Guideline: “Diagnosis and treatment of dementia and Mild cognitive impairment”

Supplementary material

GRADE and CERQual tables

Review question 1 (RQ NICE): What are the most effective methods of case finding for people at high risk of dementia?

Case finding for people at high risk of dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
New diagnosis of dementia and MCI in stage 1	1 (van den Dungen 2016)	RR 1.33 (0.70. 2.07). I^2 n.a.	647	Very Low [b,c]
New diagnosis of dementia and MCI in stage 2	1 (van den Dungen 2016)	RR 1.07 (0.60. 1.62). I^2 n.a.	145	Very Low [b,c]
QoL-AD 6m	1 (van den Dungen 2016)	MD -0.61 (-2.31. 1.09). I^2 n.a.	124	Moderate
QoL-AD 12m	1 (van den Dungen 2016)	MD -0.85 (-2.46. 0.76). I^2 n.a.	124	Moderate
95% CI: 95% confidence interval; MD: mean difference a. I^2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I^2 > 75%; n.a.: not applicable				

Review question 2a (RQ NICE). What are the most effective methods of primary assessment to decide whether a person with suspected dementia should be referred to a dementia service?

Review question 2b (New RQ). What are the most effective methods of primary assessment to decide whether a person with suspected cognitive deficit should be referred to a dementia service?

Review question 2c (RQ NICE). What are the most effective methods of diagnosing dementia and dementia subtypes in specialist dementia diagnostic services?

Review question 2d (New RQ). What are the most effective methods of diagnosing Mild cognitive impairment (MCI) in specialist dementia diagnostic services?

PRIMARY CARE

COGNITIVE TESTS	
10-Cognitive screener	General practitioner Cog
6-item screener	IQCODE
Abbreviated mental test	Memory impairment screen (MIS)
Functional Activities questionnaire	Mini mental State examination (MMSE)
Mini-Cog	Phototest

SPECIALISTS CARE

COGNITIVE AND NEUROPSYCHOLOGICAL ASSESSMENT	
Addenbrooke's cognitive examination	Letter sorting test
AD8	Memory impairment screen (MIS)
AD scale	Mini mental State examination (MMSE)
Clock drawing test	Montreal Cognitive Assessment (MoCA)
Boston naming test	Orientation
Brief neuropsychological test battery	Rowland universal dementia assessment scale (RUDAS)
CERAD test	Seven-minute screen
FCSRT-immediate recall 3-FR	Short portable mental status questionnaire
Free recall score of 5-word test	Syndrome Kurztest
Mini-Cog	Test Your Memory (TYM)
FTD scale	5-word test
IQCODE	Verbal category fluency

CLINICAL CRITERIA	
FTD Consortium criteria	DLB consensus criteria
FTD consensus criteria	Movement disorders criteria for PDD
CJD criteria	Alzheimer's diseases diagnostic and treatment centers criteria
Corticobasal degeneration consensus criteria	NINDS-AIREN

NEUROIMAGING	
Computer tomography	99mTc-ECD-SPECT
FDG-PET	^{123}I-FP-CIT-SPECT
Amyloid PET	^{123}I-IMP-SPECT
MRI	^{123}I-IMP-SPECT and ^{123}I-MIBG cardiac scintigraphy
MRI hippocampal grey matter volume	^{123}I-MIBG cardiac scintigraphy
^{99}mTc-HMPAO-SPECT	mass spectrometry

CSF BIOMARKERS	
Amyloid beta 1-42	14-3-3
Amyloid beta 1-42/p-tau	14-3-3 and Amyloid beta 1-42
Amyloid beta 1-42/t-tau	14-3-3 and t-tau
t-tau/ Amyloid beta 1-42	14-3-3 and S100B
Amyloid beta 42/40	t-tau and S100B
Amyloid beta 42/40 and p-tau	14-3-3, t-tau and p-tau
Amyloid beta 1-42 and t-tau	14-3-3, t-tau and S100B
Amyloid beta 1-42, t-tau, p-tau	Neuron-specific enolase
p-tau	RT-QuIC
p-tau/ Amyloid beta 1-42	S100B
t-tau	biomarker formulas
p-tau/t-tau	

Other tests	
Olfactory test	EEG
Short smell test	skin biopsy
Applause sign	Lewy body composite risk score
Palmo mental reflex	REM sleep behavior disorder, visual hallucination Parkinsonism, fluctuating attention and concentration
Urinary AD7c-NTP	
Apolipoprotein E	Hachinski ischemic score

DEMENTIA IN PRIMARY AND SPECIALIST CARE SETTING

10-Cognitive Screener (primary care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 10%		
10-CS ≤ 5	1 dem vs no dem	CD	230	Se 0.69	TP 7	FP 5	Low
				Sp 0.94	FN 3	TN 85	
10-CS ≤ 7	1 dem vs no dem	CD	230	Se 0.94	TP 9	FP 36	Very Low
				Sp 0.60	FN 1	TN 54	
10-CS ≤ 8	1 dem vs no dem	CD	230	Se 0.97	TP 10	FP 54	Low
				Sp 0.40	FN 0	TN 36	
TP (people with dementia. **true positives**); FN (people incorrectly classified as healthy. **false negatives**); TN (people without dementia. **true negatives**); FP (people incorrectly classified with dementia. **false positives**); CD: clinical diagnosis							

Study: Apolinario 2015

6-Items Screener (primary care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 10%		
6-IS ≥ 0	1 dem vs no dem	CC	651	Se 1	TP 10	FP 88	Very Low
				Sp 0	FN 0	TN 2	
6-IS ≥ 1	1 dem vs no dem	CC	651	Se 0.97	TP 10	FP 42	Low
				Sp 0.53	FN 0	TN 48	
6-IS ≥ 2	1 dem vs no dem	CC	651	Se 0.90	TP 9	FP 19	Moderate
				Sp 0.79	FN 1	TN 71	
6-IS ≥ 3	1 dem vs no dem	CC	651	Se 0.81	TP 8	FP 8	Moderate
				Sp 0.91	FN 2	TN 82	
6-IS ≥ 4	1 dem vs no dem	CC	651	Se 0.68	TP 7	FP 4	Moderate
				Sp 0.96	FN 3	TN 86	
6-IS ≥ 5	1 dem vs no dem	CC	651	Se 0.49	TP 5	FP 1	Low
				Sp 0.99	FN 5	TN 89	
6-IS ≥ 6	1 dem vs no dem	CC	651	Se 0.30	TP 3	FP 1	Moderate
				Sp 0.99	FN 7	TN 89	
TP (people with dementia. **true positives**); FN (people incorrectly classified as healthy. **false negatives**); TN (people without dementia. **true negatives**); FP (people incorrectly classified with dementia. **false positives**); CD: clinical diagnosis							

