	LR+	9.85 (4.39, 22.12)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.32 (0.18, 0.57)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias												
Vijverberg 2016b: 19% study population was excluded from analysis and it is unclear whether a consecutive or random group of patients was enrolled or whether inappropriate exclusions were avoided; all test results (including the index tests) were used to reach the clinical diagnosis.												

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

P.2.11.1 FDG-PET

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

P.2.12 CADASIL versus CADASIL-like syndromes

P.2.12.1 Skin biopsy

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ampuero 2009)	Prospective	90	0.96 (0.78, 0.99)	0.68 (0.56, 0.79)	LR+	3.03 (2.10, 4.39)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.05 (0.01, 0.37)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.13 CBD versus non-CBD

P.2.13.1 CBD consensus criteria

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

P.2.14 CJD versus non-CJD

P.2.14.1 Amyloid Beta 1-42 and total tau

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Fourier 2017)	Retrospective	268	0.94 (0.85, 0.97)	0.95 (0.91, 0.98)	LR+	19.84 (10.46, 37.65)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.07 (0.03, 0.16)	Not serious	n/a	Not serious	Not serious		HIGH

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

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

P.2.14.4 CSF 14-3-3 ELISA

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Kenney 2000; Leitao 2016)	1 × prospective; 1 × retrospective	292	0.94 (0.78, 0.98)	0.96 (0.91, 0.98)	LR+	22.61 (10.33, 49.47)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.07 (0.02, 0.24)	Serious	Serious	Not serious	Not serious		LOW

Notes on risk of bias

Kenney 2000: The test threshold was not pre-specified and it was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test.
Leitao 2016: It was unclear whether: a consecutive or random sample of patients was enrolled; the study avoided inappropriate exclusions; test thresholds were pre-specified.

P.2.14.5 CSF 14-3-3 immunoblotting

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
17 studies (Bahl 2008; Beudry 1998; Burkhard 2001; Chohan 2010; Coulthart 2011; Cuadrado-Corrales 2006; Fourier 2017, Foutz 2017; Hamlin 2012; Kenney 2000; Lattanzio 2017; Lemstra 2000; Rohan 2015; Tagliapietra 2013; Van Everbroeck 2003; Zerr 1998; Zerr 2000)	8 × prospective; 9 × retrospective	6,086	0.87 (0.84, 0.90)	0.83 (0.73, 0.90)	LR+	5.44 (3.28, 8.78)	Serious	Serious	Not serious	Not serious	-	LOW
					LR-	0.16 (0.13, 0.19)	Serious	Not serious	Not serious	Not serious		MODERATE
Notes on risk of bias												
<p>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.</p> <p>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.</p> <p>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.</p> <p>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.</p> <p>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.</p> <p>Cuadrado-Corrales 2006: 20% drop out due to problems with samples; <10 % excluded from analysis for possible CJD so not downgraded for this issue.</p> <p>Bahl 2008: Exclusion of possible CJD group from index tests may inflate test sensitivity</p> <p>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> <p>Coulthart 2011: Not downgraded for exclusions during data analysis as <10% population excluded.</p> <p>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.</p> <p>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.</p>												
Notes on indirectness												
Burkhard 2001: Patients do not have suspected CJD at baseline												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Chohan 2010)	Retrospective	411	0.62 (0.56, 0.68)	0.95 (0.90, 0.97)	LR+	11.72 (6.16, 22.29)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.40 (0.34, 0.47)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias												
Chohan 2010: Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Van Everbroeck 2003)	Retrospective	250	0.99 (0.87, 1.00)	0.98 (0.94, 0.99)	LR+	43.81 (17.57, 109.24)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.01 (0.00, 0.15)	Not serious	n/a	Not serious	Not serious		HIGH

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Chohan 2010)	Retrospective	351	0.75 (0.69, 0.80)	0.88 (0.82, 0.93)	LR+	6.33 (3.97, 10.09)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.28 (0.22, 0.36)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias												
Chohan 2010: Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Chohan 2010)	Retrospective	351	0.57 (0.50, 0.63)	0.96 (0.90, 0.98)	LR+	12.81 (5.81, 28.25)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.45 (0.38, 0.53)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias												
Chohan 2010: Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.												

P.2.14.10 EEG

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

P.2.14.11 European criteria for CJD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Brandel 2000)	Retrospective	236	0.91 (0.86, 0.95)	0.28 (0.16, 0.43)	LR+	1.26 (1.04, 1.53)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.32 (0.16, 0.62)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.14.12 French criteria for CJD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Brandel 2000)	Retrospective	236	0.88 (0.83, 0.92)	0.50 (0.35, 0.65)	LR+	1.77 (1.29, 2.42)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.23 (0.14, 0.38)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.14.13 Master's criteria for CJD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Brandel 2000)	Retrospective	236	0.98 (0.95, 1.00)	0.10 (0.04, 0.24)	LR+	1.09 (0.99, 1.21)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.15 (0.04, 0.66)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.14.14 MRI

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

P.2.14.15 MRI, DWI

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

P.2.14.16 Neuron-specific enolase

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Bahl 2008; Beudry 1998)	2 × prospective	295	0.74 (0.65, 0.82)	0.90 (0.85, 0.94)	LR+	8.00 (5.05, 12.69)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.28 (0.20, 0.40)	Serious	Not serious	Not serious	Not serious		MODERATE
Notes on risk of bias												
Beudry 1998: Optimised test cut-offs were used and it was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test.												
Bahl 2008: Exclusion of possible CJD group from index tests may inflate test sensitivity												

