# P.2 GRADE tables

# P.2.1 Dementia versus no dementia

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

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

## Notes on risk of bias

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

## Notes on indirectness

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

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%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 study (Austinania 0045)	December	000	0.04 (0.00, 0.07)	0.00 (0.54, 0.00)	LR+	2.34 (1.88, 2.91)	Serious	n/a	Serious	Serious		VERY LOW
1 study (Apolinario 2015)	Prospective	230	0.94 (0.88, 0.97)	0.60 (0.51, 0.68)	LR-	0.09 (0.04, 0.21)	Serious	n/a	Serious	Not serious	-	LOW

### Notes on risk of bias

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

## Notes on indirectness

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Apolipario 2015)	Droopoetivo	230	0.97 (0.92, 0.99) 0.40 (0.	0.40 (0.33, 0.40)	LR+	1.63 (1.40, 1.89)	Serious	n/a	Serious	Not serious		LOW
1 study (Apolinario 2015)	Prospective	230	0.97 (0.92, 0.99)	0.40 (0.32, 0.49)	LR-	0.07 (0.02, 0.22)	Serious	n/a	Serious	Not serious	-	LOW

## Notes on risk of bias

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

## Notes on indirectness

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

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

# **P.2.1.4** 6 item screener (≥0)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Callahan	Prospective	054	4.00 (0.00, 4.00)	0.00 (0.00, 0.03)	LR+	1.00 (0.99, 1.01)	Serious	n/a	Not serious	Not serious		MODERATE
2002)	Prospective	651	1.00 (0.98, 1.00)	0.00 (0.00, 0.03)	LR-	0.89 (0.02, 44.58)	Serious	n/a	Not serious	V. serious	-	VERY LOW

## Notes on risk of bias

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

# **P.2.1.5** 6 item screener (≥1)

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

## Notes on risk of bias

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

# **P.2.1.6** 6 item screener (≥2)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	!Ε											
1 study (Callahan	Prospective	054	0.00 (0.00 0.00)	0.70 (0.75, 0.04)	LR+	4.35 (3.48, 5.44)	Serious	n/a	Not serious	Not serious		MODERATE
2002)	Prospective	651	0.90 (0.86, 0.92)	0.79 (0.75, 0.84)	LR-	0.13 (0.10, 0.18)	Serious	n/a	Not serious	Not serious	-	MODERATE

## Notes on risk of bias

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

# **P.2.1.7** 6 item screener (≥3)

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

## Notes on risk of bias

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

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

# **P.2.1.8** 6 item screener (≥4)

						Summary	of bias	Inconsistency	ectness	ecision	er siderations	
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	of findings (95%CI)	Risk	Inco	Indir	lm pr	Othe	Quality
SECONDARY CAR	RE											
1 study (Callahan	Prospective	651	0.68 (0.62, 0.72)	0.06 (0.03, 0.09)	LR+	17.22 (9.84, 30.13)	Serious	n/a	Not serious	Not serious		MODERATE
2002)	Flospective	001	0.00 (0.02, 0.72)	0.96 (0.93, 0.98)	LR-	0.34 (0.29, 0.39)	Serious	n/a	Not serious	Not serious	-	MODERATE

#### Notes on risk of bias

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

# P.2.1.9 6 item screener (≥5)

	- \ - /											
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Callahan	Prognostivo	651	0.40 (0.44, 0.54)		LR+	37.47 (14.07, 99.80)	Serious	n/a	Not serious	Not serious		MODERATE
2002)		001	0.49 (0.44, 0.54)	0.99 (0.97, 1.00)	LR-	0.52 (0.47, 0.57)	Serious	n/a	Not serious	Serious	-	LOW

## Notes on risk of bias

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

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

# P.2.1.10 6 item screener (≥6)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAI	RE											
1 study	Prognactiva	651	0.30 (0.26, 0.35)	0.00 (0.07.1.00)	LR+	46.57 (11.59, 187.06)	Serious	n/a	Not serious	Not serious		MODERATE
(Callahan 2002)	Prospective	001	0.30 (0.26, 0.33)	0.99 (0.97, 1.00)	LR-	0.70 (0.65, 0.75)	Serious	n/a	Not serious	Not serious	-	MODERATE

## Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 atudu (Abdal A== 2045)	Dunamantiiva	045	0.00 (0.75, 0.04)	0.70 (0.70, 0.00)	LR+	4.01 (3.01, 5.33)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Abdel-Aziz 2015)	Prospective	245	0.88 (0.75, 0.94)	0.78 (0.72, 0.83)	LR-	0.16 (0.08, 0.34)	Not serious	n/a	Not serious	Not serious	-	HIGH

# P.2.1.12 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA												
1 study (Dahart 2005)	Dragnostivo	24	0.90 (0.65, 0.07)	0.22 (0.09, 0.72)	LR+	1.33 (0.74, 2.40)	Serious	n/a	Not serious	Serious		LOW
1 study (Dobert 2005)	Prospective	24	0.89 (0.65, 0.97)	0.33 (0.08, 0.73)	LR-	0.33 (0.06, 1.88)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of bias  Dobert 2005: It is unclear wh	nether a consecutiv	ve or rand	lom sample of patie	nts was enrolled and	d whether in	appropriate exclusion	ns were a	oided.				

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

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
2 studies (Larner 2007;	2 ×	424	0.91 (0.67, 0.98)	0.84 (0.29, 0.98)	LR+	5.62 (0.81, 39.07)	Serious	Serious	Not serious	Serious		VERY LOW	
Mathuranath 2000)	prospective	424	0.91 (0.07, 0.96)	0.04 (0.29, 0.96)	LR-	0.12 (0.04, 0.33)	Serious	Serious	Not serious	Not serious	-	LOW	
Notes on risk of bias Mathuranath 2000: Optimis													

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
2 studies (Larner 2007;	2 ×	404	0.00 (0.74, 4.00)	0.50 (0.00, 0.00)	LR+	2.18 (1.23, 3.85)	Serious	Serious	Not serious	Serious		VERY LOW	
Mathuranath 2000)	prospective	424	0.98 (0.71, 1.00)	0.56 (0.29, 0.80)	LR-	0.04 (0.00, 0.42)	Serious	Serious	Not serious	Not serious	-	LOW	
Notes on risk of bias Mathuranath 2000: Optimise													

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy ( lubb 2015)	Drooppotivo	ctive 59 0.81 (0.61, 0.92	0.94 (0.64, 0.02)	0.07 (0.91.1.00)	LR+	26.65 (3.83, 185.32)	Serious	n/a	Serious	Not serious		LOW
1 study (Jubb 2015)	Prospective	29	0.81 (0.61, 0.92)	0.97 (0.81, 1.00)	LR-	0.20 (0.09, 0.44)	Serious	n/a	Serious	Not serious	-	LOW

Notes on risk of bias

Jubb 2015: Optimised threshold used for analysis.

Notes on indirectness

Jubb 2015: Study population was confined to >75 years

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

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
OLOGINDAN TOAKL			1									
1 atudy ( lubb 2015)	Prospective	59	0.91 (0.61, 0.02)	0.70 (0.52, 0.92)	LR+	2.67 (1.54, 4.62)	Not serious	n/a	Serious	Serious		LOW
1 study (Jubb 2015)	Prospective	39	0.81 (0.61, 0.92)	0.70 (0.52, 0.83)	LR-	0.28 (0.12, 0.63)	Not serious	n/a	Serious	Serious	-	LOW
Notes on indirectness	,											

Jubb 2015: Study population was confined to >75 years

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 atualy ( light 2045)	Dragagativa	50	0.00 (0.74, 0.00)	0.04 (0.42, 0.70)	LR+	2.34 (1.51, 3.63)	Serious	n/a	Serious	Serious		VERY LOW
1 study (Jubb 2015)	Prospective	59	0.92 (0.74, 0.98)	0.61 (0.43, 0.76)	LR-	0.13 (0.03, 0.49)	Serious	n/a	Serious	Not serious	-	LOW

Notes on risk of bias

Jubb 2015: Optimised threshold used for analysis.

Notes on indirectness

Jubb 2015: Study population was confined to >75 years

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

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
OZGGND/IIII G/IIIZ			1									
1 study (Jubb 2015)	Prospostivo	60	0.96 (0.77, 0.99)	0.50 (0.34, 0.66)	LR+	1.92 (1.36, 2.71)	Not serious	n/a	Serious	Serious		LOW
1 Study (Jubb 2015)	b 2015) Prospective 60 0.96		0.90 (0.77, 0.99)	0.50 (0.54, 0.66)	LR-	0.08 (0.01, 0.54)	Not serious	n/a	Serious	Serious	-	LOW
Notes on indirectness												

Jubb 2015: Study population was confined to >75 years

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

Addenbiooke 3 C		A CATTONIA	au on Roviou	,710 <u>2</u> R ( 4 I)								
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Hannak 2011)	Droopoetiyo	140	0.00 (0.76, 0.06)	0.02 (0.96, 0.07)	LR+	12.95 (6.29, 26.67)	Serious	n/a	Not serious	Not serious		MODERATE
1 study (Hancock 2011)	Prospective	140	0.90 (0.76, 0.96)	0.93 (0.86, 0.97)	LR-	0.11 (0.04, 0.28)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of bias												
Hancock 2011: Optimised	test threshold.											

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

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

#### Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 atualy (Tamanina 2014)	Dana a a ativa	400	0.05 (0.70, 0.04)	0.00 (0.05, 0.00)	LR+	4.27 (2.28, 7.98)	Serious	n/a	Not serious	Not serious		MODERATE
1 study (Terpening 2011)	Prospective	122	0.85 (0.76, 0.91)	0.80 (0.65, 0.90)	LR-	0.18 (0.11, 0.32)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of bias Terpening 2011: Patients 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 atualy (Tamanina 2011)	Dunanastiva	400	0.04 (0.02, 0.00)	0.00 (0.50, 0.00)	LR+	2.81 (1.79, 4.42)	Serious	n/a	Not serious	Serious		LOW
1 study (Terpening 2011)	Prospective	122	0.91 (0.83, 0.96)	0.68 (0.52, 0.80)	LR-	0.13 (0.06, 0.27)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of bias Terpening 2011: Patients la	acking a clinical	diagnosis	s were excluded fron	n the analysis								

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

# P.2.1.24 AD8 (≥2)

ABG (22)		Total	Sens	Spec		Summary of findings	Risk of bias	consistency	directness	Imprecision	Other considerations	
Studies	Design	N	(95%CI)	(95%CI)	Measure	(95%CI)	涩	lnc	ق	트	28	Quality
SECONDARY CARE												
1 study (Larner 2015)	Prospective	212	0.97 (0.89, 0.99)	0.11 (0.07, 0.17)	LR+	1.09 (1.02, 1.17)	Not serious	n/a	Not serious	Not serious		HIGH
1 Study (Lamer 2013)	Flospective	212	0.97 (0.09, 0.99)	0.11 (0.07, 0.17)	LR-	0.26 (0.06, 1.10)	Not serious	n/a	Not serious	Serious	-	MODERATE

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

Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
	•					•					
December	000	0.07 (0.04.0.00)	0.00 (0.40, 0.00)	LR+	1.34 (1.17, 1.54)	V. serious	n/a	Not serious	Not serious		LOW
Prospective	299	0.97 (0.94, 0.99)	0.28 (0.19, 0.38)	LR-	0.10 (0.04, 0.24)	V. serious	n/a	Not serious	Not serious	-	LOW
		Design N	Design N (95%CI)	Design N (95%CI) (95 <sup>5</sup> %CI)	Design         N         (95%CI)         (95%CI)         Measure           Prospective         299         0.97 (0.94, 0.99)         0.28 (0.19, 0.38)         LR+	Design         Total N         Sens (95%CI)         Spec (95%CI)         Measure         of findings (95%CI)           Prospective         299         0.97 (0.94, 0.99)         0.28 (0.19, 0.38)         LR+         1.34 (1.17, 1.54)	Design         Total N         Sens (95%CI)         Spec (95%CI)         Measure         Summary of findings (95%CI)         Summary of findings (95%CI)           Prospective         299         0.97 (0.94, 0.99)         0.28 (0.19, 0.38)         LR+         1.34 (1.17, 1.54)         V. serious	Total N   Sens (95%CI)   Spec (95%CI)   Measure   Summary of findings (95%CI)   Serious   N/2   Summary of findings (95%CI)   Summary of findings (95%CI)	Total N   Sens (95%CI)   Spec (95%CI)   Measure   Summary of findings (95%CI)   Summary of fin	Design         Total N         Sens (95%CI)         Spec (95%CI)         Measure         Summary of findings (95%CI)         Summary of findings (95%CI)         V. serious         Not serious         Not serious	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

#### Notes on risk of bias

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

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

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

#### Notes on risk of bias

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

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

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

## Notes on risk of bias

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

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

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

#### Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
1 study (Frisoni	Prospective	94	0.42 (0.21, 0.55)	0.70 (0.60, 0.00)	LR+	1.98 (0.92, 4.25)	Serious	n/a	Not serious	Serious		LOW
2009)	Flospective	94	0.42 (0.31, 0.55)	0.79 (0.60, 0.90)	LR-	0.73 (0.55, 0.97)	Serious	n/a	Not serious	Not serious	-	MODERATE

## Notes on risk of bias

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

**P.2.1.30** Applause sign (<3)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 atudu (Danalla 2040)	Description	075	0.54 (0.40, 0.67)	0.05 (0.00, 0.00)	LR+	3.64 (2.43, 5.45)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Bonello 2016)	Prospective	275	0.54 (0.40, 0.67)	0.85 (0.80, 0.89)	LR-	0.54 (0.40, 0.73)	Not serious	n/a	Not serious	Serious	-	MODERATE

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Beinhoff	Dragnactive	232	0.20 (0.29, 0.52)	0.03 (0.99, 0.06)	LR+	5.94 (3.12, 11.33)	Serious	n/a	Not serious	Not serious		MODERATE
2005)		232	0.39 (0.28, 0.52)	0.93 (0.88, 0.96)	LR-	0.65 (0.53, 0.79)	Serious	n/a	Not serious	Not serious	-	MODERATE

#### Notes on risk of bias

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

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

#### Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	E											
1 study (Beinhoff	Prophostivo	232	0.71 (0.50, 0.91)	0.62 (0.55, 0.70)	LR+	1.91 (1.49, 2.45)	Serious	n/a	Not serious	Serious		LOW
2005)	Prospective	232	0.71 (0.59, 0.81)	0.63 (0.55, 0.70)	LR-	0.46 (0.31, 0.68)	Serious	n/a	Not serious	Serious	_	LOW

## Notes on risk of bias

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

P.2.1.34 Brief Neuropsychological Test Battery

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Coutinho 2012)	Propositivo	131	0.01 (0.70, 0.06)	0.92 (0.72 0.00)	LR+	5.43 (3.28, 8.99)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Coutinho 2013)	Prospective	131	0.91 (0.79, 0.96)	0.83 (0.73, 0.90)	LR-	0.11 (0.05, 0.26)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
RE											
Dragnostiva	222	0.96 (0.76, 0.03)	0.52 (0.45, 0.60)	LR+	1.81 (1.51, 2.19)	Serious	n/a	Not serious	Serious		LOW
Prospective	232	0.00 (0.76, 0.93)	0.52 (0.45, 0.60)	LR-	0.26 (0.14, 0.49)	Serious	n/a	Not serious	Not serious	-	MODERATE
	•	Design N	Design N (95%CI)	Design N (95%CI) (95 <sup>5</sup> %CI)	Design N (95%CI) (95%CI) Measure  RE  Prospective 232 0.86 (0.76, 0.93) 0.52 (0.45, 0.60)	Design   N   Sens (95%CI)   Spec (95%CI)   Measure   Offindings (95%CI)	Design   Total   Sens   Spec   Measure   Summary of findings (95%CI)   ER	Total   Sens   Spec   Measure   Summary of findings   95%CI)   RE	Total N   Sens (95%CI)   Spec (95%CI)   Measure   Summary of findings (95%CI)   Serious   Seri	Total N   Sens (95%CI)   Spec (95%CI)   Measure   Summary of findings (95%CI)   Serious   Seri	Total   Sens (95%CI)   Spec (95%CI)   Measure   Summary of findings (95%CI)   Serious   Seriou

#### Notes on risk of bias

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

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

## Notes on risk of bias

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

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

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

## Notes on risk of bias

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

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

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

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

Olock Blawing I	oot, ob 1, 11	atoon v	sooning moune	a (* <del>1</del> )								
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Pargar 2009)	Prophostivo	462	0.72 (0.67, 0.76)	0.64 (0.55, 0.72)	LR+	2.00 (1.57, 2.54)	Serious	n/a	Not serious	Serious		LOW
1 study (Berger 2008)	Prospective	402	0.72 (0.67, 0.76)	0.64 (0.55, 0.72)	LR-	0.44 (0.35, 0.54)	Serious	n/a	Not serious	Serious	_	LOW
Notes on risk of bias												

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

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality		
SECONDARY CARE														
1 study (Parger 2009)	Prophostivo	462	0.59 (0.52, 0.62)	0.01 (0.74, 0.07)	LR+	3.10 (2.14, 4.49)	Serious	n/a	Not serious	Not serious		MODERATE		
1 study (Berger 2008)	Prospective	402	0.58 (0.53, 0.63)	0.81 (0.74, 0.87)	LR-	0.52 (0.44, 0.60)	Serious	n/a	Not serious	Serious	-	LOW		
Notes on risk of bias Berger 2008: People wh														

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 abody (Carrar 2000)	Description	204	0.70 (0.00 0.77)	0.02 (0.74, 0.00)	LR+	4.10 (2.68, 6.28)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Sager 2006)	Prospective	364	0.72 (0.66, 0.77)	0.83 (0.74, 0.89)	LR-	0.34 (0.28, 0.42)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
4 -tt (D 0000)	December	400	0.04 (0.77, 0.05)	0.00 (0.54, 0.00))	LR+	2.04 (1.64, 2.54)	Serious	n/a	Not serious	Serious		LOW	
1 study (Berger 2008)	Prospective	462	0.81 (0.77, 0.85)	0.60 (0.51, 0.68))	LR-	0.31 (0.24, 0.41)	Serious	n/a	Not serious	Not serious	-	MODERATE	
Notes on risk of bias Berger 2008: People wh	Notes on risk of bias Berger 2008: People who received a final diagnosis of FTD, DLB or MCI were excluded from the study												

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Pargar 2009)	Prophostivo	462	0.03 (0.00, 0.05)	0.27 (0.20, 0.45)	LR+	1.47 (1.29, 1.68)	V. serious	n/a	Not serious	Not serious		LOW	
1 study (Berger 2008)	Prospective	402	0.93 (0.90, 0.95)	0.37 (0.29, 0.45)	LR-	0.19 (0.12, 0.30)	V. serious	n/a	Not serious	Not serious	-	LOW	
Notes on risk of bias Berger 2008: People wh	otes on risk of bias erger 2008: People who received a final diagnosis of FTD, DLB or MCI were excluded from the study and an optimised threshold was used.												

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 atudu (Damas 2000)	Duagnactive	400	0.00 (0.04, 0.04)	0.40 (0.44, 0.50)	LR+	1.73 (1.45, 2.07)	Serious	n/a	Not serious	Serious		LOW
1 study (Berger 2008)	Prospective	462	0.88 (0.84, 0.91)	0.49 (0.41, 0.58)	LR-	0.24 (0.17, 0.34)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of bias			: (570.010. •	101								

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

# P.2.1.45 CERAD battery

	,											
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	ι <b>Ε</b>											
1 study	Prospective	100	0.74 (0.60, 0.84)	0.98 (0.87, 1.00)	LR+	37.00 (5.28, 259.34)	V. serious	n/a	Not serious	Not serious	_	LOW
(Hentschel 2005)	, , , , ,		, ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	, , , , , ,	LR-	0.27 (0.17, 0.42)	V. serious	n/a	Not serious	Serious		LOW

## Notes on risk of bias

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

P.2.1.46 Computed Tomography, CT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (O'Prion 2000)	(O'Brien 2000) Prospective 116 0.54 (0.45	0.54 (0.45, 0.64)	0.77 (0.49, 0.02)	LR+	2.36 (0.86, 6.46)	Not serious	n/a	Not serious	Serious		MODERATE	
1 study (O'Brien 2000)	riospective	110	0.54 (0.45, 0.64)	0.77 (0.48, 0.92)	LR-	0.59 (0.41, 0.85)	Not serious	n/a	Not serious	Serious	-	MODERATE

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Cruz-Orduna 2012)	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
1 Study (Gruz-Gruuria 2012)	Flospective	100	0.67 (0.59, 0.97)	0.62 (0.73, 0.67)	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.												

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

# P.2.1.48 FDG-PET

		}										
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
3 studies (Dobert 2005;	3 ×	000	0.87 (0.46,	0.77 (0.69,	LR+	3.70 (2.62, 5.22)	Not serious	Not serious	Not serious	Not serious		HIGH
Frisoni 2009; Silverman 2001)	prospective	386	0.98)	0.84)	LR-	0.16 (0.03, 0.79)	Serious	Serious	Not serious	Serious	-	VERY LOW

## Notes on risk of bias

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

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 at refer (Marrier and 2042)	Dunamantina	4.45	0.70 (0.00, 0.05)	0.00 (0.70, 0.00)	LR+	7.66 (3.31, 17.69)	V. serious	n/a	Not serious	Not serious		LOW
1 study (Mormont 2012)	Prospective	145	0.78 (0.69, 0.85)	0.90 (0.78, 0.96)	LR-	0.24 (0.16, 0.36)	V. serious	n/a	Not serious	Not serious	-	LOW
Notes on risk of bias Mormont 2012: Exclusion	of >35% popula	tion at an	alysis and use of opt	imised test threshold	S.							

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Garcia	2 ×	436	0.03 (0.00, 0.06)	0.65 (0.27, 0.01)	LR+	2.80 (0.97, 8.10)	Serious	Serious	Not serious	Serious		VERY LOW
2002; Knaefelc 2003)	prospective	430	0.93 (0.90, 0.96)	6) 0.65 (0.27, 0.91)	LR-	0.12 (0.07, 0.18)	Serious	Not serious	Not serious	Not serious	-	MODERATE

### Notes on risk of bias

Garcia 2002: Inappropriate exclusions at patient selection stage.