Study: Callahan 2002

6-Items Cognitive Impairment Test (primary care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 10%		
6-IS-CIT >9	1 dem vs no dem	CC	245	Se 0.88	TP 9	FP 20	High
				Sp 0.78	FN 1	TN 70	
6-IS-CIT >7	1 dem vs no dem	CD	240	Se 0.76			Moderate
				Sp 0.70			
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis							

Studies: Abdel-Aziz 2015, Creavin 2023

Abbreviated Mental Test (primary care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 10%		
AMT < 10	1 dem vs no dem	CD	299	Se 0.97	TP 10	FP 65	Low
				Sp 0.28	FN 0	TN 25	
AMT < 9	1 dem vs no dem	CD	299	Se 0.88	TP 9	FP 42	Very Low
				Sp 0.53	FN 1	TN 48	
AMT < 8	1 dem vs no dem	CD	299	Se 0.73	TP 7	FP 26	Very Low
				Sp 0.71	FN 3	TN 64	
AMT < 7	1 dem vs no dem	CD	299	Se 0.58	TP 6	FP 12	Very Low
				Sp 0.87	FN 4	TN 78	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis							

Study: Flicker 1997

Functional Activities Questionnaire (primary care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 10%		
FAQ > 9	1 dem vs no dem	CC	160	Se 0.87	TP 9	FP 16	Low
				Sp 0.82	FN 1	TN 74	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis							

Study: Cruz-Orduña 2012

Addenbrooke's Cognitive Examination (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
ACE<75	1 dem vs no dem	CC	285	Se 0.85	TP 26	FP 12	High
				Sp 0.83	FN 4	TN 58	
ACE<83	2 dem vs no dem	CD	424	Se 0.82 to 0.96	TP 25 to 29	FP 3 to 26	Very Low
				Sp 0.63 to 0.96	FN 1 to 5	TN 44 to 67	
ACE<88	2 dem vs no dem	CD	424	Se 0.93 to 1	TP 28 to 30	FP 20 to 40	Very Low
				Sp 0.43 to 0.71	FN 0 to 2	TN 30 to 50	
ACE-III<81	1 dem vs no dem	CC	59	Se 0.81	TP 24	FP 2	Low
				Sp 0.97	FN 6	TN 68	
ACE-III<82	1 dem vs no dem	CC	59	Se 0.81	TP 24	FP 21	Low
				Sp 0.70	FN 6	TN 49	
ACE-III<84	1 dem vs no dem	CC	59	Se 0.92	TP 28	FP 27	Very Low
				Sp 0.61	FN 2	TN 43	
ACE-III<88	1 dem vs no dem	CC	59	Se 0.96	TP 29	FP 35	Low
				Sp 0.50	FN 1	TN 35	
ACE-R<74	1 dem vs no dem	CD	140	Se 0.90	TP 27	FP 6	Moderate
				Sp 0.93	FN 3	TN 84	
ACE-R<83	2 dem vs no dem	CD	442	Se 0.79 to 0.92	TP 24 to 28	FP 14 to 22	Moderate
				Sp 0.69 to 0.80	FN 2 to 6	TN 48 to 56	
ACE-R<85	1 dem vs no dem	CC	122	Se 0.85	TP 26	FP 14	Moderate
				Sp 0.80	FN 4	TN 56	
ACE-R<89	1	CC	122	Se 0.91	TP 27	FP 22	Low

	dem vs no dem			Sp 0.68	FN 3	TN 48	
ACE<75	2 dem vs no dem **(1 LG DEM)**	1 CC 1 CD	859	Se 0.98 to 0.99	TP 29 to 30	FP 46 to 46	Moderate
				Sp 0.34 to 0.35	FN 0 to 1	TN 24 to 24	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis; CC: clinical criteria							

Studies: Larner 2007, Mathuranath 2000, Jubb 2015, Hancock 2011, Bastide 2012, Terpening 2011, Williamson 2018

AD8 (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
AD8 ≥ 2	1 dem vs no dem	CC	212	Se 0.97	TP 29	FP 62	Moderate
				Sp 0.11	FN 1	TN 8	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis							

Studies: Larner 2015

AD Scale (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
AD Scale	1 AD vs other dem	NP	190	Se 0.80	TP 24	FP 9	High
				Sp 0.87	FN 6	TN 61	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); NP: neuropathology							

Studies: Gustafson 2010

Clock Drawing Test (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CDT > 0 Schulman	1 dem vs no dem	CC	232	Se 0.86	TP 26	FP 34	Low
				Sp 0.52	FN 4	TN 36	
CDT > 1 Schulman	1 dem vs no dem	CC	232	Se 0.71	TP 21	FP 8	Moderate
				Sp 0.88	FN 9	TN 62	
CDT > 2 Schulman	2 dem vs no dem	CC	734	Se 0.29 to 0.78	TP 9 to 23	FP 1 to 2	Very Low
				Sp 0.97 to 0.98	FN 7 to 21	TN 68 to 69	
CDT > 3 Schulman	1 dem vs no dem	CC	462	Se 0.90	TP 27	FP 31	Low
				Sp 0.56	FN 3	TN 39	
CDT > 4 Watson	1 dem vs no dem	CC	462	Se 0.72	TP 22	FP 25	Low
				Sp 0.64	FN 8	TN 45	
CDT < 7 Wolf-Klein	1 dem vs no dem	CC	462	Se 0.58	TP 17	FP 13	Low
				Sp 0.81	FN 13	TN 57	
CDT < 8 Unclear scoring method	1 dem vs no dem	CC	364	Se 0.72	TP 22	FP 12	High
				Sp 0.83	FN 8	TN 58	
CDT < 8 Manos and Wu	1 dem vs no dem	CC	462	Se 0.81	TP 24	FP 28	Low
				Sp 0.60	FN 6	TN 42	
CDT < 9 Manos and Wu	1 dem vs no dem	CC	462	Se 0.93	TP 28	FP 44	Low
				Sp 0.37	FN 2	TN 26	
CDT < 3 Lin	1 dem vs no dem	CC	462	Se 0.88	TP 26	FP 36	Low
				Sp 0.49	FN 4	TN 34	
				Se 0.86	TP 26	FP 34	

TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria

Studies: Ravaglia 2005, Yamamoto 2004, Ramlall 2014, Lee 2008, Beinhoff 2005

Applause Sign (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
AS < 3	1 dem vs no dem	CD	275	Se 0.54	TP 16	FP 10	Moderate
				Sp 0.85	FN 14	TN 60	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis							

Studies: Bonello 2016

Boston Naming Test (primary care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 10%		
BNT <13	1 dem vs no dem	CC	232	Se 0.39	TP 12	FP 5	Moderate
				Sp 0.93	FN 18	TN 65	
BNT <14	1 dem vs no dem	CC	232	Se 0.55	TP 17	FP 11	Low
				Sp 0.84	FN 13	TN 59	
BNT <15	1 dem vs no dem	CC	232	Se 0.71	TP 21	FP 26	Low
				Sp 0.63	FN 9	TN 44	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis							

Studies: Beinhoff 2005

Brief Neuropsychological Test Battery (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
BNTB	1 dem vs no dem	CC	131	Se 0.91	TP 27	FP 12	High
				Sp 0.83	FN 3	TN 58	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria							

Studies: Coutinho 2013

CERAD test (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CERAD	1 dem vs no dem	CC	100	Se 0.74	TP 22	FP 1	Low
				Sp 0.98	FN 8	TN 69	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria							

Studies: Hentschel 2005

Brain Computerized Tomography (primary care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CTdms	1 dem vs no dem	CC	116	Se 0.54	TP 16	FP 16	Moderate
				Sp 0.77	FN 14	TN 54	
	1 AD vs VaD	CC	94	Se 0.51	TP 15	FP 48	Low
				Sp 0.32	FN 15	TN 22	
	1 AD vs other dem	CC	103	Se 0.51	TP 15	FP 43	Low
				Sp 0.38	FN 15	TN 27	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria							

Studies: O'Brien 2000

Free and Cued Selective Reminding Test-Immediate Recall 3-FR (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
FCSRT-IR 3-FR ≤ 22	1 PDD vs no PDD	CD	40	Se 0.84	TP 25	FP 15	Low
				Sp 0.78	FN 5	TN 55	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis							

Studies: Kiesmann 2013

Free Recall Score of 5-word Test (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
FRS5-W ≤ 6	1 dem vs no dem	CD	145	Se 0.78	TP 23	FP 7	Low
				Sp 0.90	FN 7	TN 63	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis							

Studies: Mormont 2012

Mini-Cog (primary and specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 10%, 30%		
Primary care							
Mini-Cog ≤ 2	1* dem vs no dem	CD	142	Se 0.99	TP 10	FP 54	Moderate
				Sp 0.40	FN 0	TN 36	
Mini-Cog < 3	1** dem vs no dem	CD	240	Se 0.70			Moderate
				Sp 0.73			
Specialist care setting							
Mini-Cog Scanlan & Borson	1*** dem vs no dem	CC	502	Se 0.87	TP 26	FP 1	Moderate
				Sp 0.99	FN 4	TN 69	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis; CC: clinical criteria							

Studies: *Carnero-Pardo 2013, **Creavin 2023, ***Milian 2012

FDG-PET (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
FDG-PET	3 dem vs no dem	2CD 1NP	386	Se 0.54 to 1	TP 16 to 30	FP 12 to 17	Very Low
				Sp 0.76 to 0.83	FN 0 to 14	TN 53 to 58	
	6 AD vs no AD	CD	544	Se 0.38 to 0.94	TP 11 to 28	FP 4 to 22	Very Low
				Sp 0.69 to 0.94	FN 2 to 19	TN 48 to 66	
	1	CC	83	Se 0.58	TP 17	FP 15	Very Low

	AD vs FTD			Sp 0.78	FN 13	TN 55	
	1 AD vs DLB	CC	70	Se 0.58	TP 17	FP 56	Very Low
				Sp 0.20	FN 13	TN 14	
	6 AD vs other dem	3CD 2NP 1CC	300	Se 0.58 to 0.93	TP 17 to 28	FP 0 to 31	Very Low
				Sp 0.55 to 1	FN 2 to 13	TN 39 to 70	
	3 Studies DLB vs no DLB **(1 LG DEM)**	2CD 1NP	387	Se 0.20 to 0.89	TP 6 to 27	FP 1 to 4	Low
				Sp 0.95 to 0.99	FN 3 to 24	TN 66 to 69	
	1 DLB vs other dem	CC	98	Se 0.20	TP 6	FP 3	Very Low
				Sp 0.95	FN 24	TN 67	
	1 FTD vs DLB	CC	23	Se 0.34	TP 10	FP 6	Very Low
				Sp 0.92	FN 20	TN 64	
	2 FTD vs no FTD	1CD 1NP	255	Se 0.33 to 0.53	TP 10 to 16	FP 4 to 6	Very Low
				Sp 0.91 to 0.95	FN 14 to 20	TN 64 to 66	
	1 bvFTD vs no bvFTD	CD	111	Se 0.89	TP 27	FP 2	Low
				Sp 0.68	FN 3	TN 48	
	2 FTD vs other dem	2CD	146	Se 0.33 to 0.47	TP 10 to 14	FP 8 to 25	Very Low
				Sp 0.65 to 0.88	FN 16 to 20	TN 45 to 62	
	1 AD vs no dem	CC	46	Se 0.79	TP 24	FP 6	Low
				Sp 0.91	FN 6	TN 64	
	1 PPA vs PPA	CC	102	Se 0.50	TP 15	FP 1	Low
				Sp 0.99	FN 15	TN 69	

TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis; CC: clinical criteria; NP: neuropathology

Studies: Yakushev 2010, Arslan 2015; Frisoni 2009; Hoffman 2000; Jagust 2007; Ossenkoppele 2013, Panegyres 2009, Döbert 2005, Silverman 2001, Vijverberg 2016b, Caminiti 2019

FTD Consortium Criteria (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
FTDCC Overall	1 bvFDT vs no bvFTD	NP	147	Se 0.79	TP 24	FP 3	Moderate
				Sp 0.96	FN 6	TN 67	
FTDCC Probabile	1 bvFDT vs no bvFTD	CD	116	Se 0.85	TP 26	FP 51	Low
				Sp 0.27	FN 4	TN 19	
FTDCC	1	CD	116	Se 0.85	TP 26	FP 13	Low