P.2.14.17 New criteria for sporadic CJD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Zerr 2009)	Retrospective	74	0.98 (0.87, 1.00)	0.71 (0.50, 0.85)	LR+	3.36 (1.80, 6.28)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.03 (0.00, 0.20)	V. serious	n/a	Not serious	Not serious		LOW
Notes on risk of bias												
Zerr 2009: Unclear whether patients were selected randomly or consecutively or whether inappropriate exclusions were avoided; the optimal index test thresholds were determined during the study and a subgroup analysis was used to determine test sensitivity and specificity.												

P.2.14.18 p-tau 181/total tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Bahl 2008; Leitao 2016)	1 × prospective; 1 × retrospective	282	0.93 (0.71, 0.99)	0.89 (0.84, 0.93)	LR+	8.10 (5.35, 12.26)	V. serious	Not serious	Not serious	Not serious	-	LOW
					LR-	0.08 (0.02, 0.37)	V. serious	Serious	Not serious	Not serious		VERY LOW
Notes on risk of bias												
Bahl 2008: Exclusion of possible CJD group from index tests may inflate test sensitivity; test cut off not pre-specified												
Leitao 2016: It was unclear whether: a consecutive or random sample of patients was enrolled; the study avoided inappropriate exclusions; test thresholds were pre-specified.												

P.2.14.19 RT-QuIC

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Foutz 2017; Lattanzio 2017)	1 × prospective; 1 × retrospective	779	0.89 (0.69, 0.97)	0.99 (0.96, 1.00)	LR+	99.38 (26.52, 372.49)	Not serious	Not serious	Not serious	Not serious	-	HIGH

P.2.14.20 S100B, 1.0ng/ml

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Chohan 2010)	Retrospective	412	0.65 (0.59, 0.71)	0.90 (0.84, 0.94)	LR+	6.46 (4.08, 10.24)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.39 (0.33, 0.47)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias												
Chohan 2010: Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.												

P.2.14.21 S100B, 2.5ng/ml

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Beudry 1998; Coulthart 2011)	2 × prospective	1,053	0.87 (0.82, 0.91)	0.87 (0.84, 0.89)	LR+	6.65 (5.52, 8.00)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.15 (0.10, 0.21)	Serious	Not serious	Not serious	Not serious		MODERATE
Notes on risk of bias												
Beudry 1998: Optimised test cut-offs were used and it was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test.												
Coulthart 2011: Optimised threshold used to analyse S100B results; unclear whether the reference standards would correctly classify non-CJD cases as not specified; not downgraded for exclusions during data analysis as <10% population excluded.												

P.2.14.22 S100B, 4.2ng/ml

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Coulthart 2011)	Prospective	924	0.52 (0.43, 0.60)	0.97 (0.96, 0.98)	LR+	17.26 (11.23, 26.52)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.50 (0.41, 0.60)	Not serious	n/a	Not serious	Serious		MODERATE
Notes on risk of bias												
Coulthart 2011: Unclear whether the reference standards would correctly classify non-CJD cases as not specified; not downgraded for exclusions during data analysis as <10% population excluded and standard threshold used to analyse S100B results.												

P.2.14.23 Total Tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
11 studies (Bahl 2008; Chohan 2010; Coulthart 2011; Foutz 2017; Hamlin 2012; Lattanzio 2017; Leitao 2016; Rohan 2015; Tagliapietra 2013; Van Everbroeck 2003; Van Everbroeck 2004)	4 × prospective; 7 × retrospective	3,614	0.87 (0.84, 0.90)	0.88 (0.80, 0.93)	LR+	7.22 (4.34, 11.60)	Serious	Serious	Not serious	Not serious	-	LOW
					LR-	0.15 (0.12, 0.19)	Serious	Serious	Not serious	Not serious		LOW
Notes on risk of bias												
Van Everbroeck 2004: > 10% population excluded from analysis												
Bahl 2008: Exclusion of possible CJD group from index tests may inflate test sensitivity; test cut off not pre-specified												
Chohan 2010: Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.												
Coulthart 2011: Optimised threshold used to analyse Tau results; unclear whether the reference standards would correctly classify non-CJD cases as not specified; not downgraded for exclusions during data analysis as <10% population excluded.												
Hamlin 2012: Multiple thresholds were tested and unclear whether researchers were blind to reference test results or that the reference test was interpreted without knowledge of index test.												
Rohan 2015: It was unclear whether: a consecutive or random sample of patients was enrolled; the index test results were interpreted without knowledge of the results of the reference standard; a pre-specified cut-off was used for the index tests; the reference standard results were interpreted without knowledge of the index test results.												
Leitao 2016: It was unclear whether: a consecutive or random sample of patients was enrolled; the study avoided inappropriate exclusions; test thresholds were pre-specified.												
Lattanzio 2017: An optimised threshold was used for the assay.												

P.2.14.24 Total Tau and S100B

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Chohan 2010)	Retrospective	351	0.59 (0.52, 0.65)	0.95 (0.90, 0.98)	LR+	11.34 (5.46, 23.53)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.43 (0.37, 0.51)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias												
Chohan 2010: Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.												