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Consolves 2011)	Dragnostiva	204	0.72 (0.64, 0.79)	0.67 (0.54, 0.70)	LR+	2.19 (1.47, 3.28)	Serious	n/a	Not serious	Serious		LOW
1 study (Goncalves 2011)	Prospective	204	0.72 (0.64, 0.78)	0.67 (0.54, 0.79)	LR-	0.42 (0.31, 0.58)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of bias												

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

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

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

## Notes on risk of bias

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

Hancock 2009: An optimised test threshold was used.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Cruz-Orduna	Dusanastiva	100	0.80 (0.53,	0.77 (0.69,	LR+	3.14 (2.31, 5.03)	Serious	n/a	Not serious	Not serious		MODERAT E
012) Prospe	Prospective	160	0.93)	0.83)	LR-	0.26 (0.09, 0.72)	Serious	n/a	Not serious	Serious		LOW
SECONDARY CARE												
4 ahudu (Fliakaa 4007)	Dusanastiva	200	0.81 (0.76,	0.61 (0.51,	LR+	2.11 (1.60, 2.79)	V. serious	n/a	Not serious	Serious		VERY LOW
1 study (Flicker 1997)	Prospective	299	0.86)	0.71)	LR-	0.30 (0.22, 0.42)	V. serious	n/a	Not serious	Not serious		LOW
ALL EVIDENCE POOLED \	V. serious											
2 studies (Cruz-Orduna	2x	459	0.81 (0.76,	0.70 (0.53,	LR+	2.63 (1.65, 4.20)	V. serious	Serious	Not serious	Serious		VERY LOW
	prospective	409	0.86)	0.82	LR-	0.30 (0.22, 0.41)	V. serious	Not serious	Not serious	Not serious	-	LOW

## Notes on risk of bias

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

Cruz-Orduna 2012: Thresholds were not pre-specified but were calculated to give optimum sensitivity and specificity

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY C	ARE											
1 study (Flicker	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
1997)	Flospective	299	0.76 (0.72, 0.63)	0.65 (0.54, 0.75)	LR-	0.34 (0.25, 0.46)	V. serious	n/a	Not serious	Not serious	-	LOW

#### Notes on risk of bias

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

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

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

#### Notes on risk of bias

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

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

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

## Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY C	ARE											
1 study (Flicker	Prospective	299	0.65 (0.58, 0.71)	0.90 (0.60, 0.97)	LR+	3.16 (2.05, 4.89)	V. serious	n/a	Not serious	Not serious		LOW
1997)	riospective	299	0.05 (0.56, 0.71)	) 0.80 (0.69, 0.87)	LR-	0.44 (0.36, 0.55)	V. serious	n/a	Not serious	Serious	_	VERY LOW

#### Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
1 study (Flicker	Prognostivo	200	0.59 (0.52, 0.65)	0.92 (0.74, 0.00)	LR+	3.46 (2.12, 5.65)	V. serious	n/a	Not serious	Not serious		LOW
1997)	Prospective 299 0.58 (0.52, 0.65)	0.56 (0.52, 0.65)	0.83 (0.74, 0.90)	LR-	0.50 (0.42, 0.60)	V. serious	n/a	Not serious	Serious		VERY LOW	

## Notes on risk of bias

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

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

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

#### Notes on risk of bias

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAL	RE											
1 study (Beinhoff	Dunamantika	000	0.44 (0.22.0.50)	0.03 (0.00, 0.00)	LR+	6.08 (3.30, 11.18)	Serious	n/a	Not serious	Not serious		MODERATE
2005)	Prospective	232	0.44 (0.33, 0.56)	0.93 (0.88, 0.96)	LR-	0.60 (0.49, 0.75)	Serious	n/a	Not serious	Serious	-	LOW

## Notes on risk of bias

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

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

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

## Notes on risk of bias

# P.2.1.62 Mini-ACE (<26)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Larger 2017)	Dragnostiva	260	0.09 (0.95, 1.00)	0.25 (0.20, 0.42)	LR+	1.50 (1.35, 1.67)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Larner 2017)	Prospective	200	0.98 (0.85, 1.00)	0.35 (0.29, 0.42)	LR-	0.07 (0.01, 0.46)	Not serious	n/a	Not serious	Not serious	-	HIGH

# P.2.1.63 Mini-Cog (≤2)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnera Darde 2012)	Dragnactive	142	0.00 (0.96, 4.00)	0.40 (0.34, 0.50)	LR+	1.65 (1.39, 1.95)	Serious	n/a	Not serious	Not serious		MODERATE
1 study (Carnero-Pardo 2013)	Prospective	142	0.99 (0.86, 1.00)	0.40 (0.31, 0.50)	LR-	0.03 (0.00, 0.40)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of bias Carnero-Pardo 2013: The test the	Notes on risk of bias Carnero-Pardo 2013: The test threshold was not pre-specified, but was optimised based on the data obtained.											

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

Studies SECONDARY O	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
1 study (Milian		500	0.07 (0.02. 0.00)	0.00 (0.00 4.00)	LR+	112.68 (7.12, 1782.71)	Serious	n/a	Not serious	Not serious		MODERATE
2012)	Retrospective	502	0.87 (0.83, 0.90)	0.99 (0.89, 1.00)	LR-	0.13 (0.11, 0.17)	Serious	n/a	Not serious	Not serious	-	MODERATE

## Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
4 atualy (Company Davida 2011)	Prospective 117 0.93 (0		0.02 (0.77, 0.00)	0.00 (0.74, 0.07)	LR+	4.78 (3.09, 7.39)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Carnero-Pardo 2011)			0.93 (0.77, 0.98)	0.80 (0.71, 0.87)	LR-	0.08 (0.02, 0.32)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies	Design	Tota I N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnero-	Description	447	0.97 (0.80,	0.71 (0.61,	LR+	3.36 (2.40, 4.71)	Not serious	n/a	Not serious	Not serious		HIGH
Pardo 2011)	Prospective	117	1.00)	0.80)	LR-	0.05 (0.01, 0.32)	Not serious	n/a	Not serious	Not serious	-	HIGH
SECONDARY CAR	RE											
1 study (Beinhoff	Dragonactiva	232	0.82 (0.71,	0.81 (0.75,	LR+	4.38 (3.13, 6.14)	Serious	n/a	Not serious	Not serious		MODERATE
2005)	Prospective	232	0.89)	0.87)	LR-	0.22 (0.13, 0.37)	Serious	n/a	Not serious	Not serious	-	MODERATE
ALL EVIDENCE PO	OOLED											
2 studies (Beinhoff 2005;	2 ×	240	0.90 (0.61,	0.77 (0.66,	LR+	3.84 (2.96, 4.97)	Serious	Not serious	Not serious	Not serious		MODERATE
,	prospective 34			0.85)	LR-	0.14 (0.03, 0.57)	Serious	Serious	Not serious	Serious	-	VERY LOW

## Notes on risk of bias

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Beinhoff	Danamantika	222	0.00 (0.70, 0.04)	0.70 (0.00 0.70)	LR+	2.92 (2.28, 3.74)	Serious	n/a	Not serious	Not serious		MODERATE
2005)	Prospective	Prospective 232 0.88 (0.78, 0.94)		0.70 (0.62, 0.76)	LR-	0.17 (0.09, 0.33)	Serious	n/a	Not serious	Not serious	-	MODERATE

## Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Beinhoff	Dragnostiva	222	0.02 (0.02.0.07)	0.63 (0.45, 0.60)	LR+	1.97 (1.65, 2.34)	Serious	n/a	Not serious	Serious		LOW
2005)	Prospective	232	0.92 (0.83, 0.97)	0.53 (0.45, 0.60)	LR-	0.14 (0.06, 0.34)	Serious	n/a	Not serious	Not serious	-	MODERATE

## Notes on risk of bias

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

Studies SECONDARY CAR	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDART CAR	\L											
1 study (Beinhoff	Prospective	232	0.98 (0.90, 1.00)	0.22 (0.25, 0.20)	LR+	1.45 (1.30, 1.61)	Serious	n/a	Not serious	Not serious		MODERATE
2005)	Prospective	232	0.96 (0.90, 1.00)	0.32 (0.25, 0.39)	LR-	0.05 (0.01, 0.34)	Serious	n/a	Not serious	Not serious	-	MODERATE

Notes on risk of 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%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
4 atualis (Campana Danda 2012)	Description	200	0.70 (0.50, 0.70)	0.02 (0.00, 0.05)	LR+	9.92 (6.35, 15.52)	Serious	n/a	Not serious	Not serious		MODERATE
1 study (Carnero-Pardo 2013)	Prospective	360	0.70 (0.59, 0.79)	0.93 (0.89, 0.95)	LR-	0.32 (0.23, 0.45)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of bias Carnero-Pardo 2013: Multiple to	est thresholds v	vere use	d									

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
4 about (Oron Ordon 2012)	December	200	0.81 (0.70,	0.92 (0.88,	LR+	9.91 (6.60, 14.88)	Serious	n/a	Not serious	Not serious		MODERAT E
study (Cruz-Orduna 2012)	Prospective	360	0.88)	0.95)	LR-	0.21 (0.13, 0.33)	Serious	n/a	Not serious	Not serious	-	MODERAT E
SECONDARY CARE												
4 shorts (Flisher 4007)	December	000	0.50, 0.43,	0.90 (0.82,	LR+	5.19 (2.65, 10.16)	V. serious	n/a	Not serious	Not serious		LOW
1 study (Flicker 1997)	Prospective	299	0.57)	0.95)	LR-	0.55 (0.48, 0.64)	V. serious	n/a	Not serious	Serious	-	VERY LOW
ALL EVIDENCE POOLED V.	serious											
2 studies (Cruz-Orduna	2x	659	0.67 (0.33,	0.92 (0.88,	LR+	7.59 (4.07, 14.17)	V. serious	Serious	Not serious	Not serious		VERY LOW
2012; Flicker 1997)	prospective	009	0.89)	0.94)	LR-	0.35 (0.14, 0.90	V. serious	Serious	Not serious	Serious	-	VERYLOW

### Notes on risk of bias

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

Cruz-Orduna 2012: Thresholds were not pre-specified but were calculated to give optimum sensitivity and specificity

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

# P.2.1.72 MMSE (<19)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
2 studies (Carnero-Pardo			0.87 (0.83,	LR+	6.46 (4.97, 8.38)	Serious	Not serious	Not serious	Not serious		MODERAT E	
013, Cruz-Orduna 2012)	prospective	520	0.92)	0.90)	LR-	0.16 (0.09, 0.26)	Serious	Not serious	Not serious	Not serious	-	MODERAT E
SECONDARY CARE												
4 atualy (Fliatras 4007)	Dragnastiva	200	0.56 (0.49,	0.97 (0.78,	LR+	4.19 (2.39, 7.36)	V. serious	n/a	Not serious	Not serious		LOW
1 study (Flicker 1997)	Prospective	299	0.62)	0.93)	LR-	0.51 (0.43, 0.61)	V. serious	n/a	Not serious	Serious	-	VERY LOW
ALL EVIDENCE POOLED V	. serious											
2 studies (Carnero-Pardo	3x	819	0.76 (0.46,	0.87 (0.83,	LR+	5.95 (4.64, 7.62)	Serious	Not serious	Not serious	Not serious		MODERAT E
2013; Cruz-Orduna 2012; Flicker 1997)	prospective	019	0.93)	0.89)	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

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

# P.2.1.73 MMSE (<20)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Carnero-Pardo	Dragnastiva	360	0.94 (0.85,	0.82 (0.77,	LR+	5.19 (4.02, 6.70)	Serious	n/a	Not serious	Not serious		MODERAT E
013)	Prospective	360	0.97)	0.86)	LR-	0.08 (0.03, 0.19)	Serious	n/a	Not serious	Not serious	-	MODERAT E
SECONDARY CARE												
4 ahudu (Fliakaa 1007)	Dragnastiva	200	0.62 (0.55,	0.84 (0.75,	LR+	3.96 (2.38, 6.60)	V. serious	n/a	Not serious	Not serious		LOW
1 study (Flicker 1997)	Prospective	299	0.68)	0.91)	LR-	0.45 (0.37, 0.55)	V. serious	n/a	Not serious	Serious	-	VERY LOW
ALL EVIDENCE POOLED V	. serious											
2 studies (Carnero-Pardo	2x	659	0.82 (0.36,	0.82 (0.78,	LR+	4.92 (3.91, 6.18)	Serious	Not serious	Not serious	Not serious		MODERAT E
2013; Flicker 1997)	prospective	009	0.98)	0.86)	LR-	0.20 (0.04, 1.09)	V. serious	Serious	Not serious	Serious	-	VERYLOW

### Notes on risk of bias

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

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

## 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	Danasativa	200	0.95 (0.87,	0.73 (0.68,	LR+	3.53 (2.89, 4.31)	Serious	n/a	Not serious	Not serious		MODER ATE
study (Carnero-Pardo 013)	Prospective	360	0.98)	0.78)	LR-	0.07 (0.03, 0.18)	Serious	n/a	Not serious	Not serious	-	MODER ATE
SECONDARY CARE												
4 at at (50 days 4007)	Danasativa	200	0.69 (0.63,	0.76 (0.66,	LR+	2.86 (1.93, 4.24)	V. serious	n/a	Not serious	Serious		VERY LOW
1 study (Flicker 1997)	Prospective	299	0.75)	0.84)	LR-	0.41 (0.32, 0.52)	V. serious	n/a	Not serious	Serious	-	VERY LOW
ALL EVIDENCE POOLED	V. serious											
2 studies (Carnero-	2x	659	0.86 (0.43,	0.74 (0.69,	LR+	3.38 (2.83, 4.04)	Serious	Not serious	Not serious	Not serious		MODER ATE
Pardo 2013; Flicker 1997)	prospective	659	0.98)	0.78)	LR-	0.18 (0.03, 1.00)	V. serious	Serious	Not serious	Serious	-	VERYLO W

### Notes on risk of bias

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

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

### P.2.1.75 MMSE (<22)

Studies PRIMARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
4 abody (Compare Davida 2012)	Prospectiv	360	0.96 (0.89,	0.67 (0.61,	LR+	2.92 (2.46, 3.48)	Serious	n/a	Not serious	Not serious		MODERA TE
1 study (Carnero-Pardo 2013)	е	360	0.99)	0.72)	LR-	0.06 (0.02, 0.18)	Serious	n/a	Not serious	Serious	-	MODERA TE
3 studies (Callahan 2002; Flicker	3x	1,	0.69 (0.60,	0.94 (0.64,	LR+	12.43 (1.75, 88.49)	Very serious	Serious	Not serious	Serious		VERY LOW
1997; Kukull 1994)	prospective	089	0.78)	0.99)	LR-	0.35 (0.26, 0.46)	Serious	Serious	Not serious	Serious	-	LOW
ALL EVIDENCE POOLED												
4 studies (Callahan 2002;	4 ×	1,44	0.76 (0.64,	0.89 (0.67,	LR+	6.54 (2.67, 16.01)	Serious	Serious	Not serious	Not serious		LOW
Carnero-Pardo 2013; Flicker 1997; Kukull 1994)	prospective	3	0.85)	0.97)	LR-	0.30 (0.21, 0.43)	Serious	Serious	Not serious	Not serious	-	LOW

### Notes on risk of bias

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

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

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

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

### P.2.1.76 MMSE (<23)

Studies	Design	Tot al N	Sens (95%CI)	Spec (95%CI)	Meas ure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
4 study (Corners Dords 2042)	1 ×	360	0.99 (0.91,	0.57 (0.51,	LR+	2.29 (2.00, 2.62)	Serious	n/a	Not serious	Serious		LOW
1 study (Carnero-Pardo 2013)	prospect ive	300	1.00)	0.63)	LR-	0.02 (0.00, 0.16)	Serious	n/a	Not serious	Not serious	-	MODE RATE
SECONDARY CARE												
5 studies (Abdel-Aziz 2015; Callahan 2002; Flicker 1997;	5 ×	1,3	0.67 (0.55,	0.89 (0.75,	LR+	6.79 (2.70, 15.00)	Very serious	Serious	Not serious	Not serious		VERY LOW
Kukull 1994; Nielsen 2013)	prospect ive	64	0.77)	0.96)	LR-	0.38 (0.26, 0.52)	Very serious	Serious	Not serious	Serious	-	VERY LOW
ALL EVIDENCE POOLED												
6 studies (Abdel-Aziz 2015; Callahan 2002; Carnero-Pardo	6 ×	1,7	0.75 (0.54,	0.85 (0.69,	LR+	5.47 (2.60, 10.80)	V. serious	Serious	Not serious	Not serious		VERY LOW
2013; Flicker 1997; Kukull 1994; Nielsen 2013)	prospect ive	24	0.88)	0.94)	LR-	0.31 (0.15, 0.51)	V. serious	Serious	Not serious	Serious	-	VERY LOW

### Notes on risk of bias

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

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

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

Carnero-Pardo 2013: Multiple test thresholds were used

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

Abdel-Aziz 2015: Subgroup of 6 CIT tested patients were tested with MMSE as well; MMSE cut off was not pre-specified as chosen for comparison to 6CIT test.

# P.2.1.77 MMSE (<24)

Studies PRIMARY CARE	Design	Tot al N	Sens (95%CI)	Spec (95%CI)	Meas ure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
4 shirth: (Correcte Double 2042)	Prospecti	200	0.99 (0.91,	0.46 (0.40,	LR+	1.84 (1.65 2.05)	Seriou s	n/a	Not serious	Serious		LOW
1 study (Carnero-Pardo 2013)	ve	360	1.00)	0.52)	LR-	0.08 (0.01, 1.32)	Seriou s	n/a	Not serious	Not serious	-	MODE RATE
SECONDARY CARE												
11 studies (Bastide 2012; Callahan 2002; Goncalves 2011; Flicker 1997; Hancock 2011; Knaefelc 2003; Kukull 1994;	11 ×	2,9	0.73 (0.63,	0.91 (0.83,	LR+	8.43 (4.47, 14.80)	Seriou s	Serious	Not serious	Not serious		LOW
Mathuranath 2000; Nielsen 2013; Postel-Vinay 2014; Sager 2006)	prospecti ve	75	0.81)	0.96)	LR-	0.31 (0.23, 0.40)	Seriou s	Serious	Not serious	Not serious	-	LOW
ALL EVIDENCE POOLED												
12 studies (Bastide 2012; Callahan 2002; Carnero-Pardo 2013; Flicker 1997; Goncalves 2011; Hancock 2011; Knaefelc 2003;	12 ×	3,3	0.75 (0.65,	0.88 (0.78,	LR+	6.65 (3.70, 11.00)	Seriou s	Serious	Not serious	Not serious		LOW
Kukull 1994; Mathuranath 2000; Nielsen 2013; Postel-Vinay 2014; Sager 2006)	prospecti ve	5	0.84)	0.94)	LR-	0.29 (0.20, 0.38)	Seriou s	Serious	Not serious	Not serious	-	LOW

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

### Dementia

Appendix P: Diagnosis evidence tables & GRADE

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

### Notes on risk of bias

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

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

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

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

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

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

Hancock 2011: Optimised test threshold.

Bastide 2012: Optimised test cut-offs used.

Carnero-Pardo 2013: Multiple test thresholds were used

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

Postel-Vinay 2014: Optimised cut-off was used; the study was not downgraded for exclusions as <10% population was excluded

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

# P.2.1.78 MMSE (<25)

Studies PRIMARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measu re	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMART CARE												
1 study (Carnero-Pardo 2013)	1 × prospectiv	360	0.99 (0.91,	0.38 (0.33,	LR+	1.61 (1.46, 1.76)	Serious	n/a	Not serious	Not serious		MODER ATE
1 Study (Camero-Fardo 2013)	e	300	1.00)	0.44)	LR-	0.02 (0.00, 0.27)	Serious	n/a	Not serious	Serious	-	MODER ATE
SECONDARY CARE												
7 studies (Callahan 2002; Flicker 1997;	6 × prospectiv				LR+	5.18 (2.74, 9.37)	V. serious	Serious	Not serious	Not serious		VERY LOW
Kukull 1994; Larner 2015; Milian 2012; Nielsen 2013; Yeung 2014)	e; 1 × retrospecti ve	2,02	0.82 (0.73, 0.87)	0.83 (0.70, 0.91)	LR-	0.22 (0.14, 0.33)	V. serious	Serious	Not serious	Not serious	-	VERY LOW
ALL EVIDENCE POOLED												
	7 × prospectiv				LR+	4.41 (2.31, 8.1)	V. serious	Serious	Not serious	Not serious		VERY LOW
8 studies (Callahan 2002; Carnero-Pardo 2013; Flicker 1997; Kukull 1994; Larner 2015; Milian 2012; Nielsen 2013; Yeung 2014)	e; 1 × retrospecti ve	2,38	0.85 (0.75, 0.91)	0.80 (0.62, 0.90)	LR-	0.20 (0.12, 0.31)	V. serious	Serious	Not serious	Not serious	-	VERY LOW

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

### Dementia

Appendix P: Diagnosis evidence tables & GRADE

		Total	Sens	Spec	Measu	Summary of findings	Risk of bias	consistency	directness	precision	her nsiderations	
Studies	Design	N	(95%CI)	(95%CI)	re	(95%CI)	æ	Ĕ	_ <u>ĕ</u>	ੁ	<b>5</b> 8	Quality

#### Notes on risk of bias

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

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

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

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

Carnero-Pardo 2013: Multiple test thresholds were used

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

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

## P.2.1.79 MMSE (<26)

11111102 ( 120)												
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE		•					·	·	·	·		
4 studies (Callahan 2002;	3 × prospective;	4.500	0.85 (0.77,	0.78 (0.53,	LR+	3.84 (1.68, 8.76)	V. serious	Serious	Not serious	Serious		VERY LOW
Flicker 1997; Milian 2012;	1 × retrospective	1,583	0.91)	0.92)	LR-	0.19 (0.14, 0.28)	V. serious	Serious	Not serious	Not serious	-	VERY LOW

### Notes on risk of bias

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

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

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

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

### P.2.1.80 MMSE (<27)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	Risk of bias	nconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE	Design		(50,651)	(50,651)		(00700.)					0 3	quanty
4 studies (Bastide 2012; Callahan	4 ×	4 044	0.86 (0.73,	0.75 (0.66,	LR+	3.43 (2.43, 4.85)	Serious	Serious	Not serious	Not serious		LOW
2002; Mathuranath 2000; Nielsen 2013)	prospective	1,241	0.94)	0.82)	LR-	0.17 (0.09, 0.33)	Serious	Serious	Not serious	Not 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)	Measur e	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Callahan	2 ×	796	0.96 (0.87,	0.70 (0.57,	LR+	3.13 (2.22, 4.41)	Serious	Not serious	Not serious	Not serious		MODERAT E
	prospective	790	0.99)	0.81)	LR-	0.05 (0.02, 0.16)	V. serious	Serious	Not serious	Not serious	-	VERY LOW

### Notes on risk of bias

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

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	E											
2 studies (Chen	2 ×	405	0.93 (0.90,	0.81 (0.44,	LR+	5.18 (1.32, 20.41)	V. serious	Serious	Not serious	Serious		VERY LOW
2011; Yeung 2014)	prospective 495 0.96) 0.96) 0.96)	0.96)	LR-	0.09 (0.06, 0.13)	V. serious	Not serious	Not serious	Not serious	-	LOW		

### Notes on risk of bias

Chen 2011: Unclear whether inappropriate exclusions were avoided or if a pre-specified test threshold was used; unclear whether index and reference tests were interpreted without knowledge of each other and whether all participants were included in the analysis.