Possibile	bvFDT vs no bvFTD			Sp 0.82	FN 4	TN 57	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis; NP: neuropathology							

Studies: Harris 2013, Vijverberg 2016a

FTD Consensus Criteria (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
FTDCoC	1 FDT vs no FTD	CD	134	Se 0.37	TP 11	FP 1	High
				Sp 0.99	FN 19	TN 69	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis							

Studies: Mendez 2007

FTD Scale (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
FTD Scale	1 FDT vs other dem	NP	190	Se 0.92	TP 28	FP 6	High
				Sp 0.92	FN 2	TN 64	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); NP: neuropathology							

Studies: Gustafson 2010

PET amiloide (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
Amy-PET	1 AD vs no AD **(2 LG DEM)**	CD	11.729	Se 0.52 to 0.76	TP 16 to 23	FP 24 to 36	Low
				Sp 0.48 to 0.66	FN 7 to 14	TN 34 to 46	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis							

Studies: Zwan 2017, Rabinovinci 2019, Matsuda 2022

General Practitioner Cog (primary care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 10%		
GPCOG <11	1 dem no dem **(1 LG DEM)**	CAMCOG	1.717	Se 0.79	TP 8	FP 7	Moderate
				Sp 0.92	FN 2	TN 83	
GPCOG <8	1 dem no dem **(1 LG DEM)**	CD	240	Se 0.93			Low
				Sp 0.52			
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CAMCOG: clinical scale							

Studies: Brodaty 2016, Creavin 2023

Informant Questionnaire on Cognitive Decline in the Elderly (primary and specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 10%, 30%		
Primary care							
IQCODE26-item >3.6	1 dem vs no dem	CD	160	Se 0.80	TP 8	FP 21	Low
				Sp 0.77	FN 2	TN 69	
Specialist care setting							
IQCODE16-item >3.2	1 AD vs no dem	CC	269	Se 0.96	TP 29	FP 41	Low
				Sp 0.42	FN 1	TN 29	
IQCODE16-item >3.3	1 AD vs no dem	CC	269	Se 0.96	TP 29	FP 37	Very Low
				Sp 0.47	FN 1	TN 33	
IQCODE16-item >3.4	1 AD vs no dem	CC	269	Se 0.92	TP 28	FP 26	Very Low
				Sp 0.63	FN 2	TN 44	
IQCODE16-item >3.5	1 AD vs no dem	CC	269	Se 0.89	TP 27	FP 22	Low
				Sp 0.69	FN 3	TN 48	
IQCODE16-item >3.6	1 AD vs no dem	CC	269	Se 0.86	TP 26	FP 18	Low
				Sp 0.74	FN 4	TN 52	
IQCODE16-item >3.5	2 dem vs no dem	CD	436	Se 0.92 to 0.94	TP 28 to 28	FP 12 to 37	Moderate
				Sp 0.47 to 0.83	FN 2 to 2	TN 33 to 58	
IQCODE16-item >4.1	1 dem vs no dem	CD	204	Se 0.72	TP 22	FP 23	Low
				Sp 0.67	FN 8	TN 47	

IQCODE26-item >3.5	2 dem vs no dem	CD	443	Se 0.86 to 0.87 Sp 0.39 to 0.83	TP 28 to 28 FN 2 to 2	FP 12 to 37 TN 33 to 58	Very Low
IQCODE26-item >3.6	1 dem vs no dem	CD	299	Se 0.81 Sp 0.61	TP 24 FN 6	FP 27 TN 43	Very Low
IQCODE26-item >3.7	1 dem vs no dem	CD	299	Se 0.78 Sp 0.65	TP 23 FN 7	FP 25 TN 45	Very Low
IQCODE26-item >3.8	1 dem vs no dem	CD	299	Se 0.75 Sp 0.71	TP 22 FN 8	FP 20 TN 50	Very Low
IQCODE26-item >3.9	1 dem vs no dem	CD	299	Se 0.70 Sp 0.75	TP 21 FN 9	FP 18 TN 52	Very Low
IQCODE26-item >4	1 dem vs no dem	CD	299	Se 0.65 Sp 0.80	TP 20 FN 10	FP 14 TN 56	Very Low
IQCODE26-item >4.1	1 dem vs no dem	CD	299	Se 0.58 Sp 0.83	TP 17 FN 13	FP 12 TN 58	Very Low

TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis; CC: clinical criteria

Studies: Garcia 2002, Knaefelc 2003, Flicker 1997, Hancock 2009, Sikkes 2010, Cruz-Orduña 2012, Gonçalves 2011

Letter Sorting Test (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
LST < 1	1 dem vs no dem	CC	232	Se 0.12 Sp 0.99	TP 4 FN 26	FP 1 TN 69	Moderate
LST < 2	1 dem vs no dem	CC	232	Se 0.44 Sp 0.93	TP 13 FN 17	FP 5 TN 65	Low
LST < 3	1 dem vs no dem	CC	232	Se 0.80 Sp 0.69	TP 24 FN 6	FP 27 TN 48	Low

TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria

Studies: Beinhoff 2005

Memory Impairment Screen (primary and specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 10%, 30%		
Primary care							
MIS < 4	1 dem vs no dem	CD	117	Se 0.93	TP 9	FP 18	High
				Sp 0.80	FN 1	TN 72	
MIS < 5	1 dem vs no dem	CD	117	Se 0.97	TP 10	FP 26	High
				Sp 0.71	FN 0	TN 64	
Specialist care setting							
MIS<5	1 dem vs no dem	CD	232	Se 0.82	TP 25	FP 13	Moderate
				Sp 0.81	FN 5	TN 57	
MIS<6	1 dem vs no dem	CD	232	Se 0.88	TP 26	FP 13	Moderate
				Sp 0.70	FN 4	TN 21	
MIS<7	1 dem vs no dem	CD	232	Se 0.92	TP 28	FP 33	Low
				Sp 0.53	FN 2	TN 37	
MIS<8	1 dem vs no dem	CD	232	Se 0.98	TP 29	FP 48	Moderate
				Sp 0.32	FN 1	TN 22	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria							