P.2.14.25 WHO CJD criteria

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Heath 2010; Zerr 2009)	2 × retrospective	306	0.90 (0.85, 0.94)	0.71 (0.61, 0.79)	LR+	3.14 (2.29, 4.30)	V. serious	Not serious	Serious	Not serious	-	VERY LOW
					LR-	0.14 (0.09, 0.21)	V. serious	Not serious	Serious	Not serious		VERY LOW
Notes on risk of bias												
Zerr 2009: Unclear whether patients were selected randomly or consecutively or whether inappropriate exclusions were avoided; the optimal index test thresholds were determined during the study and a subgroup analysis was used to determine test sensitivity and specificity.												
Heath 2010: It was unclear whether the index test was interpreted without knowledge of the results of the reference test; whether a consecutive or random sample of patients was enrolled or inappropriate exclusions were avoided.												
Notes on indirectness												
Heath 2010: Mean age at onset < 40 years old												

P.2.15 DLB versus AD

P.2.15.1 Lewy body composite risk score, LBCRS, ≥ 3

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Galvin 2015)	Prospective	153	0.94 (0.84, 0.98)	0.78 (0.69, 0.85)	Measure	LR+	4.29 (2.95, 6.24)	Serious	n/a	Not serious	Not serious	-	MODERATE
						LR-	0.07 (0.02, 0.22)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias													
Galvin 2015: Subgroup analysis was carried out excluding >30% study population.													

P.2.15.2 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Koikkalainen 2016)	Prospective	270	0.43 (0.29, 0.57)	0.71 (0.65, 0.77)	Measure	LR+	1.48 (1.00, 2.19)	Serious	n/a	Not serious	Serious	-	LOW
						LR-	0.81 (0.62, 1.04)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias													
Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.													

P.2.16 DLB versus FTD

P.2.16.1 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	139	0.43 (0.29, 0.57)	0.86 (0.77, 0.92)	LR+	3.01 (1.65, 5.51)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.67 (0.52, 0.87)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias												
Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.												

P.2.17 DLB versus non-DLB

P.2.17.1 123I-FP-CIT SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
1 study (Walker 2009)	Retrospective	23	0.95 (0.55, 1.00)	0.89 (0.61, 0.98)	LR+	8.91 (1.95, 40.64)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.05 (0.00, 0.77)	Serious	n/a	Not serious	Serious		LOW
MULTIPLE CAMERA												
2 studies (Kemp 2011; O'Brien 2009; Thomas 2017)	1x prospective, 2x retrospective	161	0.78 (0.59, 0.89)	0.95 (0.87, 0.98)	LR+	15.40 (6.24, 38.01)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.25 (0.13, 0.48)	Not serious	Serious	Not serious	Not serious		MODERATE
ALL EVIDENCE POOLED												
3 studies (Kemp 2011; O'Brien 2009; Walker 2009; Thomas 2017)	1x prospective, 2 x retrospective	184	0.83 (0.52, 0.96))	0.94 (0.86, 0.98)	LR+	13.34 (6.14, 29.01)	Serious	Not serious	Not serious	Not serious	-	MODERATE
					LR-	0.22 (0.11, 0.44)	Not serious	Not serious	Not serious	Not serious		HIGH
Notes on risk of bias												
Walker 2009: Some of the included individuals had a presumed dementia diagnosis at baseline Kemp 2011: Index test used as part of the reference standard												

P.2.17.2 123I-IMP SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA												
1 study (Sakamoto 2014)	Retrospective	101	0.62 (0.42, 0.78)	0.75 (0.64, 0.83)	LR+	2.43 (1.48, 3.98)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.52 (0.31, 0.85)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias												
Sakamoto 2014: It was unclear whether the study avoided inappropriate exclusions or whether the reference standard results were interpreted without knowledge of the results of the index test.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA												
1 study (Sakamoto 2014)	Retrospective	100	0.88 (0.70, 0.96)	0.86 (0.77, 0.93)	LR+	6.55 (3.62, 11.84)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.13 (0.05, 0.39)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias												
Sakamoto 2014: It was unclear whether the study avoided inappropriate exclusions or whether the reference standard results were interpreted without knowledge of the results of the index test.												

P.2.17.4 123I-MIBG cardiac scintigraphy

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
5 studies (Estorch 2008; Manabe 2017; Sakamoto 2014; Sakamoto 2017, Slaets 2015)	4 × prospective; 1 × retrospective	607	0.89 (0.81, 0.93)	0.91 (0.82, 0.96)	LR+	10.80 (4.89, 21.50)	Serious	Serious	Not serious	Not serious	-	LOW
					LR-	0.13 (0.07, 0.21)	V. serious	Not serious	Not serious	Not serious		LOW
Notes on risk of bias												
Estorch 2008: Significant proportion of people not given a final reference standard diagnosis												
Sakamoto 2014: It was unclear whether the study avoided inappropriate exclusions or whether the reference standard results were interpreted without knowledge of the results of the index test.												
Slaets 2015: The diagnosing physicians were not blind to the index test results.												
Manabe 2017: Optimised test cut-offs were calculated and it was unclear whether the reference standard was interpreted without knowledge of the results of the index test or the index test was interpreted without knowledge of the results of the reference test.												
Sakamoto 2017: Selective reporting of sensitivity and specificity of outcome variables and it was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; whether the reference standard results were interpreted without knowledge of the results of the index test or whether the test cut-off was pre-specified.												