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

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

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

### Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 atualy (Calabatain 2044)	Dunamantiva	04	0.00 (0.70, 0.00)	0.24 (0.24, 0.45)	LR+	1.41 (1.16, 1.71)	Not serious	n/a	Serious	Not serious		MODERATE
1 study (Goldstein 2014)	Prospective	81	0.96 (0.78, 0.99)	0.31 (0.21, 0.45)	LR-	0.12 (0.02, 0.84)	Not serious	n/a	Serious	Serious	-	LOW
Notes on indirectness												

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Caldatain 2014)	Dragnostiva	81	0.09 (0.77, 1.00)	0.22 (0.14, 0.26)	LR+	1.27 (1.09, 1.48)	Not serious	n/a	Serious	Not serious		MODERATE
1 study (Goldstein 2014)	Prospective	01	0.98 (0.77, 1.00)	0.23 (0.14, 0.36)	LR-	0.08 (0.00, 1.28)	Not serious	n/a	Serious	Serious	-	LOW
Notes on indirectness Goldstein 2014: Study only recruited African Americans ≥ 50 years old.												

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

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

### P.2.1.87 MRI

IVIIXI							1					
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Frisoni 2009;	2 ×	004	0.83 (0.49,	0.57 (0.47,	LR+	1.87 (1.45, 2.37)	V. serious	Not serious	Not serious	Serious		VERY LOW
	prospective	234	0.96)	0.66)	LR-	0.30 (0.09, 1.04)	V. serious	Serious	Not serious	Serious	-	VERY LOW

### Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAI	RE											
1 study (Beinhoff	Droopostivo	232	0.30 (0.39, 0.53)		LR+	32.70 (7.99, 133.88)	Serious	n/a	Not serious	Not serious		MODERATE
2005)	005) Prospective	232	0.39 (0.28, 0.52)	0.99 (0.95, 1.00)	LR-	0.61 (0.50, 0.75)	Serious	n/a	Not serious	Not serious	-	MODERATE

### Notes on risk of bias

P.2.1.89 Orientation, OR (<8)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAL	RE											
1 study (Beinhoff	Droopostivo	222	0.65 (0.53, 0.76)	0.00 (0.85, 0.04)	LR+	6.76 (4.11, 11.12)	Serious	n/a	Not serious	Not serious		MODERATE
2005)	Prospective 232 0.65 (0.53, 0.76)	0.00 (0.03, 0.76)	0.90 (0.85, 0.94)	LR-	0.39 (0.28, 0.54)	Serious	n/a	Not serious	Serious	-	LOW	

### Notes on risk of bias

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

### P.2.1.90 Palmo-Mental Reflex

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

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

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDART CARE												
1 study (Streit 2015)	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
1 Study (Strell 2015)	Reliospective	154	0.71 (0.40, 0.67)	0.04 (0.05, 0.71)	LR-	0.46 (0.22, 0.98)	Serious	n/a	Not serious	Serious	_	LOW
Notes on risk of bias												

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Strait 2015)	Potroppostivo	154	0.24 (0.00, 0.40)	0.02 (0.00 0.07)	LR+	3.58 (1.24, 10.38)	Serious	n/a	Not serious	Serious		LOW
1 study (Streit 2015)	Retrospective	154	0.24 (0.09, 0.49)	9) 0.93 (0.88, 0.97)	LR-	0.82 (0.63, 1.07)	Serious	n/a	Not serious	Not serious	-	MODERATE

Notes on risk of bias

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

Notes on indirectness

Streit 2015: Patients had to have cognitive complaints, but score as normal on the MMSE and CDT tests.

## P.2.1.93 Phototest (<27)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
4 atualis (Campana Danda 2014)	dy (Cornero Derde 2011) Prespective 140	110	0.04 (0.00, 0.00)	0.00 (0.04, 0.04)	LR+	7.48 (4.10, 13.63)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Carnero-Pardo 2011)	Prospective	140	0.81 (0.68, 0.90)	0.89 (0.81, 0.94)	LR-	0.21 (0.12, 0.38)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
ARE											
5 "	00.4	0.00 (0.50, 0.70)	0.00 (0.70, 0.00)	LR+	6.84 (2.95, 15.87)	Serious	n/a	Not serious	Not serious		MODERATE
Prospective	204	0.66 (0.58, 0.73)	0.90 (0.79, 0.96)	LR-	0.38 (0.30, 0.48)	Serious	n/a	Not serious	Not serious	-	MODERATE
	Design CARE Prospective	Design N	Design N (95%CI)	Design N (95%CI) (95%CI)	Design N (95%CI) (95%CI) Measure  CARE  Prospective 204 0.66 (0.58, 0.73) 0.90 (0.79, 0.96)	Design   Total   Sens   Spec   Measure   Offindings   (95%CI)    CARE   Prospective   204   0.66 (0.58, 0.73)   0.90 (0.79, 0.96)   LR+   6.84 (2.95, 15.87)	Design   Total   Sens (95%CI)   Spec (95%CI)   Measure   Summary of findings (95%CI)   Serious	Design   Total   Sens   Spec   Measure   Summary of findings   (95%CI)   Serious   N/a	Design   Total   Sens   Spec   Measure   Summary of findings   (95%CI)   Design   Total   Sens   (95%CI)   Measure   Summary of findings   (95%CI)   Design   Total   Sens   Sens   (95%CI)   Design   Total   Sens   Sens	Design   Total   Sens   Spec   Measure   Summary of findings   (95%CI)   Serious   Not serious   Not serious   Not serious   Serious   Not s	Total   Sens (95%CI)   Spec (95%CI)   Measure   Summary of findings (95%CI)   Serious   Seriou

### Notes on risk of bias

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

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

				70010, 1102110	\/							
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
1 study	Droopoetivo	137	0.40 (0.27, 0.60)	0.01 (0.81, 0.06)	LR+	5.27 (2.37, 11.70)	V. serious	n/a	Not serious	Not serious		LOW
(Nielsen 2013)	Prospective	137	0.49 (0.37, 0.60)	0.91 (0.81, 0.96)	LR-	0.57 (0.45, 0.72)	V. serious	n/a	Not serious	Serious	-	VERY LOW

### Notes on risk of bias

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

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

Studies SECONDARY CA	<b>D</b> esign ARE	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
1 study (Nielsen	Dan and the	407	0.04 (0.50, 0.74)	0.00 (0.70, 0.00)	LR+	3.78 (2.14, 6.65)	V. serious	n/a	Not serious	Not serious		LOW
1 study (Nielsen 2013)	Prospective	137	0.64 (0.52, 0.74)	0.83 (0.72, 0.90)	LR-	0.43 (0.31, 0.60)	V. serious	n/a	Not serious	Serious	-	VERY LOW

### Notes on risk of bias

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

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

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

### Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
1 study (Nielsen	Prospective	107	0.76 (0.65, 0.95)	0.66 (0.54, 0.77)	LR+	2.26 (1.57, 3.25)	V. serious	n/a	Not serious	Serious		VERY LOW
2013)	Prospective	137	0.76 (0.65, 0.85)	0.66 (0.54, 0.77)	LR-	0.36 (0.23, 0.56)	V. serious	n/a	Not serious	Serious	-	VERY LOW

### Notes on risk of bias

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

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

			, 1000001110111	, ca.c, . (CD/ (C	(,							
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
1 study (Nielsen	Decementive	407	0.00 (0.74, 0.00)	0.05 (0.50, 0.75)	LR+	2.32 (1.64, 3.27)	V. serious	n/a	Not serious	Serious		VERY LOW
2013)	Prospective	137	0.82 (0.71, 0.89)	0.65 (0.52, 0.75)	LR-	0.28 (0.17, 0.47)	V. serious	n/a	Not serious	Not serious	-	LOW

### Notes on risk of bias

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

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

				1	1	1	1			1		
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Chianta 2008)	Dragnostiva	05	0.72 (0.64, 0.92)	0.65 (0.46, 0.94)	LR+	2.09 (1.21, 3.62)	Serious	n/a	Not serious	Serious		LOW
1 study (Skjerve 2008)	Prospective	95	0.72 (0.61, 0.82)	0.65 (0.46, 0.81)	LR-	0.42 (0.26, 0.68)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of bias												

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skionyo 2009)	Prophostivo	95	0.72 (0.61, 0.92)	0.60 (0.40, 0.84)	LR+	2.36 (1.30, 4.27)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Skjerve 2008)	Prospective	90	0.72 (0.61, 0.82)	0.69 (0.49, 0.84)	LR-	0.40 (0.25, 0.63)	Not serious	n/a	Not serious	Serious	-	MODERATE

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

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

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

### 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												
4 -turk (Otro # 0045)	Determention	454	0.50 (0.00, 0.74)	0.75 (0.07.0.00)	LR+	2.13 (1.25, 3.64)	Serious	n/a	Serious	Serious		VERY LOW
1 study (Streit 2015)	Retrospective	154	0.53 (0.30, 0.74)	0.75 (0.67, 0.82)	LR-	0.63 (0.37, 1.05)	Serious	n/a	Serious	Serious	-	VERY LOW

### Notes on risk of bias

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

### Notes on indirectness

Streit 2015: Patients had to have cognitive complaints, but score as normal on the MMSE and CDT tests.

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

Studies SECONDARY CAR	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDART CAL	\L									1		
1 study (Malhotra	Prospective	127	0.70 (0.70, 0.96)	0.75 (0.54, 0.88)	LR+	3.15 (1.56, 6.34)	V. serious	n/a	Not serious	Serious		VERY LOW
2013)	riospective	12/	0.79 (0.70, 0.86)	0.75 (0.54, 0.66)	LR-	0.28 (0.18, 0.44)	V. serious	n/a	Not serious	Not serious	-	LOW

### Notes on risk of bias

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

### Notes on indirectness

Malhotra 2013: Participants had ≥ 6 years education

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

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

### Notes on risk of bias

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

### Notes on indirectness

Malhotra 2013: 60% participants had < 6 years education

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Malhotra	Dragnastiva	107	0.72 (0.62, 0.90)	0.42 (0.24, 0.62)	LR+	1.23 (0.86, 1.76)	V. serious	n/a	Serious	Not serious		VERY LOW
2013)	Prospective 127 0.72 (0.62, 0.80)	0.42 (0.24, 0.62)	LR-	0.68 (0.38, 1.19)	V. serious	n/a	Serious	Serious	-	VERY LOW		

### Notes on risk of bias

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

### Notes on indirectness

Malhotra 2013: Participants had < 6 years education

P.2.1.107 Syndrom Kurztest (≥7)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skionyo 2009)	Prospective	95	0.71 (0.59, 0.80)	0.54 (0.35, 0.72)	LR+	1.54 (0.99, 2.39)	Serious	n/a	Not serious	Serious		LOW
1 study (Skjerve 2008)	Fiospective	90	0.71 (0.59, 0.60)	0.54 (0.55, 0.72)	LR-	0.54 (0.32, 0.90)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of bias Skierve 2008: Use of an a	alternative thresh	old to the	standard one and tha	t was not pre-specifie	d.							

P.2.1.108 Syndrom Kurztest (≥8)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Chianya 2009)	Droopostivo	0.E	0.65 (0.53, 0.75)	0.65 (0.46, 0.94)	LR+	1.88 (1.08, 3.28)	Serious	n/a	Not serious	Serious		LOW
1 study (Skjerve 2008)	Prospective	95	0.65 (0.53, 0.75)	0.65 (0.46, 0.81)	LR-	0.53 (0.35, 0.82)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of bias Skjerve 2008: Use of an a	alternative thresh	old to the	standard one and tha	t was not pre-specifie	d.							

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

# 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 (Chionic 2000)	Dragnactive	95	0.50 (0.46, 0.60)	0.60 (0.40, 0.84)	LR+	1.88 (1.02, 3.47)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Skjerve 2008)	Prospective	90	0.58 (0.46, 0.69)	0.69 (0.49, 0.84)	LR-	0.61 (0.42, 0.89)	Not serious	n/a	Not serious	Serious	-	MODERATE

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Marmont 2012)	Dragnostiva	145	0.04 (0.70, 0.00)	0.00 (0.79, 0.06)	LR+	7.96 (3.45, 18.37)	V. serious	n/a	Not serious	Not serious		LOW	
1 study (Mormont 2012)	Prospective	145	0.81 (0.72, 0.88)	0.90 (0.78, 0.96)	LR-	0.21 (0.14, 0.32)	V. serious	n/a	Not serious	Not serious	-	LOW	
Notes on risk of bias Mormont 2012: Exclusion of	lotes on risk of bias  formont 2012: Exclusion of >35% population at analysis and use of optimised test thresholds.												

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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 atudy (Marmont 2012)	Droopoetiyo	115	0.75 (0.65, 0.93)	0.06 (0.95, 0.00)	LR+	18.38 (4.71, 71.75)	V. serious	n/a	Not serious	Not serious		LOW
1 study (Mormont 2012)	Prospective	145	0.75 (0.65, 0.83)	0.96 (0.85, 0.99)	LR-	0.26 (0.18, 0.37)	V. serious	n/a	Not serious	Not serious	-	LOW
Notes on risk of bias Mormont 2012: Exclusion	of >35% popula	tion at ar	nalysis and use of op	timised test threshold	ls.							

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 -4	December	004	0.70 (0.00, 0.00)	0.00 (0.04, 0.00)	LR+	5.93 (3.77, 9.32)	Serious	n/a	Not serious	Not serious		MODERATE
1 study (Hancock 2011)	Prospective	224	0.73 (0.62, 0.82)	0.88 (0.81, 0.92)	LR-	0.31 (0.21, 0.44)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of bias Hancock 2011: Optimised	test threshold.											

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

P.2.1.113 Test Your Memory, TYM (≤42)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 abody (Hanasak 2044)	Description	004	0.05 (0.07, 0.00)	0.45 (0.07, 0.50)	LR+	1.73 (1.48, 2.02)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Hancock 2011)	Prospective	224	0.95 (0.87, 0.98)	0.45 (0.37, 0.53)	LR-	0.11 (0.04, 0.30)	Not serious	n/a	Not serious	Not serious	-	HIGH

**P.2.1.114** Test Your Memory (≤39)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Postel-Vinay 2014)	Prospective	201	0.90 (0.80, 0.95)	0.70 (0.62, 0.77)	LR+	2.98 (2.27, 3.91)	Serious	n/a	Not serious	Not serious	_	MODERATE	
1 Study (1 Oster-Villay 2014)	Trospective	201	0.90 (0.00, 0.93)	0.70 (0.02, 0.77)	LR-	0.15 (0.07, 0.30)	Serious	n/a	Not serious	Not serious	_	MODERATE	
Notes on risk of bias Postel-Vinay 2014: Optimised	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												

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4	Dunamantiiva	204	0.05 (0.00, 0.00)	0.00 (0.50, 0.00)	LR+	2.14 (1.68, 2.72)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Sager 2006)	Prospective	364	0.85 (0.80, 0.89)	89) 0.60 (0.50, 0.69)	LR-	0.25 (0.18, 0.35)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
ι <b>Ε</b>				•						•	
Dragnostiva	222	0.95 (0.74, 0.02)	0.62 (0.56, 0.70)	LR+	2.31 (1.85, 2.89)	Serious	n/a	Not serious	Serious		LOW
Prospective 2	232	0.85 (0.74, 0.92)	0.63 (0.56, 0.70)	LR-	0.24 (0.13, 0.43)	Serious	n/a	Not serious	Not serious	-	MODERATE
	Design RE Prospective	Design N	Design N (95%CI)	Design N (95%CI) (95%CI)	Design N (95%CI) (95%CI) Measure  RE  Prospective 232 0.85 (0.74, 0.92) 0.63 (0.56, 0.70)	Design   N   Sens (95%CI)   Spec (95%CI)   Measure   Offindings (95%CI)	Design   Total   Sens   Spec   Measure   Summary of findings   95%CI)   E	Design   Total   Sens   Spec   Measure   Summary of findings (95%CI)   ER+   2.31 (1.85, 2.89)   Serious   n/a	Design   Total   Sens   Spec   (95%CI)   Measure   Summary of findings   (95%CI)   E	Total   Sens   Spec   (95%CI)   Measure   Summary of findings   (95%CI)   Serious   Serious	Total   Sens (95%CI)   Spec (95%CI)   Measure   Summary of findings (95%CI)   Serious   Seriou

### Notes on risk of bias

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

		100000	ai iiaiiiiig/, vi	17			i .					
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Beinhoff	Droopostivo	222	0.04 (0.95, 0.09)	0.59 (0.50, 0.65)	LR+	2.23 (1.85, 2.69)	Serious	n/a	Not serious	Serious		LOW
2005)		0.94 (0.85, 0.98)	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%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Beinhoff	(Beinhoff Prospective 232 0.94 (0.85, 0.98	0.04 (0.95, 0.09)	0) 0.52 (0.45, 0.60)	LR+	1.97 (1.66, 2.34)	Serious	n/a	Not serious	Serious		LOW	
2005)		232	0.94 (0.85, 0.98) 0	0.52 (0.45, 0.60)	LR-	0.12 (0.04, 0.30)	Serious	n/a	Not serious	Not serious	-	MODERATE

#### Notes on risk of bias

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

		/	ai maiiiig,, vi									
Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Beinhoff	Drooppotivo	222	0.05 (0.97, 0.00)	0.46 (0.30, 0.53)	LR+	1.76 (1.52, 2.04)	Serious	n/a	Not serious	Serious		LOW
2005)	Prospective	Prospective 232 0.95 (0.87, 0.99)	9) 0.46 (0.38, 0.53)	LR-	0.10 (0.03, 0.30)	Serious	n/a	Not serious	Not serious	-	MODERATE	

### Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%Cl)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Beinhoff	Prophostivo	222	0.07 (0.80, 0.00)	0.20 (0.21, 0.46)	LR+	1.58 (1.39, 1.79)	Serious	n/a	Not serious	Not serious		MODERATE
2005) Pro	Prospective 2	tive 232	32 0.97 (0.89, 0.99) 0.	0.39 (0.31, 0.46)	LR-	0.08 (0.02, 0.31)	Serious	n/a	Not serious	Not serious	-	MODERATE

#### Notes on risk of bias

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

	<u> </u>	<b>\</b> -	aag,,	( = .,								
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	RE											
1 study (Beinhoff	Droopoetivo	222	0.98 (0.90, 1.00)	0.24 (0.24, 0.29)	LR+	1.42 (1.28, 1.58)	Serious	n/a	Not serious	Not serious		MODERATE
2005) Pro	Prospective 2	ve 232	0.90 (0.90, 1.00)	0.31 (0.24, 0.38)	LR-	0.05 (0.01, 0.35)	Serious	n/a	Not serious	Not serious	-	MODERATE

### Notes on risk of bias

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

## P.2.2 AD versus DLB

P.2.2.1 Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Androson 2001)	Droopoetiyo	170	0.65 (0.57, 0.72)	0.67 (0.22, 0.90)	LR+	1.95 (0.77, 4.95)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Andreasen 2001)	Prospective	172	0.65 (0.57, 0.72)	0.67 (0.33, 0.89)	LR-	0.52 (0.32, 0.87)	Not serious	n/a	Not serious	Serious	-	MODERATE

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

### P.2.2.2 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study	Prospective	70	0.58 (0.46, 0.70)	0.20 (0.03, 0.69)	LR+	0.73 (0.45, 1.19)	V. serious	n/a	Serious	Serious	_	VERY LOW	
(Ossenkoppele 2013)	Prospective	Prospective	70	0.50 (0.40, 0.70)	0.20 (0.03, 0.09)	LR-	2.08 (0.35, 12.27)	V. serious	n/a	Serious	V. serious	-	VERY LOW

### Notes on risk of bias

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

### Notes on indirectness

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

### P.2.2.3 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Prognostivo	270	0.20 (0.24, 0.25)	0.72 (0.59, 0.92)	LR+	1.05 (0.64, 1.75)	Serious	n/a	Not serious	Not serious		MODERATE
Koikkalainen 2016)	Prospective 2	270	0.29 (0.24, 0.35)	) 0.72 (0.58, 0.83)	LR-	0.98 (0.81, 1.19)	Serious	n/a	Not serious	Not serious	-	MODERATE

### Notes on risk of bias

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

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

### P.2.3 AD versus FTD

### P.2.3.1 99mTc-HMPAO SPECT

Studies SINGLE CAMERA	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
2 studies (Launes 1991; Velakoulis 1997)	2 × prospective	59	0.73 (0.42, 0.91)	0.71 (0.43, 0.89)	LR+ LR-	2.78 (1.20, 6.42) 0.41 (0.23, 0.74)	V. serious Serious	Not serious	Not serious	Serious Serious	-	VERY LOW
MULTIPLE CAMERA						0.11 (0.20, 0.11)	3033		1101 0011000	30000		
1 study (Boutoleau- Bretonniere 2012)	Prospective	29	0.78 (0.54, 0.91)	0.73 (0.41, 0.91)	LR+ LR-	2.85 (1.05, 7.72) 0.31 (0.12, 0.78)	V. serious V. serious	n/a n/a	Not serious Not serious	Serious Serious	-	VERY LOW VERY LOW
ALL EVIDENCE POOLED												
3 studies (Boutoleau- Bretonniere 2012; Launes 1991; Velakoulis 1997)	3 × prospective	88	0.72 (0.56, 0.83)	0.72 (0.51, 0.86)	LR+ LR-	2.81 (1.48, 5.33) 0.38 (0.23, 0.62)	V. serious V. serious	Not serious	Not serious	Serious Serious	-	VERY LOW VERY LOW

### Notes on risk of bias

Launes 1991: Subgroup analysis used with >10% study population excluded.