Studies: Carnero Pardo 2011, Beinhoff 2005

Mini Mental State Examination (primary care e specialistico)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 10%, 30%		
Primary care							
MMSE<17	1 dem vs no dem	CD	360	Se 0.70	TP 7	FP 6	Moderate
				Sp 0.93	FN 3	TN 84	
MMSE<18	1 dem vs no dem	CD	360	Se 0.81	TP 8	FP 7	Moderate
				Sp 0.92	FN 2	TN 83	
MMSE<19	2 dem vs no dem	CD	520	Se 0.80 to 0.88	TP 8 to 9	FP 12 to 13	Low
				Sp 0.86 to 0.87	FN 1 to 2	TN 77 to 78	
MMSE<20	1 dem vs no dem	CD	360	Se 0.94	TP 9	FP 16	Moderate
				Sp 0.82	FN 1	TN 74	
MMSE<21	1	CD	360	Se 0.95	TP 10	FP 24	Moderate

	dem vs no dem			Sp 0.73	FN 0	TN 66	
MMSE<22	1 dem vs no dem	CD	360	Se 0.96	TP 10	FP 30	Moderate
				Sp 0.67	FN 0	TN 60	
MMSE<23	1 dem vs no dem	CD	360	Se 0.99	TP 10	FP 39	Low
				Sp 0.57	FN 0	TN 51	
MMSE<24	2 dem vs no dem **(1 LG DEM)**	CD	2.388	Se 0.51 to 1	TP 5 to 10	FP 3 to 49	Low
				Sp 0.46 to 0.97	FN 0 to 5	TN 41 to 87	
MMSE<25	1 dem vs no dem	CD	360	Se 1	TP 10	FP 56	Moderate
				Sp 0.38	FN 0	TN 34	
Specialist care setting							
MMSE<18	1 dem vs no dem	CD	299	Se 0.50	TP 15	FP 7	Very Low
				Sp 0.90	FN 15	TN 63	
MMSE<19	1 dem vs no dem	CD	299	Se 0.56	TP 17	FP 2	Very Low
				Sp 0.97	FN 13	TN 68	
MMSE<20	1 dem vs no dem	CD	299	Se 0.62	TP 19	FP 11	Very Low
				Sp 0.84	FN 11	TN 59	
MMSE<21	1 dem vs no dem	CD	299	Se 0.69	TP 21	FP 17	Very Low
				Sp 0.76	FN 9	TN 53	
MMSE<22	4 dem vs no dem	CD	1.214	Se 0.56 to 0.75	TP 17 to 22	FP 0 to 20	Very Low
				Sp 0.71 to 1	FN 8 to 13	TN 50 to 70	
MMSE<23	6 dem vs no dem	CD	1.489	Se 0.54 to 0.80	TP 16 to 24	FP 0 to 22	Very Low
				Sp 0.69 to 1	FN 6 to 14	TN 48 to 70	
MMSE<24	12 dem vs no dem	10CD 1NP	3.100	Se 0.39 to 0.88	TP 12 to 26	FP 1 to 28	Low
				Sp 0.60 to 0.99	FN 4 to 18	TN 42 to 69	
MMSE<25	8 dem vs no dem	5CD 1CC 1NP	2.145	Se 0.70 to 0.95	TP 21 to 28	FP 0 to 33	Very Low
				Sp 0.53 to 1	FN 2 to 9	TN 37 to 70	
MMSE<26	6 dem vs no dem **(2 LG DEM)**	4CD 2NP	1.934	Se 0.52 to 0.92	TP 17 to 28	FP 0 to 38	Very Low
				Sp 0.46 to 1	FN 2 to 13	TN 32 to 70	
MMSE<27	4 dem vs no dem	CD	1241	Se 0.74 to 0.94	TP 22 to 28	FP 3 to 26	Low
				Sp 0.63 to 0.96	FN 2 to 8	TN 44 to 67	
MMSE<28	2 dem vs no dem	CD	796	Se 0.93 to 0.98	TP 28 to 29	FP 15 to 25	Very Low
				Sp 0.65 to 0.78	FN 1 to 2	TN 45 to 55	
	1 AD vs no dem	CD	110	Se 0.98	TP 29	FP 15	Low
				Sp 0.78	FN 1	TN 55	

TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria; CD: clinical diagnosis; NP: neuropathology

Studies: Brodaty 2016, Callahan 2002, Flicker 1997, Kukull 1994, Abdel-Aziz 2015, Nielsen 2013, Bastide 2012, Gonçalves 2011, Hancock 2011, Knaefelc 2003, Mathuranath 2000, Postel-Vinay 2014, Sager 2006, Milian 2012, Yeung 2014, Mormont 2012, Carnero Pardo 2013, Cruz-Orduña 2012, Torkpoor 2022

Montreal Cognitive Assessment (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
MoCA<19	2 dem vs no dem	1CD 1CC	495	Se 0.92 to 0.94 Sp 0.66 to 0.92	TP 28 to 28 FN 2 to 2	FP 6 to 24 TN 46 to 64	Very Low
MoCA<21	1 dem vs no dem **(1 LG DEM)**	1 CD	693	Se 0.90 Sp 0.74	TP 27 FN 3	FP 19 TN 51	Moderate
MoCA<22	1 dem vs no dem	CC	272	Se 1 Sp 0.37	TP 30 FN 0	FP 44 TN 26	Moderate
MoCA<24	1 dem vs no dem	CD	81	Se 0.96 Sp 0.31	TP 29 FN 1	FP 48 TN 22	Low
MoCA<25	1 dem vs no dem	CD	81	Se 0.98 Sp 0.23	TP 29 FN 1	FP 54 TN 16	Low
MoCA<26	2 dem vs no dem **(1 LG DEM)**	1CC 1 CD	953	Se 0.98 to 0.99 Sp 0.29 to 31	TP 29 to 30 FN 0 to 1	FP 48 to 50 TN 20 to 22	Moderate
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria; CD: clinical diagnosis							

Studies: Chen 2011, Yeung 2014, Goldstein 2014, Larner 2017, Dautzenberg 2022

Brain Magnetic Resonance imaging (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
RM	2 dem vs no dem	CD	234	Se 0.69 to 0.92 Sp 0.55 to 0.58	TP 21 to 28 FN 2 to 9	FP 29 to 31 TN 39 to 41	Very Low
	2 Studies AD vs no AD	CD	637	Se 0.29 to 0.87 Sp 0.56 to 0.84	TP 9 to 26 FN 4 to 21	FP 11 to 31 TN 39 to 59	Low
	1 AD vs FTD	CC	315	Se 0.29 Sp 0.77	TP 9 FN 21	FP 16 TN 54	Moderate
	2 AD vs other dem	CD	471	Se 0.29 to 0.87 Sp 0.53 to 0.77	TP 9 to 26 FN 4 to 21	FP 16 to 33 TN 37 to 54	Very Low