P.2.17.5 EEG

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Engedal 2015)	Prospective	387	0.87 (0.59, 0.97)	0.88 (0.84, 0.91)	LR+	7.01 (5.01, 9.80)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.15 (0.04, 0.55)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.17.6 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Ossenkoppele 2013; Panegyres 2009)	2 × prospective	255	0.53 (0.06, 0.96)	0.97 (0.91, 0.99)	LR+	19.64 (1.28, 301.23)	Serious	Serious	Serious	Serious	-	VERY LOW
					LR-	0.48 (0.11, 2.13)	Serious	Serious	Serious	V. serious		VERY LOW
<p>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.</p> <p>Notes on indirectness Panegyres 2009: The study only recruited people with early onset dementia (<65 years old). Ossenkoppele 2013: It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.</p>												

P.2.17.7 MRI

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ferman 2011)	Prospective	234	0.90 (0.82, 0.94)	0.73 (0.65, 0.80)	LR+	3.30 (2.49, 4.38)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.14 (0.08, 0.25)	Not serious	n/a	Not serious	Not serious		HIGH

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ferman 2011)	Prospective	234	0.85 (0.76, 0.91)	0.73 (0.65, 0.80)	LR+	3.11 (2.34, 4.15)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.21 (0.13, 0.34)	Not serious	n/a	Not serious	Not serious		HIGH

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

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ferman 2011)	Prospective	234	0.88 (0.80, 0.93)	0.73 (0.65, 0.80)	LR+	3.23 (2.43, 4.29)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.17 (0.10, 0.29)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.18 DLB versus other dementias

P.2.18.1 123I-FP-CIT SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
1 study (Treglia 2012)	Prospective	31	0.90 (0.68, 0.97)	0.91 (0.56, 0.99)	LR+	9.90 (1.52, 64.52)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.11 (0.03, 0.42)	Not serious	n/a	Not serious	Not serious		HIGH
MULTIPLE CAMERA												
1 study (Walker 2007)	Retrospective	20	0.83 (0.46, 0.97)	0.96 (0.60, 1.00)	LR+	21.67 (1.43, 333.42)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.17 (0.04, 0.75)	Not serious	n/a	Not serious	Serious		MODERATE
ALL EVIDENCE POOLED												
2 studies (Treglia 2012; Walker 2007)	1 × prospective; 1 × retrospective	51	0.88 (0.70, 0.96)	0.93 (0.72, 0.99)	LR+	12.72 (2.71, 59.68)	Not serious	Not serious	Not serious	Not serious	-	HIGH
					LR-	0.14 (0.05, 0.36)	Not serious	Not serious	Not serious	Not serious		HIGH
Notes on risk of bias												
Treglia 2012: Specific criteria used as the reference standard not reported												

P.2.18.2 123I-MIBG cardiac scintigraphy

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Treglia 2012)	Prospective	31	0.90 (0.68, 0.97)	0.91 (0.56, 0.99)		LR+	9.90 (1.52, 64.52)	Not serious	n/a	Not serious	Serious	-	MODERATE
						LR-	0.11 (0.03, 0.42)	Not serious	n/a	Not serious	Not serious		HIGH
Notes on risk of bias													
Treglia 2012: Specific criteria used as the reference standard not reported													

P.2.18.3 DLB consensus criteria

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Skogseth 2017)	Prospective	55	0.80 (0.57, 0.92)	0.89 (0.74, 0.96)		LR+	7.20 (2.79, 18.61)	Serious	n/a	Not serious	Not serious	-	HIGH
						LR-	0.23 (0.09, 0.54)	Serious	n/a	Not serious	Serious		LOW

P.2.18.4 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ossenkoppele 2013)	Prospective	98	0.20 (0.03, 0.69)	0.95 (0.88, 0.98)	LR+	3.72 (0.53, 26.13)	V. serious	n/a	Serious	Serious	-	VERY LOW
					LR-	0.85 (0.54, 1.31)	V. serious	n/a	Serious	Not serious		VERY LOW
<p>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.</p> <p>Notes on indirectness Ossenkoppele 2013: It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.</p>												

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

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

P.2.18.6 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	386	0.43 (0.29, 0.57)	0.76 (0.72, 0.81)	LR+	1.80 (1.23, 2.65)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.75 (0.58, 0.97)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias												
Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.												

P.2.19 DLB versus VaD

P.2.19.1 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	71	0.43 (0.29, 0.57)	0.88 (0.68, 0.96)	LR+	3.40 (1.12, 10.32)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.66 (0.49, 0.88)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias												
Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.												