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

Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

P.2.3.2 Amyloid Beta 1-42 and Total Tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	nconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE			. ,	. ,		· , ,						
4 atudu (Talada 2042)	Detuces estive	100	0.00 (0.04, 0.05)	0.03 (0.05, 0.03)	LR+	5.23 (2.35, 11.65)	Serious	n/a	Not serious	Not serious		MODERATE
1 study (Toledo 2012)	Retrospective	100	0.90 (0.81, 0.95)	0.83 (0.65, 0.93)	LR-	0.12 (0.06, 0.25)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of bias												

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

# P.2.3.3 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Prospective	83	0.58 (0.46, 0.70)	0.78 (0.54, 0.91)	LR+	2.63 (1.08, 6.39)	V. serious	n/a	Serious	Serious		VERY LOW
(Ossenkoppele 2013)	Fiospective	03	0.56 (0.46, 0.70)	0.76 (0.34, 0.91)	LR-	0.53 (0.37, 0.78)	V. serious	n/a	Serious	Serious	-	VERY LOW

#### Notes on risk of bias

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

#### Notes on indirectness

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

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

#### P.2.3.4 MRI

							(0	ıcy	Ŋ		tions	
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerat	Quality
SECONDARY CARE												
1 study	Droopootivo	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
(Koikkalainen 2016)	Prospective	313	0.29 (0.24, 0.35)	0.77 (0.00, 0.00)	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												
4 -tudu (Talada 0040)	Datasasathas	400	0.00 (0.00 4.00)	0.05 (0.00, 0.04)	LR+	6.62 (2.82, 15.52)	Serious	n/a	Not serious	Not serious		MODERATI
1 study (Toledo 2012)	Retrospective	100	0.99 (0.90, 1.00)	0.85 (0.68, 0.94)	LR-	0.01 (0.00, 0.13)	Serious	n/a	Not serious	Not serious	-	MODERATI

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

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

# P.2.4 AD versus no dementia

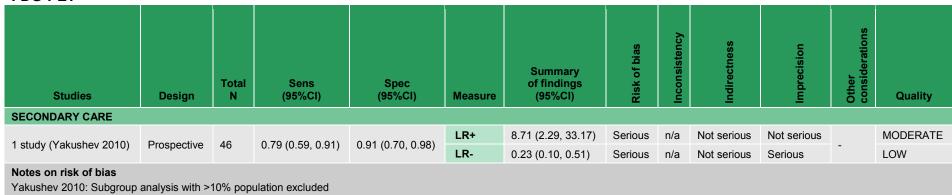
# P.2.4.1 Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE	E											
1 study	Dragnostiva	70	0.94 (0.72, 0.02)	0.94 (0.64, 0.05)	LR+	5.34 (1.88, 15.19)	Serious	n/a	Not serious	Serious		LOW
(Maddalena 2003)	Prospective	70	0.84 (0.72, 0.92)	0.84 (0.61, 0.95)	LR-	0.19 (0.10, 0.36)	Serious	n/a	Not serious	Not serious	-	MODERATE

### Notes on risk of bias

Maddalena 2003: It was unclear whether inappropriate exclusions had been made; an optimised threshold was used for each test and within each test for different analyses; it was unclear whether the index and reference tests were interpreted independently of each other.

# P.2.4.2 FDG-PET



<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Marmont 2012)	Dragnostiva	110	0.94 (0.70, 0.90)	0.00 (0.96, 1.00)	LR+	81.45 (5.15, 1287.53)	V. serious	n/a	Not serious	Not serious		LOW
1 study (Mormont 2012)	Prospective	110	0.81 (0.70, 0.89)	0.99 (0.86, 1.00)	LR-	0.19 (0.11, 0.32)	V. serious	n/a	Not serious	Not serious	-	LOW
Notes on risk of bias Mormont 2012: Exclusion	of >35% popula	ation at a	nalysis and use of o	otimised test thresho	lds.							

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

Studies SECONDARY CA	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDART CA									1			
1 study (Sikkes	Dragnostiva	260	0.06 (0.02, 0.08)		LR+	1.64 (1.38, 1.96)	V. serious	n/a	Not serious	Not serious		LOW
2010)	Prospective	269	0.96 (0.92, 0.98)	0.42 (0.32, 0.52)	LR-	0.09 (0.04, 0.20)	V. serious	n/a	Not serious	Not serious	-	LOW

#### Notes on risk of bias

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

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

Studies SECONDARY CA	<b>D</b> esign	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
1 study (Sikkes	D "	000	0.00 (0.04, 0.00)	0.47 (0.07.0.50)	LR+	1.81 (1.48, 2.21)	V. serious	n/a	Not serious	Serious		VERY LOW
2010)	Prospective	269	0.96 (0.91, 0.98)	0.47 (0.37, 0.58)	LR-	0.09 (0.05, 0.19)	V. serious	n/a	Not serious	Not serious	-	LOW

#### Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
1 study (Sikkes	Droopostivo	260	0.00 (0.07, 0.05)	0.62 (0.52, 0.72)	LR+	2.47 (1.88, 3.25)	V. serious	n/a	Not serious	Serious		VERY LOW
2010)	Prospective 269 0.92 (0.8	0.92 (0.87, 0.95)	0.63 (0.52, 0.72)	LR-	0.13 (0.08, 0.22)	V. serious	n/a	Not serious	Not serious	-	LOW	

#### Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
1 study (Sikkes	Prospective	269	0.90 (0.94, 0.03)	0.60 (0.59, 0.77)	LR+	2.84 (2.08, 3.88)	V. serious	n/a	Not serious	Not serious		LOW
2010)	Prospective	209	0.89 (0.84, 0.93)	0.69 (0.58, 0.77)	LR-	0.15 (0.10, 0.24)	V. serious	n/a	Not serious	Not serious	_	LOW

#### Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE .											
1 study (Sikkes	Prospective	269	0.86 (0.80, 0.90)	0.74 (0.64, 0.82)	LR+	3.31 (2.32, 4.73)	V. serious	n/a	Not serious	Not serious		LOW
2010)	Flospective	209	0.80 (0.80, 0.90)	0.74 (0.04, 0.02)	LR-	0.19 (0.13, 0.28)	V. serious	n/a	Not serious	Not serious	_	LOW

#### Notes on risk of bias

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

# P.2.5.6 MMSE (<28)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Marmant 2012)	Droopoetivo	110	0.09 (0.90, 1.00)	0.79 (0.64, 0.97)	LR+	4.38 (2.60, 7.38)	V. serious	n/a	Not serious	Not serious		LOW
1 study (Mormont 2012)	Prospective	110	0.98 (0.89, 1.00)	0.78 (0.64, 0.87)	LR-	0.02 (0.00, 0.15)	V. serious	n/a	Not serious	Not serious	-	LOW
Notes on risk of bias												

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

# P.2.5.7 p-tau 181

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Maddalena	Dragnostiva	70	0.67 (0.52, 0.70)	0.63 (0.40, 0.94)	LR+	1.81 (0.97, 3.36)	Serious	n/a	Not serious	Serious		LOW
2003)	Prospective	70	0.67 (0.53, 0.78)	0.63 (0.40, 0.81)	LR-	0.53 (0.31, 0.89)	Serious	n/a	Not serious	Serious		LOW

#### Notes on risk of bias

Maddalena 2003: It was unclear whether inappropriate exclusions had been made; an optimised threshold was used for each test and within each test for different analyses; it was unclear whether the index and reference tests were interpreted independently of each other.

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

p-tuu/Amyloid							<u>o</u>	ncy	SS	c	ations	
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectne	Imprecision	Other considerat	Quality
SECONDARY CARE	<b>■</b>											
1 study	Droopootivo	70	0.90 (0.67, 0.90)	0.90 (0.66, 0.07)	LR+	7.64 (2.04, 28.53)	Serious	n/a	Not serious	Not serious		MODERATE
(Maddalena 2003)	Prospective	70	0.80 (0.67, 0.89)	0.89 (0.66, 0.97)	LR-	0.22 (0.12, 0.39)	Serious	n/a	Not serious	Not serious	-	MODERATE

#### Notes on risk of bias

Maddalena 2003: It was unclear whether inappropriate exclusions had been made; an optimised threshold was used for each test and within each test for different analyses; it was unclear whether the index and reference tests were interpreted independently of each other.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Marmont 2012)	Dragnostivo	110	0.02 (0.02.0.07)	0.00 (0.79, 0.06)	LR+	9.00 (3.91, 20.71)	V. serious	n/a	Not serious	Not serious		LOW	
1 study (Mormont 2012)	Prospective	110	0.92 (0.82, 0.97)	0.90 (0.78, 0.96)	LR-	0.09 (0.04, 0.21)	V. serious	n/a	Not serious	Not serious	-	LOW	
Notes on risk of bias Mormont 2012: Exclusion													

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

# P.2.5.10 Total Tau

Total Tau						1							
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 atualy (Valuabay 2010)	Dunnanastiva	40	0.40 (0.07, 0.05)	0.05 (0.74, 0.00)	LR+	10.08 (1.42, 71.85)	V. serious	n/a	Not serious	Serious		VERY LOW	
1 study (Yakushev 2010)	Prospective	46	0.46 (0.27, 0.65)	0.95 (0.74, 0.99)	LR-	0.57 (0.39, 0.83)	V. serious	n/a	Not serious	Serious	-	VERY LOW	
Notes on risk of bias Yakushev 2010: Subgroup													

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 - to de (M t 0040)	December	440	0.00 (0.00, 0.00)	0.00 (0.05, 0.00)	LR+	22.09 (5.67, 86.05)	V. serious	n/a	Not serious	Not serious		LOW
1 study (Mormont 2012)	Prospective	110	0.90 (0.80, 0.96)	0.96 (0.85, 0.99)	LR-	0.10 (0.05, 0.22)	V. serious	n/a	Not serious	Not serious	-	LOW
Notes on risk of bias Mormont 2012: Exclusion	of >35% popula	tion at an	alysis and use of op	timised test threshold	ls.							

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

# P.2.6.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA												
1 study (Boutoleau-	Prospective	56	0.79 (0.54, 0.04)	0.66 (0.50, 0.70)	LR+	2.27 (1.37, 3.77)	Serious	n/a	Not serious	Serious		LOW
Bretonniere 2012)	Frospective	50	0.78 (0.54, 0.91)	0.66 (0.50, 0.79)	LR-	0.34 (0.14, 0.83)	Serious	n/a	Not serious	Serious	-	LOW

#### Notes on risk of bias

Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear whether consecutive or random enrolment of patients was employed; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used but <10% study population discarded

# P.2.6.2 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Boutoleau-	Droopoetivo	56	0.22 (0.16, 0.57)	0.66 (0.50, 0.70)	LR+	0.97 (0.44, 2.14)	Serious	n/a	Not serious	V. serious		VERY LOW
Bretonniere 2012)	Prospective	50	0.33 (0.16, 0.57)	0.66 (0.50, 0.79)	LR-	1.01 (0.68, 1.51)	Serious	n/a	Not serious	Not serious	-	MODERATE

#### Notes on risk of bias

Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases

# P.2.7 AD versus non-AD

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 -toda (Duite 0044)	December	4.440	0.00 (0.00, 0.00)	0.70 (0.00 0.70)	LR+	3.10 (2.68, 3.57)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Duits 2014)	Prospective	1,149	0.86 (0.83, 0.89)	0.72 (0.68, 0.76)	LR-	0.19 (0.16, 0.24)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Propdt 2009)	Detroppediye	147	0.42 (0.20, 0.56)	0.00 (0.93, 0.04)	LR+	4.13 (2.10, 8.11)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Brandt 2008)	Retrospective	147	0.42 (0.29, 0.56)	0.90 (0.82, 0.94)	LR-	0.65 (0.51, 0.83)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
	1x				LR+	6.85 (0.73, 64.28)	Serious	Seri	Not serious	Serious		VERY LOW
2008; Jahn 2011) 1>	prospective, 1x retrospective	225	0.62 (0.08, 0.97)	0.93 (0.22, 1.00)	LR-	0.39 (0.10, 1.50)	Serious	Seri ous	Not serious	Serious	-	VERY LOW

#### Notes on risk of bias

Jahn 2011: >10% population excluded from analysis; unclear whether the patients were a random or consecutive sample or whether inappropriate exclusions were avoided; unclear whether the reference standard was interpreted without knowledge of the index tests results

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMER	A											
2 studies (Kaneta	2x	000	0.70 (0.00, 0.00)	0.07 (0.40, 0.00)	LR+	4.56 (0.31, 66.33)	Serious	Serious	Not serious	V serious		VERY LOW
2016; Tripathi 2010)	prospective	206	0.72 (0.09, 0.99)	0.87 (0.49, 0.98)	LR-	0.26 (0.02, 3.24)	Serious	Serious	Not serious	V. serious		VERY LOW
Notes on risk of his	as											

Tripathi 2010: 14% of participants were lost to follow up and did not receive a reference standard; it is unclear whether the index test was interpreted without knowledge of the reference standard.

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

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

#### Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA	A											
1 study (Kaneta	Prospective	89	0.40 (0.27, 0.54)	0.93 (0.69, 0.03)	LR+	2.32 (1.08, 4.96)	Not serious	n/a	Not serious	Serious		MODERATE
2016)	Frospective	09	0.40 (0.27, 0.54)	0.83 (0.68, 0.92)	LR-	0.73 (0.56, 0.95)	Not serious	n/a	Not serious	Not serious	-	HIGH

# P.2.7.7 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA						,						
5 studies (Bergman 1997; Holman 1992; Launes 1991;	5 ×	505	0.70 (0.55, 0.81)	0.62 (0.30, 0.86)	LR+	2.07 (1.08, 4.47)	Not serious	Serious	Not serious	Serious	_	LOW
Masterman 1997; McMurdo 1994)	prospective	303	0.70 (0.55, 0.81)	0.02 (0.00, 0.00)	LR-	0.52 (0.37, 0.84)	Not serious	Serious	Not serious	Serious		LOW
MULTIPLE CAMERA												
2 studies (Dobert	1x prospective				LR+	6.80 (1.98, 23.36)	Not serious	Not serious	Not serious	Serious		MODERATE
2005; Rollin-Sillaire 2012)	1x retrospective	72	0.45 (0.24, 0.69)	0.93 (0.77, 0.98)	LR-	0.60 (0.40, 0.90)	Serious	Not serious	Not serious	Serious	-	LOW
ALL EVIDENCE POO	LED											
7 studies (Bergman 1997; Dobert 2005; Holman 1992;	6 ×				LR+	2.10 (1.29, 3.43)	Not serious	Serious	Not serious	Serious		LOW
Launes 1991; p	prospective; 1 × retrospective	577	0.63 (0.49, 0.75)	0.74 (0.45, 0.90)	LR-	0.56 (0.43, 0.73)	Not serious	Not serious	Not serious	Serious	-	MODERATE

# Notes on risk of bias

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

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

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

# P.2.7.8 Amyloid Beta 1-42

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

#### Notes on risk of bias

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

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

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

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

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

P.2.7.9 Amyloid Beta 1-42 and total tau

Studies SECONDARY C	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDART C	ARE											
1 study (Frisoni	Prognostivo	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
(1909) Prospective	Fiospective	<del>94</del>	0.7 1 (0.33, 0.63)	0.00 (0.70, 0.94)	LR-	0.33 (0.20, 0.55)	Serious	n/a	Not serious	Serious	-	LOW

#### Notes on risk of bias

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

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Duita 2014)	Dragnostiva	1 1 1 0	0.74 (0.70, 0.77)	0.96 (0.93, 0.90)	LR+	5.40 (4.33, 6.73)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Duits 2014)	Prospective	1,149	0.74 (0.70, 0.77)	0.86 (0.83, 0.89)	LR-	0.30 (0.26, 0.35)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
2 studies (Gabelle	2 ×	1,200	0.83 (0.78,	0.83 (0.79,	LR+	4.74 (3.67, 6.12)	Serious	Not serious	Not serious	Not serious		MODERAT E
(117 /I IIIA): (Janelle	prospective	1,200	0.87)	0.86)	LR-	0.21 (0.15, 0.28)	Serious	Serious	Not serious	Not serious	-	LOW

#### Notes on risk of bias

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

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

P.2.7.12 Amyloid Beta 1-42/Total Tau

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

#### Notes on risk of bias

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

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

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
3 studies (Dumurgier 2015	3 ×	007	0.83 (0.60,	0.77 (0.66,	LR+	3.33 (2.31, 4.78)	V. serious	Not serious	Not serious	Not serious		LOW
Lille); Dumurgier 2015 (Paris); numurgier 2015 (Montpellier))	prospective	367	0.94)	0.85)	LR-	0.22 (0.09, 0.54)	V. serious	Serious	Not serious	Serious	-	VERY LOW

#### Notes on risk of bias

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

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

# P.2.7.14 EEG

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Engedal 2015)	Dragnostiva	272	0.70 (0.64, 0.77)	0.40 (0.24, 0.46)	LR+	1.16 (1.00, 1.35)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Engedal 2015)	Prospective	372	0.70 (0.61, 0.77)	0.40 (0.34, 0.46)	LR-	0.76 (0.56, 1.02)	Not serious	n/a	Not serious	Not serious	-	HIGH

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

### P.2.7.15 FDG-PET

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
6 studies (Dobert 2005; Frisoni 2009;	6 ×	544	0.72 (0.53,	0.77 (0.70,	LR+	3.19 (2.05, 4.60)	Seriou s	Seriou s	Seriou s	Not serious		VERY LOW
Ossenkoppele 2013; Panegyres 2009; Silverman 2001; Yakushev 2010)	prospective	0 <del>44</del>	0.86)	0.83)	LR-	0.37 (0.18, 0.62)	Seriou s	Seriou s	Seriou s	Serious	-	VERY LOW

#### Notes on risk of bias

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

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

Yakushev 2010: Subgroup analysis with >10% population excluded

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

#### Notes on indirectness

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

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

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

# P.2.7.16 FDG-PET/CT

15012170												
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
1 study (Motara	Detroppostive	00	0.07 (0.74, 0.04)	0.06 (0.96, 0.00)	LR+	22.61 (5.78, 88.40)	Serious	n/a	Serious	Not serious		LOW
2017)	Retrospective	98	0.87 (0.74, 0.94)	0.96 (0.86, 0.99)	LR-	0.14 (0.06, 0.29)	Serious	n/a	Serious	Not serious	-	LOW

#### Notes on risk of bias

Motara 2017: There were 22 unstated reasons for exclusion; it was unclear whether a random or consecutive sample of patients was enrolled; whether the reference standard was likely to correctly classify the target condition or if it was interpreted without knowledge of the results of the index test.

#### Notes on indirectness

Motara 2017: There were 22 unstated reasons for exclusion

# P.2.7.17 [18F] flutemetamol PET

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
020011271111 071112												
1 atudy (7wan 2017)	Dragnastiva	211	0.76 (0.60, 0.93)	0.66 (0.64, 0.76)	LR+	2.23 (1.58, 3.14)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Zwan 2017)	Prospective	211	0.76 (0.69, 0.83)	0.66 (0.54, 0.76)	LR-	0.36 (0.26, 0.51)	Not serious	n/a	Not serious	Serious	-	MODERATE

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

P.2.7.18 Formula Hulstaert (biomarkers)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 -t. d. (D.:t- 2044)	Dragonactiva	1 1 1 0	0.02 (0.04.0.05)	0.74 (0.70, 0.77)	LR+	3.54 (3.06, 4.10)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Duits 2014)	Prospective	1,149	0.93 (0.91,0.95)	0.74 (0.70, 0.77)	LR-	0.09 (0.07, 0.13)	Not serious	n/a	Not serious	Not serious	-	HIGH

P.2.7.19 Formula Mattson (biomarkers)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Duita 2014)	Droopoetivo	1 1 1 0	0.00 (0.77, 0.02)	0.05 (0.01.0.00)	LR+	5.26 (4.28,6.47)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Duits 2014)	Prospective	1,149	0.80 (0.77, 0.83)	085 (0.81, 0.88)	LR-	0.24 (0.20, 0.28)	Not serious	n/a	Not serious	Not serious	-	HIGH

# P.2.7.20 Formula Mulder (biomarkers)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Duita 2014)	Droopoetivo	1 140	0.03 (0.04, 0.05)	0.72 (0.69, 0.76)	LR+	3.38 (2.93, 3.91)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Duits 2014)	Prospective	1,149	0.93 (0.91, 0.95)	0.73 (0.68, 0.76)	LR-	0.10 (0.07, 0.13)	Not serious	n/a	Not serious	Not serious	-	HIGH

# P.2.7.21 Formula Schoonenboom (biomarkers)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Duita 2014)	Droopoetivo	1 140	0.04 (0.00, 0.03)	0.79 (0.74 0.94)	LR+	4.10 (3.48, 4.82)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Duits 2014)	Prospective	1,149	0.91 (0.88, 0.93)	0.78 (0.74, 0.81)	LR-	0.12 (0.09, 0.15)	Not serious	n/a	Not serious	Not serious	-	HIGH

P.2.7.22 Mass Spectrometry

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 -tudy (Jaha 2014)	Description	00	0.07 (0.77, 0.04)	0.02 (0.02 0.02)	LR+	5.02 (2.05, 12.29)	Serious	n/a	Not serious	Serious		MODERATE
1 study (Jahn 2011)	Prospective	86	0.87 (0.77, 0.94)	0.83 (0.62, 0.93)	LR-	0.15 (0.08, 0.30)	Serious	n/a	Not serious	Serious	-	MODERATE

# P.2.7.23 MRI

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

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

# 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 atudy (Suppo 2015)	Potropootivo	100	0.61 (0.46, 0.74)	0.96 (0.74, 0.02)	LR+	4.30 (2.17, 8.50)	Serious	n/a	Not serious	Not serious		MODERATE		
1 study (Suppa 2015)	Retrospective	100	0.61 (0.46, 0.74)	0.86 (0.74, 0.93)	LR-	0.45 (0.31, 0.66)	Serious	n/a	Not serious	Serious	-	LOW		
Notes on risk of bias Suppa 2015: It was und														

5	<b>MRI</b> Hippocamp	al grey matte	r volu	me left, HVL. C	ut- off 2.69 ml								
	Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
	SECONDARY CARE					•		•			•	•	•
	4 -tt- (0 0045)	Detre en estive	400	0.70 (0.50, 0.00)	0.74 (0.50, 0.00)	LR+	2.47 (1.56, 3.89)	Serious	n/a	Not serious	Serious		LOW
	1 study (Suppa 2015)	Retrospective	100	0.70 (0.56, 0.82)	0.71 (0.58, 0.82)	LR-	0.41 (0.25, 0.67)	Serious	n/a	Not serious	Serious	-	LOW
	Notes on risk of hige												

#### Notes on risk of bias

P.2.7.25

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%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Cuppa 2015)	Detroppostive	100	0.90 (0.65, 0.90)	0.66 (0.52, 0.77)	LR+	2.34 (1.58, 3.48)	Serious	n/a	Not serious	Serious		LOW
1 study (Suppa 2015)	Retrospective	100	0.80 (0.65, 0.89)	0.66 (0.53, 0.77)	LR-	0.31 (0.17, 0.57)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of bias Suppa 2015: It was und	clear whether the ir	ndex test r	esults were interprete	d without knowledge o	of the results	of the reference stand	ard; assay c	ut-offs v	were determined	d using ROC	analysis.	