	1 AD vs DLB	CC	270	Se 0.29 Sp 0.72	TP 9 FN 21	FP 20 TN 50	Moderate
	1 DLB vs AD	CC	270	Se 0.43 Sp 0.71	TP 13 FN 17	FP 20 TN 50	Low
	1 DLB vs FTD	CC	270	Se 0.43 Sp 0.86	TP 13 FN 17	FP 10 TN 60	Low
	1 DLB vs VaD	CC	71	Se 0.43 Sp 0.88	TP 13 FN 7	FP 8 TN 62	Low
	1 DLB vs no DLB	CC	504	Se 0.43 Sp 0.76	TP 13 FN 17	FP 17 TN 53	Moderate
	1 AD vs VaD	CC	247	Se 0.29 Sp 0.88	TP 9 FN 21	FP 8 TN 62	Moderate
	1 VaD vs AD	CC	247	Se 0.71 Sp 0.97	TP 21 FN 9	FP 2 TN 68	Low
	1 VaD vs DLB	CC	71	Se 0.71 Sp 0.97	TP 21 FN 9	FP 3 TN 67	Low
	1 VaD vs FTD	CC	116	Se 0.71 Sp 0.97	TP 21 FN 9	FP 3 TN 67	Low
	1 VaD vs no VaD	CC	504	Se 0.71 Sp 0.96	TP 21 FN 9	FP 3 TN 67	Moderate
	1 VaD vs other dem	CC	386	Se 0.71 Sp 0.96	TP 21 FN 9	FP 3 TN 67	Low
	4 Studies CJD vs no CJD	3CD 1NP	564	Se 0.37 to 0.67 Sp 0.80 to 0.98	TP 11 to 20 FN 10 to 19	FP 1 to 14 TN 56 to 69	Low
	1 FTD vs AD	CC	315	Se 0.50 Sp 0.72	TP 15 FN 15	FP 20 TN 50	Low
	1 FTD vs VaD	CC	116	Se 0.50 Sp 0.96	TP 15 FN 15	FP 20 TN 3	Low
	1 FTD vs DLB	CC	139	Se 0.50 Sp 0.94	TP 15 FN 15	FP 67 TN 66	Low
	2 FTD vs no FTD	CD	638	Se 0.50 to 0.63 Sp 0.70 to 0.84	TP 15 to 19 FN 11 to 15	FP 11 to 21 TN 49 to 59	Low
	1 FTD vs other dem	CC	386	Se 0.50 Sp 0.78	TP 15 FN 15	FP 15 TN 55	Low
	1 bvFTD vs no bvFTD	CD	111	Se 0.70 Sp 0.93	TP 21 FN 9	FP 5 TN 65	Low

TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria; CD: clinical diagnosis; NP: neuropathology

Studies: Frisoni 2009, Hentschel 2005, Koikkalainen 2016, Schröter 2000, Tagliapietra 2013, Tschampa 2005, Van Everbroeck 2004, Mendez 2007

MRI Hippocampal grey matter volume (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
MRI hgmv total	1 AD vs no AD	CD	100	Se 0.61 Sp 0.86	TP 18 FN 12	FP 10 TN 60	Low
MRI hgmv left	1 AD vs no AD	CD	100	Se 0.70 Sp 0.71	TP 21 FN 9	FP 20 TN 50	Low
MRI hgmv Left/total gmv	1 AD vs no AD	CD	100	Se 0.80 Sp 0.66	TP 24 FN 6	FP 24 TN 46	Low
MRI hgmv Right	1 AD vs no AD	CD	100	Se 0.75 Sp 0.77	TP 22 FN 8	FP 16 TN 54	Low
MRI hgmv Right/total gmv	1 AD vs no AD	CD	100	Se 0.80 Sp 0.80	TP 24 FN 6	FP 14 TN 56	Moderate
MRI hgmv Total/total gmv	1 AD vs no AD	CD	100	Se 0.66 Sp 0.88	TP 20 FN 10	FP 8 TN 62	Low
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis							

Studies: Suppa 2015

Olfactory Test (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
OT ≥3	1 AD vs no AD	CD	50	Se 0.79 Sp 0.46	TP 24 FN 6	FP 38 TN 32	Moderate
OT ≥4	1 AD vs no AD	CD	50	Se 0.50 Sp 0.73	TP 15 FN 15	FP 19 TN 51	Moderate
OT ≥5	1 AD vs no AD	CD	50	Se 0.21 Sp 0.85	TP 6 FN 24	FP 10 TN 60	Low
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis							

Studies: Christensen 2017

Orientation (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
OR < 7	1 dem vs no dem	CD	232	Se 0.39	TP 12	FP 1	Moderate
				Sp 0.99	FN 18	TN 69	
OR < 8	1 dem vs no dem	CD	232	Se 0.65	TP 20	FP 7	Low
				Sp 0.90	FN 10	TN 63	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis							

Studies: Beinhoff 2005

Palmomental Reflex (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
PMR	1 dem vs no dem	CC	154	Se 0.41	TP 12	FP 13	Low
				Sp 0.82	FN 18	TN 57	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria							

Studies: Streit 2015

Palmomental Reflex and Short Smell Test (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
PMR or SST, one positive	1 dem vs no dem	CC	154	Se 0.71	TP 21	FP 25	Low
				Sp 0.64	FN 9	TN 45	
PMR and SST, both positive	1 dem vs no dem	CC	154	Se 0.24	TP 7	FP 5	Low
				Sp 0.93	FN 23	TN 65	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria							

Studies: Streit 2015

Phototest (primary care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
Phototest<27	1 dem vs no dem	CD	140	Se 0.81	TP 8	FP 10	High
				Sp 0.89	FN 2	TN 80	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis							