P.2.20 FTD versus AD

P.2.20.1 99mTc-HMPAO SPECT

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
Notes on risk of bias												
Launes 1991: Subgroup analysis used with >10% study population excluded.												
Read 1995: Subgroup analysis used with >10% study population excluded; unclear whether random or consecutive patient enrolment was used; unclear if inappropriate exclusions avoided.												
Velakoulis 1997: Subgroup analysis where >10% study population excluded and it was unclear whether: the index test results were interpreted without knowledge of the results of the reference standard; the index test threshold was pre-specified or the reference standard results interpreted without knowledge of the results of the index test.												
Talbot 1998: Unclear if avoided inappropriate exclusions; unclear whether the reference standard results were interpreted without knowledge of the index test and whether the index test was carried out without knowledge of reference test result; no pre-specified index test threshold; subgroup analysis used with >10% study population excluded.												
Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.												
Rollin-Sillaire 2012: Subgroup analysis where >10% study population excluded												

P.2.20.2 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	315	0.50 (0.40, 0.60)	0.72 (0.66, 0.78)	LR+	1.80 (1.34, 2.41)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.69 (0.56, 0.86)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias												
Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.												

P.2.20.3 FTD versus DLB

P.2.20.4 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ossenkoppele 2013)	Prospective	23	0.34 (0.17, 0.57)	0.92 (0.38, 0.99)	LR+	4.11 (0.27, 62.70)	V. serious	n/a	Serious	V. serious	-	VERY LOW
					LR-	0.72 (0.48, 1.08)	V. serious	n/a	Serious	Serious		VERY LOW
Notes on risk of bias Ossenkoppele 2013: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the index test was interpreted with knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.												
Notes on indirectness Ossenkoppele 2013: It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.												

P.2.20.5 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	139	0.50 (0.40, 0.60)	0.94 (0.82, 0.98)	LR+	7.83 (2.57, 23.86)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.53 (0.43, 0.66)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.												

P.2.21 FTD versus non-FTD dementia plus unclassifiable

P.2.21.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA												
1 study (Boutoleau-Brettonniere 2012)	Prospective	56	0.73 (0.41, 0.91)	0.78 (0.63, 0.88)	LR+	3.27 (1.70, 6.30)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.35 (0.13, 0.93)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias												
Boutoleau-Brettonniere 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-Brettonniere 2012)	Prospective	56	0.18 (0.05, 0.51)	0.62 (0.47, 0.75)	LR+	0.48 (0.13, 1.78)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	1.31 (0.92, 1.88)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias												
Boutoleau-Brettonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases.												

P.2.23 FTD versus non-FTD

P.2.23.1 99mTc-ECD SPECT, visual assessment

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA												
1 study (Tripathi 2010)	Prospective	117	0.96 (0.78, 0.99)	0.99 (0.93, 1.00)	LR+	86.67 (12.32, 609.43)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.04 (0.01, 0.26)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias												
Tripathi 2010: 14% of participants were lost to follow up and did not receive a reference standard; it is unclear whether the index test was interpreted without knowledge of the reference standard.												

P.2.23.2 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
3 studies (Launes 1991; Read 1995; Talbot 1998)	2 × prospective ; 1 × retrospective	501	0.51 (0.20, 0.81)	0.93 (0.90, 0.95)	LR+	6.05 (2.77, 13.22)	V. serious	Not serious	Not serious	Not serious	-	LOW
					LR-	0.63 (0.40, 1.01)	V. serious	Not serious	Not serious	Serious		VERY LOW
MULTIPLE CAMERA												
2 studies (Boutoleau-Bretonniere 2012; Rollin-Sillaire 2012)	1 × prospective ; 1 × retrospective	108	0.74 (0.53, 0.88)	0.90 (0.53, 0.99)	LR+	7.88 (1.14, 54.71)	Serious	Serious	Not serious	Serious	-	VERY LOW
					LR-	0.30 (0.15, 0.59)	Serious	Not serious	Not serious	Serious		LOW
ALL EVIDENCE POOLED												
5 studies (Boutoleau-Bretonniere 2012; Launes 1991; Read 1995; Rollin-Sillaire 2012; Talbot 1998)	3 × prospective ; 2 × retrospective	609	0.59 (0.37, 0.78)	0.91 (0.84, 0.95)	LR+	7.03 (3.36, 13.10)	V. serious	Not serious	Not serious	Not serious	-	LOW
					LR-	0.46 (0.24, 0.69)	V. serious	Serious	Not serious	Serious		VERY LOW
Notes on risk of bias												
<p>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.</p> <p>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>												

P.2.23.3 SPECT/PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
1 study (Mendez 2007)	Prospective	134	0.90 (0.80, 0.96)	0.75 (0.63, 0.83)	LR+	3.57 (2.38, 5.36)	Not serious	n/a	Serious	Not serious	-	HIGH
					LR-	0.13 (0.06, 0.28)	Not serious	n/a	Serious	Not serious		HIGH

P.2.23.4 FDG-PET

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

Notes on risk of bias

Ossenkoppele 2013: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the index test was interpreted with knowledge of the reference diagnosis.

Notes on indirectness

Panegyres 2009: The study only recruited people with early onset dementia (<65 years old).