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
aturdu (Cuma a 2015)	Detuces estive	100	0.75 (0.00, 0.00)	0.77 (0.04, 0.00)	LR+	3.23 (1.95, 5.36)	Serious	n/a	Not serious	Serious		LOW
tudy (Suppa 2015) I	Retrospective	100	0.75 (0.60, 0.86)	0.77 (0.64, 0.86)	LR-	0.33 (0.19, 0.55)	Serious	n/a	Not serious	Serious	-	LOW

Notes on risk of bias

P.2.7.27

Suppa 2015: It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; assay cut-offs were determined using ROC analysis.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Cuppa 2015)	Detroppediye	100	0.90 (0.65, 0.90)	0.90 (0.69, 0.90)	LR+	4.05 (2.34, 7.02)	Serious	n/a	Not serious	Not serious		MODERATE
1 study (Suppa 2015)	Retrospective	100	0.80 (0.65, 0.89)	0.80 (0.68, 0.89)	LR-	0.25 (0.14, 0.46)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of bias	l a a u la a t la a u t la a . ; u			والمرادية والمراجع والمتارية		ulta af tha wafawanaa	-4		.t affaana alat	i J.,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	200	i.

Suppa 2015: It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; assay cut-offs were determined using ROC analysis.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Suppo 2015)	Potroppostivo	100	0.66 (0.51, 0.79)	0.99 (0.76, 0.04)	LR+	5.27 (2.55, 10.88)	Serious	n/a	Not serious	Not serious		MODERATE
1 study (Suppa 2015)	Retrospective	100	0.66 (0.51, 0.78)	0.88 (0.76, 0.94)	LR-	0.39 (0.26, 0.59)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of bias												

Suppa 2015: It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; assay cut-offs were determined using ROC analysis.

P.2.7.30 Olfactory Test ≥ 3 errors

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
1 study			2 -2 (2 -2 2 2 4)		LR+	1.47 (0.97, 2.22)	Not serious	n/a	Not serious	Serious		MODERATE
(Christensen 2017)	Prospective	50	0.79 (0.59, 0.91)	0.46 (0.28, 0.65)	LR-	0.45 (0.19, 1.09)	Not serious	n/a	Not serious	Serious	-	MODERATE
Notes on risk of	bias											
Christensen 2017	: Although the th	reshold	was not pre-specified	, data was presented	I for all possi	ble cut offs.						

P.2.7.31 Olfactory Test ≥ 4 errors

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	RE											
1 study		50	0.50 (0.04, 0.00)	0.70 (0.50 0.07)	LR+	1.86 (0.88, 3.93)	Not serious	n/a	Not serious	Serious		MODERATE
(Christensen 2017)	Prospective	50	0.50 (0.31, 0.69)	0.73 (0.53, 0.87)	LR-	0.68 (0.43, 1.09)	Not serious	n/a	Not serious	Serious	-	MODERATE
Notes on risk of Christensen 2017		reshold v	was not pre-specified	, data was presented	for all possi	ble cut offs.						

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

Olfactory Test ≥ 5 errors P.2.7.32

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	RE											
1 study	Describes	50	0.04 (0.00, 0.44)	0.05 (0.05, 0.04)	LR+	1.35 (0.41, 4.46)	Not serious	n/a	Not serious	Serious		MODERATE
(Christensen 2017)	Prospective	50	0.21 (0.09, 0.41)	0.85 (0.65, 0.94)	LR-	0.94 (0.72, 1.22)	Not serious	n/a	Not serious	Serious	-	MODERATE

Christensen 2017: Although the threshold was not pre-specified, data was presented for all possible cut offs...

p-tau 181 P.2.7.33

Studies ALL EVIDENCE POOLED	Design	Tot al N	Sens (95%CI)	Spec (95%CI)	Meas ure	Summar y of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
9 studies (Brandt 2008; Duits 2014; Dumurgier 2015 (Lille); Dumurgier 2015 (Paris); Dumurgier 2015 (Montpellier); Gabelle 2012 (Lille and	7 × prospecti ve;	3,44	0.75 (0.62,	0.84 (0.76,	LR+	4.87 (3.37, 6.92)	V. seriou s	Serio us	Not serious	Not serious		VERY LOW
Paris); Gabelle 2012 (Montpellier); Knapskgog 2016; Mulder 2010)	2 × retrospe ctive	8	0.84)	0.90)	LR-	0.30 (0.20, 0.43)	V. seriou s	Serio us	Not serious	Not serious	-	VERY LOW

#### Notes on risk of bias

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

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

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

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

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	E											
1 study	Droopostivo	220	0.00 (0.00 0.00)	0.01 (0.86, 0.05)	LR+	10.29 (6.41, 16.50)	V. serious	n/a	Not serious	Not serious		LOW
(Dumurgier 2015)	Prospective	329	0.88 (0.82, 0.92)	0.91 (0.86, 0.95)	LR-	0.13 (0.08, 0.20)	V. serious	n/a	Not serious	Not serious	-	LOW

#### Notes on risk of bias

Dumurgier 2015: The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study; the timing of the reference and index tests is unclear and a subgroup analysis was carried out that excluded >10% population (with indeterminate results).

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	E											
1 study	Droopoetivo	303	0.97 (0.91, 0.02)	0.01 (0.96, 0.05)	LR+	9.79 (6.01, 15.93)	V. serious	n/a	Not serious	Not serious		LOW
(Dumurgier 2015)	Prospective	303	0.87 (0.81, 0.92)	0.91 (0.86, 0.95)	LR-	0.14 (0.09, 0.22)	V. serious	n/a	Not serious	Not serious	_	LOW

#### Notes on risk of bias

Dumurgier 2015: The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study; the timing of the reference and index tests is unclear and a subgroup analysis was carried out that excluded >10% population (with indeterminate results).

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

P-tad/Amyrold Bett		Total	Sens	Spec		Summary of findings	Risk of bias	consistency	Indirectness	Imprecision	rther onsiderations	Quality
Studies	Design	N	(95%CI)	(95%CI)	Measure	(95%CI)	<u>~</u>	<u> ۽</u>	드	=	5 8	Quality
SECONDARY CARE												
2 studies (Duits 2014;	2 ×	1 424	0.87 (0.81,	0.90 (0.74,	LR+	8.77 (2.95, 26.08)	V. serious	Serious	Not serious	Not serious		VERY LOW
Dumurgier 2015)	prospective	1,434	0.92)	0.97)	LR-	0.14 (0.08, 0.25)	V. serious	Serious	Not serious	Not serious		VERY LOW

#### Notes on risk of bias

Dumurgier 2015: The reference standard diagnosis included consideration of the CSF results; the test cut offs were not pre-specified; patients with unknown clinical diagnoses or MCI were excluded from the study; the timing of the reference and index tests is unclear and a subgroup analysis was carried out that excluded >10% population (with indeterminate results).

## P.2.7.37 Total Tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
ALL EVIDENCE POOLED												
9 studies (Brandt 2008; Duits 2014; Dumurgier (Lille) 2015; Dumurgier 2015	7 ×				LR+	3.62 (3.14, 4.17)	Serious	Serious	Not serious	Not serious		LOW
(Paris); Dumurgier 2015 (Montpellier); Gabelle 2012 (Lille and Paris); Gabelle 2012 (Montpellier); Knapskgog 2016; Mulder 2010)	prospective; 2 × retrospective	3,447	0.78 (0.71, 0.84)	0.78 (0.74, 0.82)	LR-	0.28 (0.21, 0.36)	V. serious	Serious	Not serious	Not serious	-	VERY LOW

#### Notes on risk of bias

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

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

Dumurgier 2015: The reference standard diagnosis included consideration of the CSF results; the test cut-offs were optimised; patients with unknown clinical diagnoses or MCI were excluded from the study and the timing of the reference and index tests is unclear and it is unclear whether a consecutive or random sample of patients was enrolled.

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Duita 2014)	Droopoetiyo	1 1 1 0	0.05 (0.02, 0.00)	0.02 (0.70, 0.05)	LR+	4.78 (3.96, 5.77)	Not serious	Not serious	Not serious	Not serious		HIGH
1 study (Duits 2014)	Prospective	1,149	0.85 (0.82, 0.88)	0.82 (0.79, 0.85)	LR-	0.18 (0.15, 0.22)	Not serious	Not serious	Not serious	Not serious	-	HIGH

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 at adv. (Candon an 2007)	Detrees estive	100	0.50 (0.40, 0.60)	0.72 (0.02 0.04)	LR+	2.15 (1.45, 3.19)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Goodman 2007)	Retrospective	168	0.59 (0.49, 0.69)	0.73 (0.62, 0.81)	LR-	0.56 (0.42, 0.75)	Not serious	n/a	Not serious	Serious	-	MODERATE

# P.2.8 AD versus other dementias

# P.2.8.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
1 study	Dunnannativa	22	0.00 (0.50, 0.00)	0.71 (0.50, 0.95)	LR+	3.05 (1.57, 5.93)	V. serious	n/a	Not serious	Serious		VERY LOW
(Velakoulis 1997)	Prospective	33	0.89 (0.50, 0.98)	0.71 (0.50, 0.85)	LR-	0.16 (0.02, 1.01)	V. serious	n/a	Not serious	Serious	-	VERY LOW

## Notes on risk of bias

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

# P.2.8.2 AD scale (≥6)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 -turk (Ourteform 0040)	D	400	0.00 (0.74, 0.07)	0.07 (0.70, 0.00)	LR+	6.18 (3.53, 10.82)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Gustafson 2010)	Prospective	190	0.80 (0.71, 0.87)	0.87 (0.78, 0.93)	LR-	0.23 (0.16, 0.34)	Not serious	n/a	Not serious	Not serious	-	HIGH
Notes on risk of bias												

Gustafson 2010: The study was not downgraded for subgroup analysis as <10% population was excluded.

# P.2.8.3 Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
3 studies (Boutoleau-Bretonniere 2012; Ibach 2006; Maddalena 2003)	3 × prospective	249	0.74 (0.67, 0.81)	0.62 (0.53, 0.71)	LR+	1.96 (1.46, 2.62)	V. serious	Not serious	Not serious	Serious		VERY LOW
					LR-	0.41 (0.29, 0.58)	V. serious	Not serious	Not serious	Serious	-	VERY LOW

#### Notes on risk of bias

Maddalena 2003: It was unclear whether inappropriate exclusions had been made; an optimised threshold was used for each test and within each test for different analyses; it was unclear whether the index and reference tests were interpreted independently of each other.

Ibach 2006: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the test thresholds were not pre-specified and it is unclear whether the index test was interpreted without knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.

Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.

P.2.8.4 Amyloid Beta 1-42 and total tau

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY C	ARE											
1 study (Frisoni	tudy (Frisoni	0.00 (0.70, 0.00)	LR+	19.89 (2.87, 137.80)	V. serious	n/a	Not serious	Not serious		LOW		
2009) Prospective	Prospective	ospective 66	0.71 (0.55, 0.83)	0.96 (0.79, 0.99)	LR-	0.30 (0.18, 0.50)	V. serious	n/a	Not serious	Not serious	-	LOW

#### Notes on risk of bias

Frisoni 2009: Subgroup analysis with >10% population excluded; patients whose cognitive deficit reverted (regarded as primarily depressed with secondary cognitive impairment) were excluded from the study; unclear whether reference test was interpreted without knowledge of index test and unclear whether results of index test interpreted without knowledge of reference test.

P.2.8.5 Apo E (≥1 allele)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Mayouy 1009)	Detroppositive	2 100	0.65 (0.62, 0.67)	0.69 (0.64, 0.72)	LR+	2.03 (1.75, 2.34)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Mayeux 1998)	Retrospective	2,188	0.65 (0.62, 0.67)	0.68 (0.64, 0.72)	LR-	0.52 (0.48, 0.57)	Not serious	n/a	Not serious	Serious	-	MODERATE

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

001 14 0 0; total 144			li .	l .	i e				l .			
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE		•						•	•	•		
1 study (Boutoleau- Bretonniere 2012)	Dunamantina		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
	Prospective	44			LR-	0.04 (0.00, 0.60)	V. serious	n/a	Not serious	Serious	-	VERY LOW
N. 4												

#### Notes on risk of bias

Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.

P.2.8.7 Computed Tomography, CT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 atuativ (OIDsian 2000)	Dunamantina	100	0.54 (0.30, 0.03)	0.20 (0.24, 0.55)	LR+	0.82 (0.58, 1.17)	Serious	n/a	Not serious	Not serious		MODERATE
1 study (O'Brien 2000)	Prospective	103	0.51 (0.39, 0.62)	0.38 (0.24, 0.55)	LR-	1.29 (0.79, 2.10)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of bias O'Brien 2000: Subgroup	analysis with >1	0% popu	ılation excluded									

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

### P.2.8.8 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
6 studies (Arslan 2015; Frisoni 2009; Hoffman 2000; Jagust 2007;	4 × prospective;		0.71 (0.60,	0.66 (0.57,	LR+	2.07 (1.52, 2.78)	Serious	Not serious	Not serious	Serious		LOW
Ossenkoppele 2013; Yakushev 2010)	2 × retrospectiv e	300	0.80)			0.46 (0.30, 0.64)	Serious	Serious	Not serious	Serious	-	VERY LOW

#### Notes on risk of bias

Frisoni 2009: Subgroup analysis with >10% population excluded; patients whose cognitive deficit reverted (regarded as primarily depressed with secondary cognitive impairment) were excluded from the study; unclear whether reference test was interpreted without knowledge of index test and unclear whether results of index test interpreted without knowledge of reference test.

Yakushev 2010: Subgroup analysis with >10% population excluded

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

Arslan 2015: Unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard and if the imaging patterns were pre-specified; the reference standard results were interpreted independently of the index test results.

#### Notes on indirectness

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

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

### P.2.8.9 MRI

WITCH												
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE									·			·
2 studies (Frisoni 2009;	2 ×	471	0.62 (0.09,	0.67 (0.40,	LR+	1.54 (1.08, 2.19)	Serious	Serious	Not serious	Serious		VERY LOW
Koikkalainen 2016)	prospective	4/1	0.96)	0.86)	LR-	0.50 (0.14, 1.84)	Serious	Serious	Not serious	Serious	-	VERY LOW

### Notes on risk of bias

Frisoni 2009: Subgroup analysis with >10% population excluded; patients whose cognitive deficit reverted (regarded as primarily depressed with secondary cognitive impairment) were excluded from the study; unclear whether reference test was interpreted without knowledge of index test.

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

## P.2.8.10 p-tau 181

p tau ioi												
Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
3 studies (Boutoleau-Bretonniere	3 ×	2240	0.75 (0.64,	0.74 (0.61,	LR+	2.97 (1.73, 5.09)	V. serious	Serious	Not serious	Serious		VERY LOW
2012; Ibach 2006; Maddalena 2003)	prospective	2249	0.84)	0.83)	LR-	0.35 (0.21, 0.57)	V. serious	Not serious	Not serious	Serious	-	VERY LOW

#### Notes on risk of bias

Maddalena 2003: It was unclear whether inappropriate exclusions had been made; an optimised threshold was used for each test and within each test for different analyses; it was unclear whether the index and reference tests were interpreted independently of each other.

lbach 2006: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the test thresholds were not pre-specified and it is unclear whether the index test was interpreted without knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.

Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.

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

p												
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Ibach 2006;	2 ×	205	0.79 (0.71,	0.74 (0.64,	LR+	3.07 (2.08, 4.52)	V. serious	Not serious	Not serious	Not serious		LOW
Maddalena 2003)	prospective	205	0.85)	0.83)	LR-	0.29 (0.20, 0.41)	V. serious	Not serious	Not serious	Not serious	-	LOW

### Notes on risk of bias

Maddalena 2003: It was unclear whether inappropriate exclusions had been made; an optimised threshold was used for each test and within each test for different analyses; it was unclear whether the index and reference tests were interpreted independently of each other.

lbach 2006: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the test thresholds were not pre-specified and it is unclear whether the index test was interpreted without knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.

### P.2.8.12 Total tau

										1		
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE	·	•			·		·	•	•	•		
3 studies (Boutoleau-Bretonniere	3 ×	205	0.71 (0.52,	0.82 (0.63,	LR+	4.28 (1.75, 9.99)	V. serious	Not serious	Not serious	Not serious		LOW
2012; Ibach 2006; Yakushev 2010)	prospectiv e	205	0.85)	0.93)	LR-	0.38 (0.24, 0.61)	V. serious	Serious	Not serious	Serious	-	VERY LOW

#### Notes on risk of bias

Ibach 2006: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the test thresholds were not pre-specified and it is unclear whether the index test was interpreted without knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded. Yakushev 2010: Subgroup analysis with >10% population excluded; use of optimised thresholds for test

Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.

## 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 C	ARE											
1 study (Ibach	Prophostivo	124	0.75 (0.64, 0.83)	0.75 (0.61, 0.95)	LR+	3.00 (1.81, 4.98)	V. serious	n/a	Not serious	Serious		VERY LOW
2006) Prospective	124	0.75 (0.04, 0.03)	0.75 (0.61, 0.85)	LR-	0.33 (0.22, 0.51)	V. serious	n/a	Not serious	Serious	-	VERY LOW	

#### Notes on risk of bias

lbach 2006: It is unclear whether a consecutive or random sample of patients was enrolled and whether inappropriate exclusions were avoided; the test thresholds were not pre-specified and it is unclear whether the index test was interpreted without knowledge of the reference diagnosis; a subgroup analysis was used where >10% study population was excluded.

### P.2.9 AD versus VaD

### P.2.9.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
2 studies (Launes 1991;	2 ×	97	0.61 (0.49,	0.85 (0.69,	LR+	4.13 (1.85, 9.21)	Serious	Not serious	Not serious	Serious		LOW
cMurdo 1994)	prospective	97	0.72)	0.93)	LR-	0.45 (0.31, 0.66)	Serious	Not serious	Not serious	Serious	-	LOW
MULTIPLE CAMERA												
1 study (Boutoleau-Bretonniere	December	00	0.78 (0.54,	0.50 (0.20,	LR+	1.56 (0.75, 3.25)	V. serious	n/a	Not serious	Serious		VERY LOW
2012)	Prospective	26	0.91)	0.80)	LR-	0.44 (0.15, 1.35)	V. serious	n/a	Not serious	Serious	-	VERY LOW
ALL EVIDENCE POOLED												
3 studies (Boutoleau-Bretonniere	3 ×	123	0.64 (0.53,	0.74 (0.45,	LR+	2.54 (1.19, 5.41)	V. serious	Not serious	Not serious	Serious		VERY LOW
112: Lauros 1001: McMurdo	prospective	123	0.74)	0.91)	LR-	0.45 (0.32, 0.64)	Serious	Not serious	Not serious	Serious	-	LOW

#### Notes on risk of bias

Launes 1991: Subgroup analysis used with >10% study population excluded. McMurdo 1994: Subgroup analysis used with >10% study population discarded.

Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded

P.2.9.2 Amyloid Beta 1-42

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Androson 2001)	Prophostivo	106	0.65 (0.57, 0.72)	0.49 (0.20, 0.69)	LR+	1.25 (0.83, 1.87)	Not serious	n/a	Not serious	Not serious		HIGH
i study (Andreasen 2001)	(Andreasen 2001) Prospective 186 0.65 (0.57, 0.7	0.00 (0.07, 0.72)	0.48 (0.29, 0.68)	LR-	0.73 (0.45, 1.18)	Not serious	n/a	Not serious	Serious	-	MODERATE	

P.2.9.3 Computed Tomography, CT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE							•	<u>'</u>				
4 -tt- (OID-i 0000)	Danasation	0.4	0.54 (0.00, 0.00)	0.00 (0.47, 0.50)	LR+	0.75 (0.52, 1.06)	Serious	n/a	Not serious	Not serious		MODERATE
1 study (O'Brien 2000)	Prospective	94	0.51 (0.39, 0.62)	0.32 (0.17, 0.52)	LR-	1.54 (0.83, 2.86)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of bias O'Brien 2000: Subgroup	analysis with >1	0% popu	lation excluded									

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

### 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	Dunnanativa	247	0.00 (0.04, 0.05)	0.00 (0.00 0.00)	LR+	2.33 (0.79, 6.85)	Serious	n/a	Not serious	Serious		LOW
(Koikkalainen 2016)	Prospective	247	0.29 (0.24, 0.35)	0.88 (0.68, 0.96)	LR-	0.81 (0.68, 0.96)	Serious	n/a	Not serious	Not serious	-	MODERATE

#### Notes on risk of bias

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

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

### P.2.10.1 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE	<b>≣</b>											
1 study (Vijverberg	Droopostivo	111	0.90 (0.71, 0.06)	0.69 (0.67, 0.77)	LR+	2.77 (1.97, 3.88)	Serious	n/a	Not serious	Serious		LOW
2016b)	Prospective	111	0.89 (0.71, 0.96)	0.68 (0.57, 0.77)	LR-	0.16 (0.06, 0.48)	Serious	n/a	Not serious	Not serious	-	MODERATE

### Notes on risk of bias

Vijverberg 2016b: 19% study population was excluded from analysis and it is unclear whether a consecutive or random group of patients was enrolled or whether inappropriate exclusions were avoided; all test results (including the index tests) were used to reach the clinical diagnosis.