Studies: Carnero-Pardo 2011

Rowland Universal Dementia Assessment Scale (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
RUDAS<19	1 dem vs no dem **(1 LG DEM)**	CC	116	Se 0.67	TP 20	FP 12	Low
				Sp 0.83	FN 10	TN 58	
RUDAS<20	1 dem vs no dem **(1 LG DEM)**	CC	116	Se 0.74	TP 22	FP 13	Low
				Sp 0.82	FN 8	TN 57	
RUDAS<21	2 dem vs no dem **(1 LG DEM)**	1CD 1CC	320	Se 0.66	TP 20	FP 7	Moderate
				Sp 0.90	FN 10	TN 63	
RUDAS<22	3 dem vs no dem **(2 LG DEM)**	CC	376	Se 0.49 to 0.92	TP 15 to 28	FP 6 to 17	Low
				Sp 0.75 to 0.91	FN 2 to 15	TN 53 to 64	
RUDAS<23	3 dem vs no dem **(2 LG DEM)**	CC	376	Se 0.61 to 0.97	TP 18 to 29	FP 12 to 27	Very Low
				Sp 0.62 to 0.83	FN 1 to 12	TN 43 to 58	
RUDAS<24	3 dem vs no dem **(2 LG DEM)**	CC	376	Se 0.69 to 1	TP 21 to 30	FP 14 to 31	Very Low
				Sp 0.56 to 0.80	FN 0 to 9	TN 39 to 56	
RUDAS<25	2 dem vs no dem **(1 LG DEM)**	CC	260	Se 0.76 to 0.92	TP 23 to 28	FP 24 to 28	Very Low
				Sp 0.60 to 0.66	FN 2 to 7	TN 42 to 46	
RUDAS<26	2 dem vs no dem **(1 LG DEM)**	CC	260	Se 0.82 to 0.90	TP 25 to 27	FP 25 to 35	Very Low
				Sp 0.50 to 0.65	FN 3 to 5	TN 35 to 45	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis; CC: clinical criteria							

Studies: Gonçalves 2011; Nielsen 2013; Torkpoor 2022, Daniel 2022

Seven Minute Screen (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
SMS>0,6	1 dem vs no dem	CD	95	Se 0.72	TP 22	FP 25	Low
				Sp 0.65	FN 8	TN 45	
SMS>0,7	1 dem vs no dem	CD	95	Se 0.72	TP 22	FP 22	Low
				Sp 0.69	FN 8	TN 48	
SMS>0,8	1 dem vs no dem	CD	95	Se 0.71	TP 21	FP 19	Low
				Sp 0.73	FN 9	TN 51	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis							

Studies: Skjerve 2008

Short Smell Test (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
SST	1 dem vs no dem	CC	154	Se 0.53	TP 16	FP 18	Very Low
				Sp 0.75	FN 14	TN 52	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria							

Studies: Streit 2015

Short Portable Mental Status Questionnaire (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
SPMSQ ≥ 4	1 dem vs no dem	CD	127	Se 0.79	TP 24	FP 18	Very Low
				Sp 0.75	FN 6	TN 52	
SPMSQ ≥ 5	1 dem vs no dem	CD	127	Se 0.78	TP 23	FP 18	Very Low
				Sp 0.75	FN 7	TN 52	

SPMSQ ≥ 6	1 dem vs no dem	CD	127	Se 0.72 Sp 0.42	TP 22 FN 8	FP 41 TN 29	Very Low
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis							

Studies: Malhotra 2013

Syndrome Kurztest (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested** **Pre-test probability of 30%**		**Certainty of evidence (GRADE)**
SK ≥ 7	1 dem vs no dem	CD	95	Se 0.71 Sp 0.54	TP 21 FN 9	FP 32 TN 38	Low
SK ≥ 8	1 dem vs no dem	CD	95	Se 0.65 Sp 0.65	TP 20 FN 10	FP 25 TN 45	Low
SK ≥ 9	1 dem vs no dem	CD	95	Se 0.58 Sp 0.69	TP 17 FN 13	FP 22 TN 48	Low
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis							

Studies: Skjerve 2008

5-word Test (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested** **Pre-test probability of 30%**		**Certainty of evidence (GRADE)**
5-wT total recall ≤ 9	1 dem vs no dem	CD	145	Se 0.81 Sp 0.90	TP 24 FN 6	FP 7 TN 63	Low
	1 AD vs no dem	CD	110	Se 0.92 Sp 0.90	TP 28 FN 2	FP 7 TN 63	Low
5-wT Total weighted ≤ 15	1 dem vs no dem	CD	145	Se 0.75 Sp 0.96	TP 22 FN 8	FP 3 TN 67	Low
	1 AD vs no dem	CD	110	Se 0.90 Sp 0.96	TP 27 FN 3	FP 3 TN 67	Low
5-wT ≤ 5	1	CD	110	Se 0.81	TP 24	FP 1	Low

	AD vs no dem			Sp 0.99	FN 6	TN 69	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis							

Studies: Mormont 2012

Test Your Memory (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
TYM≤30	1 dem vs no dem	CD	224	Se 0.73	TP 22	FP 8	Moderate
				Sp 0.88	FN 8	TN 62	
TYM≤39	1 dem vs no dem	CD	201	Se 0.90	TP 27	FP 21	Moderate
				Sp 0.70	FN 3	TN 49	
TYM≤42	1 dem vs no dem	CD	224	Se 0.95	TP 28	FP 38	Moderate
				Sp 0.45	FN 2	TN 32	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis							

Studies: Hancock 2011, Postel-Vinay 2014

Verbal Category Fluency (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
VCF<14	1 dem vs no dem	CC	364	Se 0.85	TP 26	FP 28	Moderate
				Sp 0.60	FN 4	TN 42	
VCF<19	1 dem vs no dem	CD	232	Se 0.85	TP 26	FP 26	Low
				Sp 0.63	FN 4	TN 44	
VCF<20	1 dem vs no dem	CD	232	Se 0.94	TP 28	FP 29	Low
				Sp 0.58	FN 2	TN 41	
VCF<21	1 dem vs no dem	CD	232	Se 0.94	TP 28	FP 34	Low
				Sp 0.52	FN 2	TN 36	
VCF<22	1 dem vs no dem	CD	232	Se 0.95	TP 28	FP 38	Low
				Sp 0.46	FN 2	TN 32	

VCF<23	1 dem vs no dem	CD	232	Se 0.97 Sp 0.39	TP 29 FN 1	FP 43 TN 27	Moderate
VCF<24	1 dem vs no dem	CD	232	Se 0.98 Sp 0.31	TP 29 FN 1	FP 48 TN 22	Moderate
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis; CC: clinical criteria							