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

P.2.23.5 FTD consensus criteria

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Mendez 2007)	Retrospective	134	0.37 (0.26, 0.49)	0.99 (0.90, 1.00)	LR+	52.88 (3.28, 853.00)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.64 (0.53, 0.77)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.23.6 MRI

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

P.2.24 FTD versus other dementias

P.2.24.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
1 study (Velakoulis 1997)	Prospective	33	0.56 (0.25, 0.82)	0.96 (0.76, 0.99)	LR+	13.33 (1.79, 99.08)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.46 (0.22, 0.97)	V. serious	n/a	Not serious	Serious		VERY LOW
Notes on risk of bias												
Velakoulis 1997: Subgroup analysis where >10% study population excluded and it was unclear whether: the index test results were interpreted without knowledge of the results of the reference standard; the index test threshold was pre-specified or the reference standard results interpreted without knowledge of the results of the index test.												

P.2.24.2 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Arslan 2015; Ossenkoppele 2013)	1 × prospective; 1 × retrospective	146	0.40 (0.25, 0.57)	0.78 (0.49, 0.93)	LR+	1.78 (0.91, 3.51)	V. serious	Not serious	Serious	Serious	-	VERY LOW
					LR-	0.78 (0.59, 1.03)	V. serious	Not serious	Serious	Not serious		VERY LOW
Notes on risk of bias												
Ossenkoppele 2013: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the index test was interpreted with knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.												
Arslan 2015: Unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard and if the imaging patterns were pre-specified; the reference standard results were interpreted independently of the index test results.												
Notes on indirectness												
Ossenkoppele 2013: It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.												

P.2.24.3 FTD scale (≥6)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Gustafson 2010)	Prospective	190	0.92 (0.81, 0.97)	0.92 (0.86, 0.96)	LR+	11.58 (6.53, 20.52)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.08 (0.03, 0.21)	Not serious	n/a	Not serious	Not serious		HIGH
Notes on risk of bias												
Gustafson 2010: The study was not downgraded for subgroup analysis as <10% population was excluded.												

P.2.24.4 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	386	0.50 (0.40, 0.60)	0.78 (0.72, 0.82)	LR+	2.23 (1.66, 2.99)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.64 (0.52, 0.80)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias												
Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.												

P.2.25 FTD versus VaD

P.2.25.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
2 studies (Launes 1991; Talbot 1998)	2 × prospective	196	0.46 (0.36, 0.57)	0.85 (0.51, 0.97)	LR+	2.58 (0.77, 8.64)	V. serious	Serious	Not serious	Serious	-	VERY LOW
					LR-	0.72 (0.58, 0.91)	V. serious	Not serious	Not serious	Not serious		LOW
MULTIPLE CAMERA												
1 study (Boutoleau-Bretonniere 2012)	Prospective	19	0.73 (0.41, 0.91)	0.75 (0.38, 0.94)	LR+	2.91 (0.83, 10.19)	V. serious	n/a	Not serious	Serious	-	VERY LOW
					LR-	0.36 (0.13, 1.03)	V. serious	n/a	Not serious	Serious		VERY LOW
ALL EVIDENCE POOLED												
3 studies (Boutoleau-Bretonniere 2012; Launes 1991; Talbot 1998)	3 × prospective	215	0.51 (0.35, 0.67)	0.82 (0.61, 0.93)	LR+	2.23 (1.20, 4.16)	V. serious	Not serious	Not serious	Serious	-	VERY LOW
					LR-	0.70 (0.56, 0.88)	V. serious	Not serious	Not serious	Not serious		LOW
Notes on risk of bias												
Launes 1991: Subgroup analysis used with >10% study population excluded.												
Talbot 1998: Unclear if avoided inappropriate exclusions; unclear whether the reference standard results were interpreted without knowledge of the index test and whether the index test was carried out without knowledge of reference test result; no pre-specified index test threshold; subgroup analysis used with >10% study population excluded.												
Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.												

P.2.25.2 MRI

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

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

P.2.26.1 HIV dementia scale (<10)

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

P.2.26.2 HIV dementia scale (<11)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skinner 2009)	Prospective	33	0.62 (0.34, 0.83)	0.80 (0.57, 0.92)	LR+	3.08 (1.16, 8.17)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.48 (0.23, 0.99)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Skinner 2009: Use of an optimised threshold.												

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

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

P.2.26.4 Grooved pegboard test

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Davis 2002)	Prospective	455	0.70 (0.62, 0.77)	0.71 (0.66, 0.76)	LR+	2.42 (1.98, 2.97)	Serious	n/a	Serious	Serious	-	VERY LOW
					LR-	0.42 (0.32, 0.55)	Serious	n/a	Serious	Serious		VERY LOW

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

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

P.2.27 Neurosyphilis versus not neurosyphilis

P.2.27.1 CSF EIA

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Chan 2014)	Prospective	45	0.97 (0.68, 1.00)	0.47 (0.30, 0.64)	LR+	1.82 (1.28, 2.58)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.06 (0.00, 0.94)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.27.2 FTA-ABS

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Dumaresq 2013)	Retrospective	100	0.97 (0.65, 1.00)	0.11 (0.06, 0.20)	LR+	1.09 (0.97, 1.22)	Not serious	n/a	Serious	Not serious	-	MODERATE
					LR-	0.28 (0.02, 4.62)	Not serious	n/a	Serious	V. serious		VERY LOW
Notes on indirectness Dumaresq 2013: >99% men who have sex with men												

P.2.27.3 INNO-LIA

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Dumaresq 2013)	Retrospective	83	0.96 (0.60, 1.00)	0.12 (0.06, 0.21)	LR+	1.09 (0.95, 1.25)	Not serious	n/a	Serious	Not serious	-	MODERATE
					LR-	0.33 (0.02, 5.31)	Not serious	n/a	Serious	V. serious		VERY LOW
Notes on indirectness Dumaresq 2013: >99% men who have sex with men												

P.2.27.4 PCR for T. pallidum genes: poIA, Tpp47, and bmp.