### P.2.10.2 FDG-PET and MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE	≣											
1 study (Vijverberg	Dragnostiva	111	0.06 (0.79, 0.00)	0.72 (0.62, 0.94)	LR+	3.52 (2.46, 5.02)	Serious	n/a	Not serious	Not serious		MODERATE
2016b)	Prospective	111	0.96 (0.78, 0.99)	0.73 (0.62, 0.81)	LR-	0.05 (0.01, 0.35)	Serious	n/a	Not serious	Not serious	-	MODERATE

### Notes on risk of bias

Vijverberg 2016b: 19% study population was excluded from analysis and it is unclear whether a consecutive or random group of patients was enrolled or whether inappropriate exclusions were avoided; all test results (including the index tests) were used to reach the clinical diagnosis.

### P.2.10.3 FTDC criteria for by FTD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 - 4	Detroconstitue	4.47	0.70 (0.00 0.07)	0.00 (0.00, 0.00)	LR+	18.48 (6.07, 56.26)	Serious	n/a	Not serious	Not serious		MODERATE
1 study (Harris 2013)	Retrospective	147	0.79 (0.69, 0.87)	0.96 (0.88, 0.99)	LR-	0.22 (0.14, 0.34)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of bias												

Harris 2013: Study excludes third of sample at initial screening

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

P.2.10.4 FTDC criteria for possible bvFTD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Vijverberg	Prospective	116	0.85 (0.67, 0.94)	0.27 (0.10, 0.27)	LR+	1.17 (0.95, 1.43)	Serious	n/a	Not serious	Not serious		MODERATE
2016a)	Frospective	110	0.65 (0.67, 0.94)	0.27 (0.19, 0.37)	LR-	0.55 (0.21, 1.44)	Serious	n/a	Not serious	Serious	-	LOW

#### Notes on risk of bias

Vijverberg 2016a: 19% study population was excluded from analysis and it is unclear whether a consecutive or random group of patients was enrolled or whether the reference standard results were interpreted without knowledge of the results of the index test.

P.2.10.5 FTDC criteria for probable bvFTD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE	<b>E</b>											
1 study (Vijverberg	Droopootivo	116	0.95 (0.67, 0.04)	0.92 (0.72, 0.90)	LR+	4.74 (2.96, 7.59)	Serious	n/a	Not serious	Not serious		MODERATE
2016a)	Prospective	116	0.85 (0.67, 0.94)	) 0.82 (0.73, 0.89)	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.

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

### P.2.10.6 MRI

1411 (1												
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE	E											
1 study (Vijverberg	Droopostivo	111	0.70 (0.51, 0.94)	0.02 (0.05, 0.07)	LR+	9.85 (4.39, 22.12)	Serious	n/a	Not serious	Not serious		MODERATE
2016b)	Prospective	111	0.70 (0.51, 0.84)	0.93 (0.85, 0.97)	LR-	0.32 (0.18, 0.57)	Serious	n/a	Not serious	Serious	-	LOW

### Notes on risk of bias

Vijverberg 2016b: 19% study population was excluded from analysis and it is unclear whether a consecutive or random group of patients was enrolled or whether inappropriate exclusions were avoided; all test results (including the index tests) were used to reach the clinical diagnosis.

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

# P.2.11.1 FDG-PET

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDAIL! CAILE												
1 study (Kerklaan 2014)	Retrospective	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
i Study (Nerkladii 2014)	Reliospective	32	0.47 (0.24, 0.71)	0.92 (0.76, 0.97)	LR-	0.58 (0.36, 0.94)	Not serious	n/a	Not serious	Serious	-	MODERATE

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

# P.2.12 CADASIL versus CADASIL-like syndromes

# P.2.12.1 Skin biopsy

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ampuero 2009)	Droopoetiyo	00	0.06 (0.79, 0.00)	0.69 (0.56, 0.70)	LR+	3.03 (2.10, 4.39)	Not serious	n/a	Not serious	Not serious		HIGH
i study (Ambuero 2009)	Prospective	90	0.96 (0.78, 0.99)	0.68 (0.56, 0.79)	LR-	0.05 (0.01, 0.37)	Not serious	n/a	Not serious	Not serious	-	HIGH

# P.2.13 CBD versus non-CBD

# P.2.13.1 CBD consensus criteria

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 - 1 - 1 - (	Determention	00	0.00 (0.70, 0.00)	0.00 (0.00 0.07)	LR+	0.96 (0.82, 1.12)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Alexander 2014)	Retrospective	33	0.93 (0.70, 0.98)	0.03 (0.00, 0.37)	LR-	2.25 (0.10, 51.46)	Not serious	n/a	Not serious	V. serious	-	LOW

# P.2.14 CJD versus non-CJD

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

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
1 study (Van Everbroeck	Determinantina	050	0.07 (0.74.0.00)	0.00 (0.05, 0.00)	LR+	42.84 (16.14, 113.67)	Not serious	n/a	Not serious	Not serious		HIGH
2003)	Retrospective	250	0.87 (0.74, 0.93)	0.98 (0.95, 0.99)	LR-	0.14 (0.07, 0.27)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Fourier 2017)	Potroppostivo	268	0.04 (0.95, 0.07)	0.05 (0.01.0.00)	LR+	19.84 (10.46, 37.65)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Fourier 2017)	Retrospective	200	0.94 (0.85, 0.97)	095 (0.91, 0.98)	LR-	0.07 (0.03, 0.16)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Tschampa	Detreserentive	474	0.04 (0.00, 0.05)	0.44 (0.20, 0.64)	LR+	1.64 (1.21, 2.21)	Not serious	n/a	Not serious	Serious		MODERATE
2005)	Retrospective	174	0.91 (0.86, 0.95)	0.44 (0.29, 0.61)	LR-	0.19 (0.10, 0.38)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
2 studies (Kenney	1 × prospective;	000	0.94 (0.78,	0.96 (0.91,	LR+	22.61 (10.33, 49.47)	Serious	Not serious	Not serious	Not serious		MODERAT E
2000; Leitao 2016)	1 × retrospective	292	0.98)	0.98)	LR-	0.07 (0.02, 0.24)	Serious	Serious	Not serious	Not serious	-	LOW

### Notes on risk of bias

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

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

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

#### Notes on risk of bias

Beudry 1998: Optimised test cut-offs were used and it was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test.

Zerr 1998: The assay used an optimised cut-off. It was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test.

Kenney 2000: It was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test.

Lemstra 2000: Unclear whether the reference and index tests were carried out blind to each other; it is unclear whether the index test (as carried out) was able to detect 14-3-3 protein at an appropriate threshold level.

Zerr 2000: It was unclear whether the index tests were interpreted independently of the reference test results; it was unclear whether a consecutive or random sample of people were enrolled or inappropriate exclusions avoided; or the index test threshold was pre-specified.

Cuadrado-Corrales 2006: 20% drop out due to problems with samples; <10 % excluded from analysis for possible CJD so not downgraded for this issue.

Bahl 2008: Exclusion of possible CJD group from index tests may inflate test sensitivity

Chohan 2010: Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.

Coulthart 2011: Not downgraded for exclusions during data analysis as <10% population excluded.

Hamlin 2012: > 28% population excluded as 14-3-3 results were ambiguous; multiple thresholds were tested and unclear whether researchers were blind to reference test results or that the reference test was interpreted without knowledge of index test.

Rohan 2015: It was unclear whether: a consecutive or random sample of patients was enrolled; the index test results were interpreted without knowledge of the results of the reference standard; a pre-specified cut-off was used for the index tests; the reference standard results were interpreted without knowledge of the index test results.

#### Notes on indirectness

Burkhard 2001: Patients do not have suspected CJD at baseline

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	RE											
1 study (Chohan	Detrespestive	444	0.00 (0.50, 0.00)	0.95 (0.90, 0.97)	LR+	11.72 (6.16, 22.29)	Serious	n/a	Not serious	Not serious		MODERATE
2010)	Retrospective	411	0.62 (0.56, 0.68)		LR-	0.40 (0.34, 0.47)	Serious	n/a	Not serious	Not serious	-	MODERATE

### Notes on risk of bias

Chohan 2010: Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.

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

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
1 study (Van Everbroeck	D	050	0.00 (0.07.4.00)	0.00 (0.04.0.00)	LR+	43.81 (17.57, 109.24)	Not serious	n/a	Not serious	Not serious		HIGH
2003)	Retrospective 250 0.99 (0.87, 1.00) 0.98 (0.94, 0.	0.98 (0.94, 0.99)	LR-	0.01 (0.00, 0.15)	Not serious	n/a	Not serious	Not serious	-	HIGH		

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

Studies SECONDARY CA	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	KE											
1 study (Chohan	Retrospective	351	0.75 (0.69, 0.80)	0.88 (0.82, 0.93)	LR+	6.33 (3.97, 10.09)	Serious	n/a	Not serious	Not serious		MODERATE
2010)	Reliospective	331	0.73 (0.09, 0.60)	0.00 (0.02, 0.93)	LR-	0.28 (0.22, 0.36)	Serious	n/a	Not serious	Not serious	-	MODERATE

#### Notes on risk of bias

Chohan 2010: Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	RE											
1 study (Chohan	Detropportive	351	0.57 (0.50, 0.63)	0.06 (0.00, 0.08)	LR+	12.81 (5.81, 28.25)	Serious	n/a	Not serious	Not serious		MODERATE
2010)	Retrospective	331	0.57 (0.50, 0.63)	0.96 (0.90, 0.98)	LR-	0.45 (0.38, 0.53)	Serious	n/a	Not serious	Serious	-	LOW

#### Notes on risk of bias

Chohan 2010: Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

# P.2.14.10 EEG

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	E											
2 studies	0				LR+	1.95 (0.42, 9.15)	Not serious	Serious	Not serious	V. serious		VERY LOW
(Tagliapietra 2013; Tschampa 2005)	etra 2 × 202 0.71 (0.05	0.71 (0.05, 0.99)	0.49 (0.00, 1.00)	LR-	0.73 (0.63, 0.84)	Not serious	Not serious	Not serious	Not serious	-	HIGH	

# P.2.14.11 European criteria for CJD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Prendel 2000)	Detroopediye	226	0.04 (0.96, 0.05)	0.29 (0.16, 0.42)	LR+	1.26 (1.04, 1.53)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Brandel 2000)	Retrospective	236	0.91 (0.86, 0.95)	0.28 (0.16, 0.43)	LR-	0.32 (0.16, 0.62)	Not serious	n/a	Not serious	Serious	-	MODERATE

# P.2.14.12 French criteria for CJD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Prandal 2000)	Detroppostive	226	0.00 (0.03 0.03)	0.50 (0.35, 0.65)	LR+	1.77 (1.29, 2.42)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Brandel 2000)	Retrospective	236	0.88 (0.83, 0.92)	0.50 (0.35, 0.65)	LR-	0.23 (0.14, 0.38)	Not serious	n/a	Not serious	Not serious	-	HIGH

# P.2.14.13 Master's criteria for CJD

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Prandal 2000)	Detroppositive	226	0.09 (0.05.4.00)	0.10 (0.04, 0.24)	LR+	1.09 (0.99, 1.21)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Brandel 2000)	2000) Retrospective 236 0.98 (0.95, 1.	0.96 (0.95, 1.00)	0.10 (0.04, 0.24)	LR-	0.15 (0.04, 0.66)	Not serious	n/a	Not serious	Serious	-	MODERATE	

# P.2.14.14 MRI

IVIIXI												
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 studies (Schroter	1 ×				LR+	5.40 (2.46, 11.88)	Not serious	Serious	Not serious	Not serious		MODERATE
2000; Tagliapietra 2013; Tschampa 2005; Van Everbroeck 2004)	prospective; 3 × retrospective	564	0.54 (0.40, 0.67)	0.90 (0.79, 0.96)	LR-	0.52 (0.37, 0.72)	Not serious	Serious	Not serious	Serious	-	LOW
Notes on risk of bias Van Everbroeck 2004:		on exclud	led 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	Detroppositive	24	0.72 (0.44, 0.04)	0.05 (0.72, 0.00)	LR+	14.55 (2.08, 101.66)	Not serious	n/a	Not serious	Not serious		HIGH
2013)	Retrospective	31	0.73 (0.41, 0.91)	0.95 (0.72, 0.99)	LR-	0.29 (0.11, 0.76)	Not serious	n/a	Not serious	Serious	-	MODERATE

# P.2.14.16 Neuron-specific enolase

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
2 studies (Bahl	2 ×	225	0.74 (0.65,	0.90 (0.85,	LR+	8.00 (5.05, 12.69)	Serious	Not serious	Not serious	Not serious		MODERAT E
2008; Beudry 1998)	prospective	295	0.82)	0.94)	LR-	0.28 (0.20, 0.40)	Serious	Not serious	Not serious	Not serious	-	MODERAT E

#### Notes on risk of bias

Beudry 1998: Optimised test cut-offs were used and it was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test.

Bahl 2008: Exclusion of possible CJD group from index tests may inflate test sensitivity

## P.2.14.17 New criteria for sporadic CJD

Studies SECONDARY (	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY C	ARE											
1 study (Zerr	Detroopediye	74	0.09 (0.97, 1.00)	0.74 (0.50, 0.95)	LR+	3.36 (1.80, 6.28)	V. serious	n/a	Not serious	Serious		VERY LOW
2009)	Retrospective	74	0.98 (0.87, 1.00)	0.71 (0.50, 0.85)	LR-	0.03 (0.00, 0.20)	V. serious	n/a	Not serious	Not serious	-	LOW

### Notes on risk of bias

Zerr 2009: Unclear whether patients were selected randomly or consecutively or whether inappropriate exclusions were avoided; the optimal index test thresholds were determined during the study and a subgroup analysis was used to determine test sensitivity and specificity.

#### p-tau 181/total tau P.2.14.18

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CAR	lΕ											
2 studies (Bahl	1 ×				LR+	8.10 (5.35, 12.26)	V. serious	Not serious	Not serious	Not serious		LOW
2008; Leitao 2016)	prospective; 1 × retrospective	282	0.93 (0.71, 0.99)	0.89 (0.84, 0.93)	LR-	0.08 (0.02, 0.37)	V. serious	Serious	Not serious	Not serious	-	VERY LOW

### Notes on risk of bias

Bahl 2008: Exclusion of possible CJD group from index tests may inflate test sensitivity; test cut off not pre-specified Leitao 2016: It was unclear whether: a consecutive or random sample of patients was enrolled; the study avoided inappropriate exclusions; test thresholds were pre-specified.

### P.2.14.19 RT-QuIC

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

P.2.14.20 S100B, 1.0ng/ml

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	RE											
1 study (Chohan	Retrospective	412	0.65 (0.50, 0.71)	0.00 (0.94, 0.04)	LR+	6.46 (4.08, 10.24)	Serious	n/a	Not serious	Not serious		MODERATE
2010)	Retrospective	412	0.65 (0.59, 0.71)	0.90 (0.84, 0.94)	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.

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

P.2.14.21 S100B, 2.5ng/ml

3 100B, 2.3Hg/H							bias	ency	ess	ion	ations	
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of b	Inconsistency	Indirectn	Imprecision	Other considera	Quality
SECONDARY CARE												
2 studies (Beudry	2 ×	1,053	0.87 (0.82,	0.87 (0.84,	LR+	6.65 (5.52, 8.00)	Serious	Not serious	Not serious	Not serious		MODERAT E
1998; Coulthart 2011)	prospective	1,055	0.91)	0.89)	LR-	0.15 (0.10, 0.21)	Serious	Not serious	Not serious	Not serious	_	MODERAT E

#### Notes on risk of bias

Beudry 1998: Optimised test cut-offs were used and it was unclear whether: a consecutive or random sample of patients was enrolled or inappropriate exclusions avoided; the index test results were interpreted without knowledge of the results of the reference standard or the reference standard results were interpreted without knowledge of the results of the index test.

Coulthart 2011: Optimised threshold used to analyse S100B results; unclear whether the reference standards would correctly classify non-CJD cases as not specified; not downgraded for exclusions during data analysis as <10% population excluded.

P.2.14.22 S100B, 4.2ng/ml

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	RE											
1 study	Prospective	924	0.52 (0.43, 0.60)	0.97 (0.96, 0.98)	LR+	17.26 (11.23, 26.52)	Not serious	n/a	Not serious	Not serious		HIGH
(Coulthart 2011)	Fiospective	924	0.52 (0.43, 0.60)	0.97 (0.90, 0.96)	LR-	0.50 (0.41, 0.60)	Not serious	n/a	Not serious	Serious	-	MODERATE

#### Notes on risk of bias

Coulthart 2011: Unclear whether the reference standards would correctly classify non-CJD cases as not specified; not downgraded for exclusions during data analysis as <10% population excluded and standard threshold used to analyse S100B results.

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

### P.2.14.23 Total Tau

Studies SECONDARY CARE	Design	Tot al N	Sens (95%CI)	Spec (95%CI)	Mea sure	Summar y of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Qua lity
11 studies (Bahl 2008; Chohan 2010; Coulthart 2011; Foutz 2017; Hamlin 2012;	4 × prospec tive;	3,	0.87	0.88	LR+	7.22 (4.34, 11.60)	Seri ous	Seri ous	Not seriou s	Not seriou s		LO W
Lattanzio 2017; Leitao 2016; Rohan 2015; Tagliapietra 2013; Van Everbroeck 2003; Van Everbroeck 2004)	7 × retrospe ctive	614	(0.84, 0.90)	(0.80, 0.93)	LR-	0.15 (0.12, 0.19)	Seri ous	Seri ous	Not seriou s	Not seriou s	-	LO W

#### Notes on risk of bias

Van Everbroeck 2004: > 10% population excluded from analysis

Bahl 2008: Exclusion of possible CJD group from index tests may inflate test sensitivity; test cut off not pre-specified

Chohan 2010: Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.

Coulthart 2011: Optimised threshold used to analyse Tau results; unclear whether the reference standards would correctly classify non-CJD cases as not specified; not downgraded for exclusions during data analysis as <10% population excluded.

Hamlin 2012: Multiple thresholds were tested and unclear whether researchers were blind to reference test results or that the reference test was interpreted without knowledge of index test.

Rohan 2015: It was unclear whether: a consecutive or random sample of patients was enrolled; the index test results were interpreted without knowledge of the results of the reference standard; a pre-specified cut-off was used for the index tests; the reference standard results were interpreted without knowledge of the index test results.

Leitao 2016: It was unclear whether: a consecutive or random sample of patients was enrolled; the study avoided inappropriate exclusions; test thresholds were pre-specified.

Lattanzio 2017: An optimised threshold was used for the assay.

### P.2.14.24 Total Tau and S100B

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	RE											
1 study (Chohan	Detropportive	251	0.50 (0.52, 0.65)	0.05 (0.00, 0.00)	LR+	11.34 (5.46, 23.53)	Serious	n/a	Not serious	Not serious		MODERATE
2010)	Retrospective	351	0.59 (0.52, 0.65)	0.95 (0.90, 0.98)	LR-	0.43 (0.37, 0.51)	Serious	n/a	Not serious	Serious	-	LOW

#### Notes on risk of bias

Chohan 2010: Subgroup analysis with >10% population excluded and in the included groups people are missing without explanation; it is unclear whether the reference and index tests were interpreted independently of each other.

### P.2.14.25 WHO CJD criteria

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE	<b>=</b>											
2 studies (Heath	2 ×	200	0.90 (0.85,	0.71 (0.61,	LR+	3.14 (2.29, 4.30)	V. serious	Not serious	Serious	Not serious		VERY LOW
2010; Zerr 2009)	retrospective	306	0.94)	0.79)	LR-	0.14 (0.09, 0.21)	V. serious	Not serious	Serious	Not serious	-	VERY LOW

#### Notes on risk of bias

Zerr 2009: Unclear whether patients were selected randomly or consecutively or whether inappropriate exclusions were avoided; the optimal index test thresholds were determined during the study and a subgroup analysis was used to determine test sensitivity and specificity.

Heath 2010: It was unclear whether the index test was interpreted without knowledge of the results of the reference test; whether a consecutive or random sample of patients was enrolled or inappropriate exclusions were avoided.

### Notes on indirectness

Heath 2010: Mean age at onset< 40 years old

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

### 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 (Calvin 2015)	Dragnastiva	150	0.04 (0.94, 0.09)	0.79 (0.60, 0.95)	LR+	4.29 (2.95, 6.24)	Serious	n/a	Not serious	Not serious		MODERATE
1 study (Galvin 2015)	Prospective	153	0.94 (0.84, 0.98)	0.78 (0.69, 0.85)	LR-	0.07 (0.02, 0.22)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of bias												

Notes on risk of bias

Galvin 2015: Subgroup analysis was carried out excluding >30% study population.

### P.2.15.2 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Droopootivo	270	0.42 (0.20, 0.57)	0.74 (0.65, 0.77)	LR+	1.48 (1.00, 2.19)	Serious	n/a	Not serious	Serious		LOW
(Koikkalainen 2016)	Prospective	210	0.43 (0.29, 0.57)	0.71 (0.65, 0.77)	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	Droopoetivo	139	0.42 (0.20, 0.57)	0.96 (0.77, 0.02)	LR+	3.01 (1.65, 5.51)	Serious	n/a	Not serious	Serious		LOW
(Koikkalainen 2016)	Prospective	139	0.43 (0.29, 0.57)	0.86 (0.77, 0.92)	LR-	0.67 (0.52, 0.87)	Serious	n/a	Not serious	Not serious	-	MODERATE

### Notes on risk of bias

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

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

# 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%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAME	RA											
1 study	Retrospective	23	0.95 (0.55, 1.00)	0.89 (0.61, 0.98)	LR+	8.91 (1.95, 40.64)	Serious	n/a	Not serious	Serious		LOW
(Walker 2009)	Reliospective	23	0.95 (0.55, 1.00)	0.69 (0.61, 0.96)	LR-	0.05 (0.00, 0.77)	Serious	n/a	Not serious	Serious	-	LOW
MULTIPLE CA	MERA											
2 studies	1x				LR+	15.40 (6.24, 38.01)	Serious	Not serious	Not serious	Not serious		MODERATE
(Kemp 2011; O'Brien 2009; Thomas 2017)	prospective, 2x retrospective	161	0.78 (0.59, 0.89)	0.95 (0.87, 0.98)	LR-	0.25 (0.13, 0.48)	Not serious	Serious	Not serious	Not serious	-	MODERATE
ALL EVIDENCE	POOLED											
3 studies					LR+	13.34 (6.14, 29.01)	Serious	Not serious	Not serious	Not serious		MODERATE
(Kemp 2011; O'Brien 2009; Walker 2009; Thomas 2017)	1x prospective, 2 × retrospective	184	0.83 (0.52, 0.96))	0.94 (0.86, 0.98)	LR-	0.22 (0.11, 0.44)	Not serious	Not serious	Not serious	Not serious	-	HIGH
Notes on risk o		led indivi	duals had a presume	ed dementia diagno	sis at baselir	ne						

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

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

1231-IIVII OI LOI												
Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA												
1 study (Sakamoto	Detroopediye	101	0.62 (0.42, 0.79)	0.75 (0.64, 0.93)	LR+	2.43 (1.48, 3.98)	Serious	n/a	Not serious	Serious		LOW
2014)	Retrospective	101	0.62 (0.42, 0.78)	0.75 (0.64, 0.83)	LR-	0.52 (0.31, 0.85)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of hige												

Notes on risk of bias

Sakamoto 2014: It was unclear whether the study avoided inappropriate exclusions or whether the reference standard results were interpreted without knowledge of the results of the index test.

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

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

Notes on risk of bias

Sakamoto 2014: It was unclear whether the study avoided inappropriate exclusions or whether the reference standard results were interpreted without knowledge of the results of the index test.

P.2.17.4 123I-MIBG cardiac scintigraphy

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
5 studies (Estorch 2008; Manabe 2017;	4 × prospective;		0.89 (0.81,	0.91 (0.82,	LR+	10.80 (4.89, 21.50)	Serious	Serious	Not serious	Not serious		LOW
Sakamoto 2014;	1 × retrospective	607	0.93)	0.96)	LR-	0.13 (0.07, 0.21)	V. serious	Not serious	Not serious	Not serious	-	LOW

### Notes on risk of bias

Estorch 2008: Significant proportion of people not given a final reference standard diagnosis

Sakamoto 2014: It was unclear whether the study avoided inappropriate exclusions or whether the reference standard results were interpreted without knowledge of the results of the index test. Slaets 2015: The diagnosing physicians were not blind to the index test results.

Manabe 2017: Optimised test cut-offs were calculated and it was unclear whether the reference standard was interpreted without knowledge of the results of the index test or the index test was interpreted without knowledge of the results of the reference test.

Sakamoto 2017: Selective reporting of sensitivity and specificity of outcome variables and it was unclear whether the index test results were interpreted without knowledge of the results of the reference standard; whether the reference standard results were interpreted without knowledge of the results of the index test or whether the test cut-off was pre-specified.

### P.2.17.5 EEG

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	nconsistency	ndirectness	Imprecision	Other considerations	Quality
SECONDARY CARE	233.9.1		(55,651)	(55,651)		(557651)	LE CONTRACTOR DE		=		0 3	<u> </u>
1 study (Engodel 2015)	Prospective	387	0.87 (0.50, 0.07)	0.88 (0.84, 0.01)	LR+	7.01 (5.01, 9.80)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Engedal 2015)	riospective	301	0.87 (0.59, 0.97)	0.88 (0.84, 0.91)	LR-	0.15 (0.04, 0.55)	Not serious	n/a	Not serious	Serious	-	MODERATE

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

### P.2.17.6 FDG-PET

Studies SECONDARY CARE	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
2 studies (Ossenkoppele	2 ×	255	0.53 (0.06,	0.97 (0.91,	LR+	19.64 (1.28, 301.23)	Serious	Serious	Serious	Serious		VERY LOW
2013; Panegyres 2009)	prospective	255	0.96)	0.99)	LR-	0.48 (0.11, 2.13)	Serious	Serious	Serious	V. serious	-	VERY LOW

### Notes on risk of bias

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

### Notes on indirectness

Panegyres 2009: The study only recruited people with early onset dementia (<65 years old). Ossenkoppele 2013: It is unclear whether the LeARN cohort consisted of people with suspected cognitive impairment.

#### MRI P.2.17.7

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen	Prospective	504	0.43 (0.20, 0.57)	0.76 (0.72, 0.80)	LR+	1.80 (1.24, 2.61)	Not serious	n/a	Not serious	Serious		MODERATE
2016)	Fiospective	504	0.43 (0.29, 0.57)	0.76 (0.72, 0.80)	LR-	0.75 (0.59, 0.97)	Not serious	n/a	Not serious	Not serious	-	HIGH

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Forman 2011)	Prophostivo	234	0.00 (0.82, 0.04)	0.72 (0.65, 0.90)	LR+	3.30 (2.49, 4.38)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Ferman 2011)	Prospective	234	0.90 (0.82, 0.94)	0.73 (0.65, 0.80)	LR-	0.14 (0.08, 0.25)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Forman 2011)	Dragnastiva	224	0.05 (0.76, 0.04)	0.72 (0.65, 0.90)	LR+	3.11 (2.34, 4.15)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Ferman 2011)	Prospective	234	0.85 (0.76, 0.91)	0.73 (0.65, 0.80)	LR-	0.21 (0.13, 0.34)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Forman 2011)	Droopoetiyo	224	0.02 (0.74, 0.00)	0.05 (0.77, 0.00)	LR+	5.35 (3.58, 8.01)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Ferman 2011)	Prospective	234	0.83 (0.74, 0.89)	0.85 (0.77, 0.90)	LR-	0.21 (0.13, 0.32)	Not serious	n/a	Not serious	Not serious	-	HIGH

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Forman 2011)	Droopoetivo	234	0.00 (0.00 0.03)	0.72 (0.65, 0.90)	LR+	3.23 (2.43, 4.29)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Ferman 2011)	Prospective	234	0.88 (0.80, 0.93)	0.73 (0.65, 0.80)	LR-	0.17 (0.10, 0.29)	Not serious	n/a	Not serious	Not serious	-	HIGH

# P.2.18 DLB versus other dementias

# P.2.18.1 123I-FP-CIT SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAME	RA											
1 study	Prospective	31	0.90 (0.68, 0.97)	0.91 (0.56, 0.99)	LR+	9.90 (1.52, 64.52)	Not serious	n/a	Not serious	Serious		MODERATE
(Treglia 2012)	Frospective	31	0.90 (0.08, 0.97)	0.91 (0.30, 0.99)	LR-	0.11 (0.03, 0.42)	Not serious	n/a	Not serious	Not serious	-	HIGH
MULTIPLE CAN	MERA											
1 study	Detroopeding	20	0.02 (0.40, 0.07)	0.00 (0.00 4.00)	LR+	21.67 (1.43, 333.42)	Not serious	n/a	Not serious	Serious		MODERATE
(Walker 2007)	Retrospective	20	0.83 (0.46, 0.97)	0.96 (0.60, 1.00)	LR-	0.17 (0.04, 0.75)	Not serious	n/a	Not serious	Serious	-	MODERATE
ALL EVIDENCE	E POOLED											
2 studies	1 ×				LR+	12.72 (2.71, 59.68)	Not serious	Not serious	Not serious	Not serious		HIGH
(Treglia 2012; Walker 2007)	prospective; 1 × retrospective	51	0.88 (0.70, 0.96)	0.93 (0.72 0.99)	LR-	0.14 (0.05, 0.36)	Not serious	Not serious	Not serious	Not serious	-	HIGH
Notes on risk of Treglia 2012: Sp		ed as the	e reference standard	not reported								

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

P.2.18.2 123I-MIBG cardiac scintigraphy

1251-WIBO cardi	ao comagi	шрпу										
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Tradia 2012)	Droopoetiyo	24	0.00 (0.69, 0.07)	0.04 (0.56, 0.00)	LR+	9.90 (1.52, 64.52)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Treglia 2012)	Prospective	31	0.90 (0.68, 0.97)	0.91 (0.56, 0.99)	LR-	0.11 (0.03, 0.42)	Not serious	n/a	Not serious	Not serious	-	HIGH
Notes on risk of bias												
Treglia 2012: Specific c	riteria used as t	he refere	nce standard not rep	ported								

# P.2.18.3 DLB consensus criteria

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skogseth	Droopoetiyo	EE	0.90 (0.57, 0.03)	0.90 (0.74, 0.06)	LR+	7.20 (2.79, 18.61)	Serious	n/a	Not serious	Not serious		HIGH
2017)	Prospective	55	0.80 (0.57, 0.92)	0.89 (0.74, 0.96)	LR-	0.23 (0.09, 0.54)	Serious	n/a	Not serious	Serious	-	LOW

### P.2.18.4 FDG-PET

150121									i			
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Ossenkoppele 2013)	Prospective	98	0.20 (0.03, 0.69)	0.95 (0.88, 0.98)	LR+	3.72 (0.53, 26.13)	V. serious	n/a	Serious	Serious	-	VERY LOW
					LR-	0.85 (0.54, 1.31)	V. serious	n/a	Serious	Not serious		VERY LOW

#### Notes on risk of bias

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

#### Notes on indirectness

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

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

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

Galvin 2015: Subgroup analysis was carried out excluding >30% study population.

### P.2.18.6 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Drooppotive	206	0.43 (0.29,	0.76 (0.72,	LR+	1.80 (1.23, 2.65)	Serious	n/a	Not serious	Serious		LOW
(Koikkalainen 2016)	Prospective	386	0.57)	0.81)	LR-	0.75 (0.58, 0.97)	Serious	n/a	Not serious	Not serious	-	MODERATE

### Notes on risk of bias

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

## P.2.19 DLB versus VaD

### P.2.19.1 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Prospective 71 0.4	0.42 (0.20, 0.57)	0.00 (0.60, 0.06)	LR+	3.40 (1.12, 10.32)	Serious	n/a	Not serious	Serious		LOW	
(Koikkalainen 2016)	Prospective	71	0.43 (0.29, 0.57)	0.88 (0.68, 0.96)	LR-	0.66 (0.49, 0.88)	Serious	n/a	Not serious	Serious	-	LOW

#### Notes on risk of bias

# P.2.20 FTD versus AD

## P.2.20.1 99mTc-HMPAO SPECT

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

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

### Dementia

Appendix P: Diagnosis evidence tables & GRADE

		Tota I	Sens	Spec	Measu	Summary of findings	Risk of bias	consistency	directness	precision	Other considerations	
Studies	Design	N	(95%CI)	(95%CI)	re	(95%CI)	涩	Ĕ	Ĕ	트	58	Quality

#### Notes on risk of bias

Launes 1991: Subgroup analysis used with >10% study population excluded.

Read 1995: Subgroup analysis used with >10% study population excluded; unclear whether random or consecutive patient enrolment was used; unclear if inappropriate exclusions avoided. Velakoulis 1997: Subgroup analysis where >10% study population excluded and it was unclear whether: the index test results were interpreted without knowledge of the results of the reference standard; the index test threshold was pre-specified or the reference standard results interpreted without knowledge of the results of the index test.

Talbot 1998: Unclear if avoided inappropriate exclusions; unclear whether the reference standard results were interpreted without knowledge of the index test and whether the index test was carried out without knowledge of reference test result; no pre-specified index test threshold; subgroup analysis used with >10% study population excluded.

Boutoleau-Bretonnière 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	Dragnastina	245	0.50 (0.40, 0.60)	0.70 (0.00 0.70)	LR+	1.80 (1.34, 2.41)	Serious	n/a	Not serious	Serious		LOW
(Koikkalainen 2016)	Prospective	315	0.50 (0.40, 0.60)	0.72 (0.66, 0.78)	LR-	0.69 (0.56, 0.86)	Serious	n/a	Not serious	Not serious	-	MODERATE

#### Notes on risk of bias

### 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	Propostivo	23	0.24 (0.17, 0.57)	0.02 (0.38, 0.00)	LR+	4.11 (0.27, 62.70)	V. serious	n/a	Serious	V. serious		VERY LOW
(Ossenkoppele 2013)	Prospective	23	0.34 (0.17, 0.57)	0.92 (0.38, 0.99)	LR-	0.72 (0.48, 1.08)	V. serious	n/a	Serious	Serious	-	VERY LOW

#### Notes on risk of bias

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

#### Notes on indirectness

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

### P.2.20.5 MRI

IALLZI												
Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Prospective	139	0.50 (0.40, 0.60)	0.94 (0.82, 0.98)	LR+	7.83 (2.57, 23.86)	Serious	n/a	Not serious	Not serious	-	MODERATE
(Koikkalainen 2016)	·		,	, , , ,	LR-	0.53 (0.43, 0.66)	Serious	n/a	Not serious	Serious		LOW

### Notes on risk of bias

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

### P.2.21.1 99mTc-HMPAO SPECT

Studies MULTIPLE CAMERA	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
MULTIPLE CAMERA												
1 study (Boutoleau-	utoleau- 2012) Prospective	56	0.72 (0.44, 0.04)	0.79 (0.62, 0.99)	LR+	3.27 (1.70, 6.30)	Serious	n/a	Not serious	Serious		LOW
Bretonniere 2012)	riospective	50	0.73 (0.41, 0.91)	0.78 (0.63, 0.88)	LR-	0.35 (0.13, 0.93)	Serious	n/a	Not serious	Serious	-	LOW

### Notes on risk of bias

Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used but <10% study population discarded

## P.2.22 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Boutoleau-	Droopoetiyo	EG	0.19 (0.05, 0.51)	0.60 (0.47, 0.75)	LR+	0.48 (0.13, 1.78)	Serious	n/a	Not serious	Serious		LOW
Bretonniere 2012)	Prospective	56	0.18 (0.05, 0.51)	0.62 (0.47, 0.75)	LR-	1.31 (0.92, 1.88)	Serious	n/a	Not serious	Not serious	-	MODERATE

### Notes on risk of bias

Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases.

## P.2.23 FTD versus non-FTD

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

Studies MULTIPLE CAMERA	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
1 study (Tripathi	Dragnactive	117	0.06 (0.79, 0.00)	0.00 (0.03, 1.00)	LR+	86.67 (12.32, 609.43)	Serious	n/a	Not serious	Not serious		MODERATE
2010)	Prospective	117	0.96 (0.78, 0.99)	0.99 (0.93, 1.00)	LR-	0.04 (0.01, 0.26)	Serious	n/a	Not serious	Not serious	-	MODERATE

#### Notes on risk of bias

Tripathi 2010: 14% of participants were lost to follow up and did not receive a reference standard; it is unclear whether the index test was interpreted without knowledge of the reference standard.

## P.2.23.2 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA									•			
	2 × prospective				LR+	6.05 (2.77, 13.22)	V. serious	Not serious	Not serious	Not serious		LOW
3 studies (Launes 1991; Read 1995; Talbot 1998)	; 1 × retrospectiv e	501	0.51 (0.20, 0.81)	0.93 (0.90, 0.95)	LR-	0.63 (0.40, 1.01)	V. serious	Not serious	Not serious	Serious	-	VERY LOW
MULTIPLE CAMERA												
	1 × prospective				LR+	7.88 (1.14, 54.71)	Serious	Serious	Not serious	Serious		VERY LOW
2 studies (Boutoleau-Bretonniere 2012; Rollin-Sillaire 2012)	; 1 × retrospectiv e	108	0.74 (0.53, 0.88)	0.90 (0.53, 0.99)	LR-	0.30 (0.15, 0.59)	Serious	Not serious	Not serious	Serious	-	LOW
ALL EVIDENCE POOLED												
5 studies (Boutoleau-Bretonniere 2012)	3 × prospective				LR+	7.03 (3.36, 13.10)	V. serious	Not serious	Not serious	Not serious		LOW
studies (Boutoleau-Bretonniere 2012; aunes 1991; Read 1995; Rollin-Sillaire 012; Talbot 1998)	; 2 × retrospectiv e	609	0.59 (0.37, 0.78)	0.91 (0.84, 0.95)	LR-	0.46 (0.24, 0.69)	V. serious	Serious	Not serious	Serious	-	VERY LOW

### Notes on risk of bias

Talbot 1998: Unclear if avoided inappropriate exclusions; unclear whether the reference standard results were interpreted without knowledge of the index test and whether the index test was carried out without knowledge of reference test result; no pre-specified index test threshold; subgroup analysis used as data on 'other' clinical diagnosis group is not reported.

Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

#### SPECT/PET P.2.23.3

OI LO 1/1 L 1												
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
1 study (Mandaz 2007)	Droopostivo	124	0.00 (0.90, 0.06)	0.75 (0.62, 0.82)	LR+	3.57 (2.38, 5.36)	Not serious	n/a	Serious	Not serious		HIGH
1 study (Mendez 2007)	Prospective	134	0.90 (0.80, 0.96)	0.75 (0.63, 0.83)	LR-	0.13 (0.06, 0.28)	Not serious	n/a	Serious	Not serious	-	HIGH

### P.2.23.4 FDG-PET

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
2 studies (Ossenkoppele	2 ×	255	0.43 (0.25,	0.93 (0.87,	LR+	6.20 (2.12, 18.11)	Seriou s	Serious	Seriou s	Not serious		VERY LOW
	prospective	200	0.63)	0.96)	LR-	0.63 (0.43, 0.92)	Seriou s	Not serious	Seriou s	Serious	-	VERY LOW

### Notes on risk of bias

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

### Notes on indirectness

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

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

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

## 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												
	Detroppostive	134	0.27 (0.26, 0.40)	0.00 (0.00, 1.00)	LR+	52.88 (3.28, 853.00)	Not serious	n/a	Not serious	Not serious		HIGH
1 study (Mendez 2007)	Retrospective	134	0.37 (0.26, 0.49)	0.99 (0.90, 1.00)	LR-	0.64 (0.53, 0.77)	Not serious	n/a	Not serious	Not serious	-	HIGH

# P.2.23.6 MRI

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

## P.2.24 FTD versus other dementias

### P.2.24.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
1 study	fudv	0.56 (0.35, 0.93)	0.06 (0.76, 0.00)	LR+	13.33 (1.79, 99.08)	V. serious	n/a	Not serious	Serious		VERY LOW	
(Velakoulis 1997)	Frospective	33	0.56 (0.25, 0.82)	0.96 (0.76, 0.99)	LR-	0.46 (0.22, 0.97)	V. serious	n/a	Not serious	Serious		VERY LOW

### Notes on risk of bias

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

## P.2.24.2 FDG-PET

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE					·		•	·	•	·		
studies (Arslan 2015; Ossenkoppele 2013)	1 × prospective;	440	0.40 (0.25,	0.78 (0.49,	LR+	1.78 (0.91, 3.51)	V. serious	Not serious	Serious	Serious		VERY LOW
	1 × retrospective	146	0.57)	0.93)	LR-	0.78 (0.59, 1.03)	V. serious	Not serious	Serious	Not serious	-	VERY LOW

### Notes on risk of bias

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

Arslan 2015: Unclear whether: a consecutive or random sample of eligible patients was enrolled and inappropriate exclusions were avoided; the index test was interpreted without knowledge of the reference standard and if the imaging patterns were pre-specified; the reference standard results were interpreted independently of the index test results.

### Notes on indirectness

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

## P.2.24.3 FTD scale (≥6)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Custofoon 2010)	Droopoetiyo	100	0.02 (0.94, 0.07)	0.02 (0.96.0.06)	LR+	11.58 (6.53, 20.52)	Not serious	n/a	Not serious	Not serious		HIGH	
1 study (Gustafson 2010)	Prospective	190	0.92 (0.81, 0.97)	0.92 (0.86, 0.96)	LR-	0.08 (0.03, 0.21)	Not serious	n/a	Not serious	Not serious	-	HIGH	
Notes on risk of bias Gustafson 2010: The study													

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

## P.2.24.4 MRI

Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
Prognactive	206	0.50 (0.40, 0.60)	0.79 (0.72, 0.92)	LR+	2.23 (1.66, 2.99)	Serious	n/a	Not serious	Serious		LOW
Frospective	300	0.50 (0.40, 0.60)	0.76 (0.72, 0.62)	LR-	0.64 (0.52, 0.80)	Serious	n/a	Not serious	Not serious	-	MODERATE
		Design N	Design N (95%CI)	Design N (95%CI) (95%CI)	Design         N         (95%CI)         (95%CI)         Measure           Prospective         386         0.50 (0.40, 0.60)         0.78 (0.72, 0.82)         LR+	Design         Total N         Sens (95%CI)         Spec (95%CI)         Measure         of findings (95%CI)           Prospective         386         0.50 (0.40, 0.60)         0.78 (0.72, 0.82)         LR+         2.23 (1.66, 2.99)	Design   Total   Sens (95%CI)   Spec (95%CI)   Measure   Summary of findings (95%CI)   Serious	Design   Total   Sens (95%CI)   Spec (95%CI)   Measure   Summary of findings (95%CI)   Serious   N/a	Total N   Sens (95%Cl)   Spec (95%Cl)   Measure   Summary of findings (95%Cl)   Serious   Not serious	Design   Total   Sens (95%CI)   Spec (95%CI)   Measure   Summary of findings (95%CI)   Serious   Serious	Design   Total   Sens (95%CI)   Spec (95%CI)   Measure   Summary of findings (95%CI)   Serious   Serious

### Notes on risk of bias

### P.2.25 FTD versus VaD

### P.2.25.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measur e	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
2 studies (Launes 1991; Talbot	2 ×	196	0.46 (0.36,	0.85 (0.51,	LR+	2.58 (0.77, 8.64)	V. serious	Serious	Not serious	Serious		VERY LOW
1998)	prospective	190	0.57)	0.97)	LR-	0.72 (0.58, 0.91)	V. serious	Not serious	Not serious	Not serious	-	LOW
MULTIPLE CAMERA												
1 study (Boutoleau-Bretonniere	Dunnanativa	10	0.73 (0.41,	0.75 (0.38,	LR+	2.91 (0.83, 10.19)	V. serious	n/a	Not serious	Serious		VERY LOW
2012)	Prospective	19	0.91)	0.94)	LR-	0.36 (0.13, 1.03)	V. serious	n/a	Not serious	Serious	-	VERY LOW
ALL EVIDENCE POOLED												
3 studies (Boutoleau-	3 ×	215	0.51 (0.35,	0.82 (0.61,	LR+	2.23 (1.20, 4.16)	V. serious	Not serious	Not serious	Serious		VERY LOW
Bretonniere 2012; Launes 1991; Talbot 1998)	prospective	213	0.67)	0.93)	LR-	0.70 (0.56, 0.88)	V. serious	Not serious	Not serious	Not serious	-	LOW

### Notes on risk of bias

Launes 1991: Subgroup analysis used with >10% study population excluded.