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Dumaresq 2013)	Retrospective	108	0.40 (0.19, 0.65)	0.61 (0.51, 0.71)	LR+	1.03 (0.53, 2.02)	Not serious	n/a	Serious	Serious	-	LOW
					LR-	0.98 (0.63, 1.53)	Not serious	n/a	Serious	Not serious		MODERATE
Notes on indirectness Dumaresq 2013: >99% men who have sex with men												

P.2.27.5 TPPA

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Dumaresq 2013)	Retrospective	100	0.67 (0.41, 0.85)	0.47 (0.37, 0.58)	LR+	1.26 (0.84, 1.90)	Not serious	n/a	Serious	Not serious	-	MODERATE
					LR-	0.71 (0.33, 1.50)	Not serious	n/a	Serious	Serious		LOW
Notes on indirectness Dumaresq 2013: >99% men who have sex with men												

P.2.28 PDD and DLB versus other dementias

P.2.28.1 123I-MIBG cardiac scintigraphy

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Hanyu 2006)	Prospective	96	0.95 (0.82, 0.99)	0.87 (0.76, 0.94)		LR+	7.47 (3.73, 14.98)	Serious	n/a	Not serious	Not serious	-	MODERATE
						LR-	0.06 (0.01, 0.22)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias													
Hanyu 2006: It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard and whether the reference standard results were interpreted without knowledge of the results of the index test.													

P.2.29 PDD versus non-PDD

P.2.29.1 FCSRT-IR 3- FR (≤ 22)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Kiesman 2013)	Prospective	40	0.84 (0.67, 0.93)	0.78 (0.42, 0.94)		LR+	3.77 (1.10, 12.94)	Serious	n/a	Not serious	Serious	-	LOW
						LR-	0.21 (0.09, 0.50)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias													
Kiesman 2013: Test threshold was not pre-specified.													

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Kiesman 2013)	Prospective	40	0.80 (0.62, 0.90)	0.95 (0.53, 1.00)	LR+	15.94 (1.06, 238.88)	Serious	n/a	Not serious	Serious	-	LOW
						0.21 (0.11, 0.43)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Kiesman 2013: Test threshold was not pre-specified.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Kiesman 2013)	Prospective	40	0.94 (0.78, 0.98)	0.78 (0.42, 0.94)	LR+	4.21 (1.24, 14.34)	Serious	n/a	Not serious	Serious	-	LOW
						0.08 (0.02, 0.33)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Kiesman 2013: Test threshold was not pre-specified.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Kiesman 2013)	Prospective	40	0.98 (0.79, 1.00)	0.45 (0.19, 0.74)	LR+	1.79 (1.02, 3.14)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.03 (0.00, 0.59)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias Kiesman 2013: Test threshold was not pre-specified.												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Kiesman 2013)	Prospective	40	0.90 (0.74, 0.97)	0.78 (0.42, 0.94)	LR+	4.06 (1.19, 13.87)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.12 (0.04, 0.39)	Serious	n/a	Not serious	Not serious		MODERATE
Notes on risk of bias Kiesman 2013: Test threshold was not pre-specified.												

P.2.30 PPA versus non-PPA

P.2.30.1 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Panegyres 2009)	Prospective	102	0.50 (0.19, 0.81)	0.99 (0.92, 1.00)	LR+	97.00 (5.54, 1697.47)	Not serious	n/a	Serious	Not serious	-	MODERATE
					LR-	0.50 (0.24, 1.05)	Not serious	n/a	Serious	Serious		LOW
Notes on indirectness Panegyres 2009: The study only recruited people with early onset dementia (<65 years old).												

P.2.31 VaD and mixed dementias versus AD

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Siritho 2006)	Prospective	214	0.86 (0.77, 0.92)	0.73 (0.65, 0.80)	LR+	3.17 (2.36, 4.25)	V. serious	n/a	Not serious	Not serious	-	LOW
					LR-	0.19 (0.11, 0.33)	V. serious	n/a	Not serious	Not serious		LOW
Notes on risk of bias Siritho 2006: Subgroup analysis excluded >45% study population; optimised test-threshold was used and it was unclear whether the index test results were interpreted without knowledge of the results of the reference standard or whether the reference standard was interpreted without knowledge of the results of the index test.												