Talbot 1998: Unclear if avoided inappropriate exclusions; unclear whether the reference standard results were interpreted without knowledge of the index test and whether the index test was carried out without knowledge of reference test result; no pre-specified index test threshold; subgroup analysis used with >10% study population excluded.

Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases; subgroup analysis used with >10% study population discarded.

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

### P.2.25.2 MRI

Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE												
Droopoetiyo	116	0.50 (0.40, 0.60)	0.06 (0.76, 0.00)	LR+	12.00 (1.74, 82.64)	Serious	n/a	Not serious	Serious		LOW	
Fiospective	110	0.50 (0.40, 0.60)	0.90 (0.76, 0.99)	LR-	0.52 (0.42, 0.65)	Serious	n/a	Not serious	Serious	-	LOW	
	<b>Design</b> Prospective	Design N	Design N (95%CI)	Design N (95%CI) (95 <sup>*</sup> %CI)	Design         N         (95%CI)         (95%CI)         Measure           Prospective         116         0.50 (0.40, 0.60)         0.96 (0.76, 0.99)	Design         Total N         Sens (95%CI)         Spec (95%CI)         Measure         of findings (95%CI)           Prospective         116         0.50 (0.40, 0.60)         0.96 (0.76, 0.99)         LR+         12.00 (1.74, 82.64)	Total N   Sens (95%CI)   Spec (95%CI)   Measure   Summary of findings (95%CI)   Serious	Design   Total   Sens (95%CI)   Spec (95%CI)   Measure   Of findings (95%CI)   Serious   Design   Total   N (95%CI)   Serious   N (95%CI)   Design   N (95%CI)   N (95%CI)   Design   N (95%CI)   De	Design   Total N   Sens (95%CI)   Spec (95%CI)   Measure   Of findings (95%CI)   Of fi	Total N   Sens (95%CI)   Spec (95%CI)   Measure   Of findings (95%CI)   Measure   Of findings (95%CI)   Measure   Of findings (95%CI)   Measure   Of findings (95%CI)   Of fin	Prospective 116 0.50 (0.40, 0.60) 0.96 (0.76, 0.99) LR+ 12.00 (1.74, 82.64) Serious n/a Not serious Serious -	

### Notes on risk of bias

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

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

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Clannor 2000)	Dragnactive	33	0.46 (0.22, 0.72)	0.90 (0.57, 0.03)	LR+	2.31 (0.80, 6.63)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Skinner 2009)	Prospective	33	0.46 (0.22, 0.72)	0.80 (0.57, 0.92)	LR-	0.67 (0.39, 1.17)	Not serious	n/a	Not serious	Serious	-	MODERATE

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

Til V dellielitia 3ca	()											
Studies	Design	Total 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 atualis (Claiman 2000)	Description	22	0.00 (0.04, 0.00)	0.00 (0.57, 0.00)	LR+	3.08 (1.16, 8.17)	Serious	n/a	Not serious	Serious		LOW
1 study (Skinner 2009)	Prospective	33	0.62 (0.34, 0.83)	0.80 (0.57, 0.92)	LR-	0.48 (0.23, 0.99)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of bias Skinner 2009: Use of an o	optimised thresho	ıld.										

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Skinner 2000)	Droopoetiyo	33	0.77 (0.49, 0.02)	0.65 (0.42, 0.92)	LR+	2.20 (1.13, 4.28)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Skinner 2009)	Prospective	33	0.77 (0.48, 0.92)	0.65 (0.43, 0.82)	LR-	0.36 (0.13, 1.01)	Not serious	n/a	Not serious	Serious	-	MODERATE

## P.2.26.4 Grooved pegboard test

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

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

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

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

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
	Dragnostivo	AEE	0.77 (0.70, 0.92)	0.40 (0.35, 0.45)	LR+	1.28 (1.13, 1.46)	Serious	n/a	Serious	Not serious		LOW
1 study (Davis 2002)	Prospective	455	0.77 (0.70, 0.83)	0.40 (0.35, 0.45)	LR-	0.57 (0.41, 0.80)	Serious	n/a	Serious	Serious	-	VERY LOW

# P.2.27 Neurosyphilis versus not neurosyphilis

## P.2.27.1 CSF EIA

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
1 atudy (Chan 2011)	Dragnastiva	4E	0.07 (0.69. 1.00)	0.47 (0.20, 0.64)	LR+	1.82 (1.28, 2.58)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Chan 2014) F	Prospective	45	0.97 (0.68, 1.00)	0.47 (0.30, 0.64)	LR-	0.06 (0.00, 0.94)	Not serious	n/a	Not serious	Serious	-	MODERATE

# P.2.27.2 FTA-ABS

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
4 study (Durasana 2010)	Datasasastina	400	0.07 (0.05, 4.00)	0.44 (0.00, 0.00)	LR+	1.09 (0.97, 1.22)	Not serious	n/a	Serious	Not serious		MODERATE	
1 study (Dumaresq 2013)	Retrospective	100	0.97 (0.65, 1.00)	0.11 (0.06, 0.20)	LR-	0.28 (0.02, 4.62)	Not serious	n/a	Serious	V. serious	-	VERY LOW	
Notes on indirectness Dumaresq 2013: >99% men	Notes on indirectness  Dumaresq 2013: >99% men who have sex with men												

# P.2.27.3 INNO-LIA

ININO-LIA												
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE							•					
4 -tudy (Dumanaa 2012)	Detuces estive	00	0.00 (0.00 4.00)	0.40 (0.00 0.04)	LR+	1.09 (0.95, 1.25)	Not serious	n/a	Serious	Not serious		MODERATE
1 study (Dumaresq 2013)	Retrospective	83	0.96 (0.60, 1.00)	0.12 (0.06, 0.21)	LR-	0.33 (0.02, 5.31)	Not serious	n/a	Serious	V. serious	-	VERY LOW
Notes on indirectness												
Dumaresq 2013: >99% me	n who have sex w	ith men										

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality		
SECONDARY CARE														
1 study (Dumarasa 2012)	Detroopediye	100	0.40 (0.10, 0.65)	0.64 (0.54, 0.74)	LR+	1.03 (0.53, 2.02)	Not serious	n/a	Serious	Serious		LOW		
1 study (Dumaresq 2013)	Retrospective	108	0.40 (0.19, 0.65)	0.61 (0.51, 0.71)	LR-	0.98 (0.63, 1.53)	Not serious	n/a	Serious	Not serious	-	MODERATE		
Notes on indirectness Dumaresq 2013: >99% me														

## P.2.27.5 TPPA

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 atd. (Dumanaa 2042)	Detrees estive	100	0.07 (0.44, 0.05)	0.47 (0.07, 0.50)	LR+	1.26 (0.84, 1.90)	Not serious	n/a	Serious	Not serious		MODERATE
1 study (Dumaresq 2013)	Retrospective	100	0.67 (0.41, 0.85)	0.47 (0.37, 0.58)	LR-	0.71 (0.33, 1.50)	Not serious	n/a	Serious	Serious	-	LOW
Notes on indirectness  Dumaresq 2013: >99% men who have sex with men												

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

## P.2.28 PDD and DLB versus other dementias

P.2.28.1 123I-MIBG cardiac scintigraphy

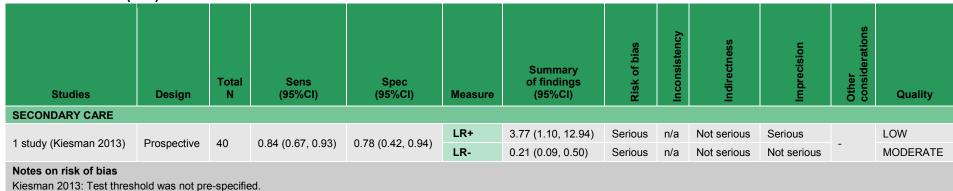
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CA	ARE											
1 study (Hanyu	Droopoetiyo	96	0.05 (0.93, 0.00)	0.87 (0.76, 0.94)	LR+	7.47 (3.73, 14.98)	Serious	n/a	Not serious	Not serious		MODERATE
2006)		90	0.95 (0.82, 0.99)	0.87 (0.76, 0.94)	LR-	0.06 (0.01, 0.22)	Serious	n/a	Not serious	Not serious	-	MODERATE

### Notes on risk of bias

Hanyu 2006: It was unclear whether the index test results were interpreted without knowledge of the results of the reference standard and whether the reference standard results were interpreted without knowledge of the results of the index test.

## P.2.29 PDD versus non-PDD

## P.2.29.1 FCSRT-IR 3- FR (≤22)



<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
4 atudu (Kiaaman 2042)	Description	40	0.00 (0.00, 0.00)	0.05 (0.52, 4.00)	LR+	15.94 (1.06, 238.88)	Serious	n/a	Not serious	Serious		LOW
1 study (Kiesman 2013)	Prospective	40	0.80 (0.62, 0.90)	0.95 (0.53, 1.00)	LR-	0.21 (0.11, 0.43)	Serious	n/a	Not serious	Not serious	-	MODERATE
Notes on risk of bias Kiesman 2013: Test thres	hold was not pr	e-specifi	ed.									

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

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality		
SECONDARY CARE					•		•							
4 - 1 - 1 - (16 0040)	Description	40	0.04 (0.70, 0.00)	0.70 (0.40, 0.04)	LR+	4.21 (1.24, 14.34)	Serious	n/a	Not serious	Serious		LOW		
1 study (Kiesman 2013)	Prospective	40	0.94 (0.78, 0.98)	0.78 (0.42, 0.94)	LR-	0.08 (0.02, 0.33)	Serious	n/a	Not serious	Not serious	-	MODERATE		
Notes on risk of bias Kiesman 2013: Test thres														

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Kissman 2012)	Droopoetivo	40	0.09 (0.70, 4.00)	0.45 (0.40, 0.74)	LR+	1.79 (1.02, 3.14)	Serious	n/a	Not serious	Serious		LOW
1 study (Kiesman 2013)	Prospective	40	0.98 (0.79, 1.00)	0.45 (0.19, 0.74)	LR-	0.03 (0.00, 0.59)	Serious	n/a	Not serious	Serious	-	LOW
Notes on risk of bias Kiesman 2013: Test thresh	old was not pre-s	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 (Kisaman 2012)	Droopostivo	40	0.00 (0.74, 0.07)	0.79 (0.42, 0.04)	LR+	4.06 (1.19, 13.87)	Serious	n/a	Not serious	Serious		LOW	
1 study (Kiesman 2013)	Prospective	40	0.90 (0.74, 0.97)	0.78 (0.42, 0.94)	LR-	0.12 (0.04, 0.39)	Serious	n/a	Not serious	Not serious	-	MODERATE	
Notes on risk of bias Kiesman 2013: Test thres	Notes on risk of bias Kiesman 2013: Test threshold was not pre-specified.												

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

## P.2.30 PPA versus non-PPA

### P.2.30.1 FDG-PET

Studies SECONDARY CARE	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
A study (December 2000)	Danagativa	400	0.50 (0.40, 0.04)	0.00 (0.00 4.00)	LR+	97.00 (5.54, 1697.47)	Not serious	n/a	Serious	Not serious		MODERATE
1 study (Panegyres 2009)	Prospective	102	0.50 (0.19, 0.81) 0.99 (0.92, 1.00)		LR-	0.50 (0.24, 1.05)	Not serious	n/a	Serious	Serious	-	LOW
Notes on indirectness												

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

## P.2.31 VaD and mixed dementias versus AD

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

Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
RE											
Dragnostiva	214	0.96 (0.77, 0.02)	0.73 (0.65, 0.90)	LR+	3.17 (2.36, 4.25)	V. serious	n/a	Not serious	Not serious		LOW
study (Siritho 006) Prospective 214	0.00 (0.77, 0.92)	0.73 (0.05, 0.80)	LR-	0.19 (0.11, 0.33)	V. serious	n/a	Not serious	Not serious	-	LOW	
F	RE	Design N RE Prospective 214	Design         N         (95%CI)           RE         Prospective         214         0.86 (0.77, 0.92)	Design         N         (95%CI)         (95%CI)           RE           Prospective         214         0.86 (0.77, 0.92)         0.73 (0.65, 0.80)	Design         N         (95%CI)         Measure           RE         Prospective         214         0.86 (0.77, 0.92)         0.73 (0.65, 0.80)         LR+           LR-         LR-         LR-	Design         Total N         Sens (95%CI)         Spec (95%CI)         Measure         of findings (95%CI)           RE           Prospective         214         0.86 (0.77, 0.92)         0.73 (0.65, 0.80)         LR+ 3.17 (2.36, 4.25)         LR- 0.19 (0.11, 0.33)	Design         Total N         Sens (95%CI)         Spec (95%CI)         Measure         Summary of findings (95%CI)         5 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	Total N   Sens (95%CI)   Spec (95%CI)   Measure   Summary of findings (95%CI)   Summary of fin	Total N   Sens (95%Cl)   Spec (95%Cl)   Measure   Summary of findings (95%Cl)   Sign of findings (95	Total N   Sens (95%CI)   Spec (95%CI)   Measure   Summary of findings (95%CI)   Summary of fin	Prospective 214 0.86 (0.77, 0.92) 0.73 (0.65, 0.80)

#### 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.

© NICE 2018. All rights reserved. See Notice of rights.

# 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%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Cold 2002)	Detropportive	00	0.70 (0.47, 0.96)	0.79 (0.67, 0.96)	LR+	3.22 (1.89, 5.48)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Gold 2002)	Retrospective	89	0.70 (0.47, 0.86)	0.78 (0.67, 0.86)	LR-	0.38 (0.19, 0.76)	Not serious	n/a	Not serious	Serious	-	MODERATE

# P.2.32.2 ADDTC (probable)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Cald 2002)	Potropoetivo	89	0.25 (0.11, 0.48)	0.91 (0.82, 0.96)	LR+	2.88 (0.98, 8.44)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Gold 2002)	Retrospective	09	0.23 (0.11, 0.46)	0.91 (0.62, 0.96)	LR-	0.82 (0.63, 1.07)	Not serious	n/a	Not serious	Not serious	-	HIGH

## P.2.32.3 ADDTC criteria

ABB 10 criteria			1									
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 -tudy (Db-tt- 2007)	Detuces estive	110	0.50 (0.40, 0.70)	0.74 (0.02, 0.02)	LR+	2.27 (1.41, 3.66)	Not serious	n/a	Serious	Serious		LOW
1 study (Bachetta 2007)	Retrospective	110	0.58 (0.42, 0.73)	0.74 (0.63, 0.83)	LR-	0.56 (0.37, 0.84)	Not serious	n/a	Serious	Serious	-	LOW
Notes on indirectness												
Bachetta 2007: Participant	s were selected to	be >90 ye	ears old									

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

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 study (Bashetta 2007)	Detroppostive	110	0.56 (0.30, 0.71)	0.66 (0.55, 0.76)	LR+	1.64 (1.07, 2.53)	Not serious	n/a	Serious	Serious		LOW	
1 study (Bachetta 2007)	Retrospective	110	0.56 (0.39, 0.71)	0.66 (0.55, 0.76)	LR-	0.67 (0.45, 1.00)	Not serious	n/a	Serious	Serious	-	LOW	
Notes on indirectness Bachetta 2007: Participants	Notes on indirectness Bachetta 2007: Participants were selected to be >90 years old												

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

## P.2.32.5 NINDS-AIREN (possible)

Studies	Design	Total N	Sens (95%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 atudy (Cold 2002)		90	0.55 (0.24, 0.75)	0.04 (0.72, 0.04)	LR+	3.45 (1.76, 6.75)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Gold 2002)	Retrospective	89	0.55 (0.34, 0.75)	0.84 (0.73, 0.91)	LR-	0.54 (0.33, 0.88)	Not serious	n/a	Not serious	Serious	-	MODERATE

# P.2.32.6 NINDS-AIREN (probable)

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
	Detroppositive	90	0.20 (0.09, 0.42)	0.03 (0.04, 0.07)	LR+	2.76 (0.82, 9.32)	Not serious	n/a	Not serious	Serious		MODERATE
1 study (Gold 2002)	Retrospective	89	0.20 (0.08, 0.43)	0.93 (0.84, 0.97)	LR-	0.86 (0.69, 1.08)	Not serious	n/a	Not serious	Not serious	-	HIGH

## P.2.32.7 NINDS-AIREN criteria

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SECONDARY CARE													
1 atudy (Pachatta 2007)	Potroppostivo	110	0.56 (0.39, 0.71)	0.72 (0.62, 0.92)	LR+	2.06 (1.28, 3.31)	Not serious	n/a	Serious	Serious		LOW	
1 study (Bachetta 2007)	Retrospective	110	0.56 (0.59, 0.71)	0.73 (0.62, 0.82)	LR-	0.61 (0.41, 0.90)	Not serious	n/a	Serious	Serious	-	LOW	
Notes on indirectness Bachetta 2007: Participant	lotes on indirectness achetta 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%Cl)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality	
SINGLE CAMERA													
2 studies (Launes 1991;	2 ×	97	0.70 (0.00 0.07)	0.77 (0.04, 0.00)	LR+	3.21 (1.90, 5.43)	Serious	Not serious	Not serious	Serious		LOW	
McMurdo 1994)	prospective	97	0.76 (0.60, 0.87)	0.77 (0.64, 0.86)	LR-	0.33 (0.18, 0.60)	Serious	Not serious	Not serious	Serious	-	LOW	
0 ,	7 Cost (0.10, 0.00) Serious Not serious Serious EOW												

<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

### P.2.33.2 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Prospective	247	0.71 (0.50,	0.97 (0.94,	LR+	22.57 (10.42, 48.88)	Serious	n/a	Not serious	Not serious	-	MODERATE
(Koikkalainen 2016)	,		0.85)	0.98)	LR-	0.30 (0.16, 0.56)	Serious	n/a	Not serious	Serious		LOW

#### Notes on risk of bias

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

## P.2.34 VaD versus DLB

### P.2.34.1 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Prospective	71	0.71 (0.50, 0.85)	0.96 (0.85, 0.99)	LR+	16.65 (4.19, 66.18)	Serious	n/a	Not serious	Not serious	_	MODERATE
(Koikkalainen 2016)	·				LR-	0.30 (0.16, 0.57)	Serious	n/a	Not serious	Serious		LOW

#### Notes on risk of bias

## P.2.35 VaD versus FTD

### P.2.35.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
atudy (Lauras 1001)	Dragnastiva	38	0.76 (0.59, 0.97)	0.60 (0.30, 0.00)	LR+	1.89 (0.64, 5.64)	Serious	n/a	Not serious	Serious		LOW
1 study (Launes 1991)	Prospective	30	0.76 (0.58, 0.87)	0.60 (0.20, 0.90)	LR-	0.40 (0.16, 1.03)	Serious	n/a	Not serious	Serious	-	LOW

### Notes on risk of bias

Launes 1991: Subgroup analysis used with >10% study population excluded.

### P.2.35.2 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Prospective	116	0.71 (0.50, 0.85)	0.96 (0.89, 0.98)	LR+	16.29 (6.04, 43.94)	Serious	n/a	Not serious	Not serious	_	MODERATE
(Koikkalainen 2016)					LR-	0.30 (0.16, 0.57)	Serious	n/a	Not serious	Serious		LOW

#### Notes on risk of bias

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

### P.2.36.1 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
PRIMARY CARE												
1 study (Boutoleau-	Prospective	56	0.88 (0.46, 0.98)	0.75 (0.61, 0.85)	LR+	3.50 (2.01, 6.10)	Serious	n/a	Not serious	Not serious		MODERATE
Bretonniere 2012)	Prospective	30	0.66 (0.46, 0.96)	0.75 (0.61, 0.65)	LR-	0.17 (0.03, 1.05)	Serious	n/a	Not serious	Serious	-	LOW

### Notes on risk of bias

Boutoleau-Bretonniere 2012: Loss to follow up of 6/69 patients; unclear about consecutive versus random enrolment of patients; reference diagnosis made at 24 month follow up with index tests carried out at baseline and again at 24 months in some cases.

## P.2.37 VaD versus non-VaD

### P.2.37.1 99mTc-HMPAO SPECT

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SINGLE CAMERA												
2 studies (Launes	2 ×	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
1991; McMurdo 1994)	prospective				LR-	0.44 (0.24, 0.81)	Not serious	Not serious	Not serious	Serious	-	MODERATE

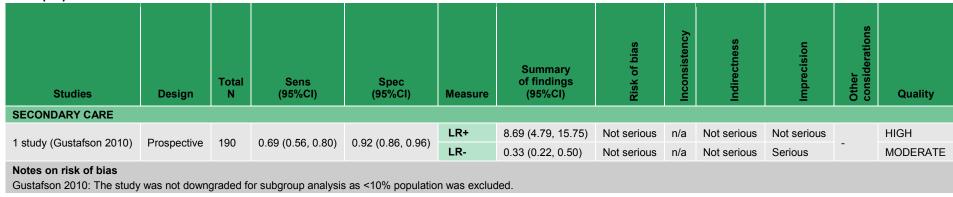
<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

## P.2.38 MRI

Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%Cl)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study (Koikkalainen		0.00 (0.04, 0.00)	LR+	18.89 (11.22, 31.80)	Not serious	n/a	Not serious	Not serious		HIGH		
2016)		504	0.71 (0.50, 0.85)	0.96 (0.94, 0.98)	LR-	0.30 (0.16, 0.57)	Not serious	n/a	Not serious	Serious	-	MODERATE

## P.2.39 VaD versus other dementias

## P.2.39.1 HIS (≥7)



<sup>©</sup> NICE 2018. All rights reserved. See Notice of rights.

### P.2.39.2 MRI

1411 X1												
Studies	Design	Total N	Sens (95%CI)	Spec (95%CI)	Measure	Summary of findings (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
SECONDARY CARE												
1 study	Prospective	386	0.71 (0.50, 0.85)	0.96 (0.94, 0.98)	LR+	19.72 (10.91, 35.66)	Serious	n/a	Not serious	Not serious	_	MODERATE
(Koikkalainen 2016)					LR-	0.30 (0.16, 0.56)	Serious	n/a	Not serious	Serious		LOW

### Notes on risk of bias