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

P.2.32.1 ADDTC (possible)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Gold 2002)	Retrospective	89	0.70 (0.47, 0.86)	0.78 (0.67, 0.86)	LR+	3.22 (1.89, 5.48)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.38 (0.19, 0.76)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.32.2 ADDTC (probable)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Gold 2002)	Retrospective	89	0.25 (0.11, 0.48)	0.91 (0.82, 0.96)	LR+	2.88 (0.98, 8.44)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.82 (0.63, 1.07)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.32.3 ADDTC criteria

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Bachetta 2007)	Retrospective	110	0.58 (0.42, 0.73)	0.74 (0.63, 0.83)	LR+	2.27 (1.41, 3.66)	Not serious	n/a	Serious	Serious	-	LOW
					LR-	0.56 (0.37, 0.84)	Not serious	n/a	Serious	Serious		LOW
Notes on indirectness Bachetta 2007: Participants were selected to be >90 years old												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Bachetta 2007)	Retrospective	110	0.56 (0.39, 0.71)	0.66 (0.55, 0.76)	LR+	1.64 (1.07, 2.53)	Not serious	n/a	Serious	Serious	-	LOW
					LR-	0.67 (0.45, 1.00)	Not serious	n/a	Serious	Serious		LOW
Notes on indirectness Bachetta 2007: Participants were selected to be >90 years old												

P.2.32.5 NINDS-AIREN (possible)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Gold 2002)	Retrospective	89	0.55 (0.34, 0.75)	0.84 (0.73, 0.91)	LR+	3.45 (1.76, 6.75)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.54 (0.33, 0.88)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.32.6 NINDS-AIREN (probable)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Gold 2002)	Retrospective	89	0.20 (0.08, 0.43)	0.93 (0.84, 0.97)	LR+	2.76 (0.82, 9.32)	Not serious	n/a	Not serious	Serious	-	MODERATE
					LR-	0.86 (0.69, 1.08)	Not serious	n/a	Not serious	Not serious		HIGH

P.2.32.7 NINDS-AIREN criteria

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

P.2.33 VaD versus AD

P.2.33.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
2 studies (Launes 1991; McMurdo 1994)	2 × prospective	97	0.76 (0.60, 0.87)	0.77 (0.64, 0.86)	LR+	3.21 (1.90, 5.43)	Serious	Not serious	Not serious	Serious	-	LOW
					LR-	0.33 (0.18, 0.60)	Serious	Not serious	Not serious	Serious		LOW
Notes on risk of bias Launes 1991: Subgroup analysis used with >10% study population excluded. McMurdo 1994: Subgroup analysis used with >10% study population discarded.												

P.2.33.2 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	247	0.71 (0.50, 0.85)	0.97 (0.94, 0.98)	LR+	22.57 (10.42, 48.88)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.30 (0.16, 0.56)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias												
Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.												

P.2.34 VaD versus DLB

P.2.34.1 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	71	0.71 (0.50, 0.85)	0.96 (0.85, 0.99)	LR+	16.65 (4.19, 66.18)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.30 (0.16, 0.57)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias												
Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.												

P.2.35 VaD versus FTD

P.2.35.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
1 study (Launes 1991)	Prospective	38	0.76 (0.58, 0.87)	0.60 (0.20, 0.90)	LR+	1.89 (0.64, 5.64)	Serious	n/a	Not serious	Serious	-	LOW
					LR-	0.40 (0.16, 1.03)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias												
Launes 1991: Subgroup analysis used with >10% study population excluded.												

P.2.35.2 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	116	0.71 (0.50, 0.85)	0.96 (0.89, 0.98)	LR+	16.29 (6.04, 43.94)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.30 (0.16, 0.57)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias												
Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.												

P.2.36 VaD versus non-VaD dementia plus unclassifiable

P.2.36.1 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
PRIMARY CARE													
1 study (Boutoleau-Brettonniere 2012)	Prospective	56	0.88 (0.46, 0.98)	0.75 (0.61, 0.85)		LR+	3.50 (2.01, 6.10)	Serious	n/a	Not serious	Not serious	-	MODERATE
						LR-	0.17 (0.03, 1.05)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias													
Boutoleau-Brettonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases.													

P.2.37 VaD versus non-VaD

P.2.37.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SINGLE CAMERA													
2 studies (Launes 1991; McMurdo 1994)	2 × prospective	204	0.76 (0.60, 0.87)	0.64 (0.40, 0.83)		LR+	2.16 (1.05, 4.45)	Not serious	Serious	Not serious	Serious	-	LOW
						LR-	0.44 (0.24, 0.81)	Not serious	Not serious	Not serious	Serious		MODERATE

P.2.38 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	504	0.71 (0.50, 0.85)	0.96 (0.94, 0.98)	LR+	18.89 (11.22, 31.80)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.30 (0.16, 0.57)	Not serious	n/a	Not serious	Serious		MODERATE

P.2.39 VaD versus other dementias

P.2.39.1 HIS (≥7)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Gustafson 2010)	Prospective	190	0.69 (0.56, 0.80)	0.92 (0.86, 0.96)	LR+	8.69 (4.79, 15.75)	Not serious	n/a	Not serious	Not serious	-	HIGH
					LR-	0.33 (0.22, 0.50)	Not serious	n/a	Not serious	Serious		MODERATE
Notes on risk of bias												
Gustafson 2010: The study was not downgraded for subgroup analysis as <10% population was excluded.												

P.2.39.2 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen 2016)	Prospective	386	0.71 (0.50, 0.85)	0.96 (0.94, 0.98)	LR+	19.72 (10.91, 35.66)	Serious	n/a	Not serious	Not serious	-	MODERATE
					LR-	0.30 (0.16, 0.56)	Serious	n/a	Not serious	Serious		LOW
Notes on risk of bias												
Koikkalainen 2016: Subgroup analysis where >10% population excluded and unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard or the reference test was interpreted independently of the index test.												