Studies: Sager 2006, Beinhoff 2005

99M-Tc-HMPAO-SPECT (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested** **Pre-test probability of 30%**		**Certainty of evidence (GRADE)**
Single camera							
99M-TC-HMPAO-SPECT	1 dem vs no dem	CD	24	Se 0.89 Sp 0.33	TP 27 FN 3	FP 47 TN 23	Low
	2 AD vs FTD	CD	59	Se 0.64 to 0.89 Sp 0.67 to 0.80	TP 19 to 27 FN 3 to 11	FP 14 to 23 TN 47 to 56	Low
	5 AD vs no AD	CD	505	Se 0.58 to 0.92 Sp 0.28 to 0.94	TP 17 to 28 FN 2 to 13	FP 4 to 50 TN 20 to 66	Low
	2 AD vs VaD	CD	97	Se 0.58 to 0.64 Sp 0.85 to 1	TP 17 to 19 FN 11 to 13	FP 0 to 10 TN 60 to 70	Low
	1 AD vs other dem	CD	33	Se 0.89 Sp 0.71	TP 27 FN 3	FP 20 TN 50	Very Low
	4 FTD vs AD	3CD 1NP	291	Se 0.40 to 1 Sp 0.96 to 1	TP 12 to 30 FN 0 to 18	FP 0 to 3 TN 67 to 70	Very Low
	3 FTD vs no FTD	2CD 1NP	501	Se 0.36 to 1 Sp 0.92 to 1	TP 11 to 30 FN 0 to 19	FP 0 to 6 TN 64 to 70	Very Low
	2 FTD vs VaD	CD	196	Se 0.40 to 0.46 Sp 0.73 to 0.94	TP 12 to 14 FN 16 to 18	FP 4 to 19 TN 51 to 66	Very Low
	1 VaD vs FTD	CC	38	Se 0.76 Sp 0.60	TP 23 FN 7	FP 28 TN 42	Low
	1 FTD vs other dem	CD	33	Se 0.56 Sp 0.96	TP 17 FN 15	FP 3 TN 67	Very Low
	2 VaD vs AD	CD	97	Se 0.76 to 1 Sp 0.72 to 0.85	TP 23 to 30 FN 0 to 7	FP 10 to 20 TN 50 to 60	Low
	2	CD	204	Se 0.76 to 1	TP 23 to 30	FP 17 to 33	Low

	VaD vs no VaD			Sp 0.53 to 0.76	FN 0 to 7	TN 37 to 53	
Multiple camera							
99M-TC-HMPAO-SPECT	1 AD vs FTD	CD	29	Se 0.78 Sp 0.73	TP 23 FN 7	FP 19 TN 51	**Low**
	2 AD vs non AD	1CD 1NP	72	Se 0.31 to 0.57 Sp 0.92 to 1	TP 9 to 17 FN 13 to 21	FP 0 to 6 TN 64 to 70	**Low**
	1 AD vs VaD	CD	26	Se 0.78 Sp 0.50	TP 23 FN 7	FP 35 TN 35	Very Low
	2 FTD vs AD	1CD 1NP	64	Se 0.73 to 0.75 Sp 0.94 to 1	TP 22 to 22 FN 8 to 8	FP 0 to 4 TN 66 to 70	Very Low
	2 FTD vs non FTD	1CD 1NP	108	Se 0.73 to 0.75 Sp 0.80 to 0.97	TP 22 to 22 FN 8 to 8	FP 2 to 14 TN 56 to 68	Very Low
	1 FTD vs VaD	CD	19	Se 0.73 Sp 0.75	TP 22 FN 8	FP 18 TN 52	Very Low

TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis; CC: clinical criteria; NP: neuropathology

Studies: Döbert 2005, Launes 1991, Velakoulis 1998, Boutoleau-Bretonnière 2012, Bergman 1997, Holman 1992, Launes 1991, Masterman 1997, McMurdo 1994, Read 1995, Talbot 1998, Rollin-Sillaire 2012

99M—Tc-ECD-SPECT (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
99M—Tc-ECD-SPECT Visual assess.	2 AD vs no AD	CD	206	Se 0.33 to 0.93 Sp 0.73 to 0.95	TP 10 to 28 FN 2 to 20	FP 4 to 19 TN 51 to 66	Very Low
	1 FTD vs no FTD	CC	117	Se 0.96 Sp 0.99	TP 29 FN 1	FP 1 TN 69	Moderate
99M—Tc-ECD-SPECT All information	1 AD vs no AD	CD	89	Se 0.71 Sp 0.68	TP 21 FN 9	FP 22 TN 48	Low
99M—Tc-ECD-SPECT Automated	1 AD vs no AD	CD	89	Se 0.40 Sp 0.83	TP 12 FN 18	FP 12 TN 58	Moderate

TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis; CC: clinical criteria

Studies: Kaneta 2016, Tripathi 2010, Velakoulis 1998

CSF beta amiloide 1-42 (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CSF Amyloid beta 1-42	8 AD vs no AD **(1 LG DEM)**	CD	4.216	Se 0.43 to 0.90	TP 13 to 27	FP 12 to 38	Low
				Sp 0.45 to 0.83	FN 3 to 17	TN 32 to 58	
	5 AD vs other dem **(2 LG DEM)**	4CD 1NP	1.099	Se 0.71 to 1	TP 21 to 30	FP 21 to 43	Low
				Sp 0.38 to 0.70	FN 0 to 9	TN 27 to 49	
	1 AD vs VaD	CC	186	Se 0.65	TP 20	FP 36	Moderate
				Sp 0.48	FN 10	TN 34	
	1 AD vs DLB	CC	172	Se 0.65	TP 20	FP 23	Moderate
				Sp 0.67	FN 10	TN 47	
	1 AD vs no dem	CC	70	Se 0.84	TP 25	FP 11	Low
				Sp 0.84	FN 5	TN 59	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis; CC: clinical criteria; NP: neuropathology							

Studies: Andreasen 2001, Brandt 2008, Boutoleau-Bretonnière 2012, Duits 2014, Dumurgier 2015, Gabelle 2012, Ibach 2006, Knapskgog 2016, Maddalena 2003, Mulder 2010, Van Everbroeck 2003, Mattsson-Carlgren 2022, Tariciotti 2018

CSF beta amiloide 1-42/p-tau (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CSF beta amiloide 1-42/p-tau	1 AD vs no AD	CD	1.200	Se 0.81 to 0.85	TP 24 to 26	FP 11 to 14	Moderate
				Sp 0.80 to 0.84	FN 4 to 6	TN 56 to 59	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis							

Studies: Gabelle 2012 (the study had two different indipendent datasets from two clinics)

CSF beta amiloide 1-42/t-tau (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CSF beta amiloide 1-42/t-tau	1 AD vs no AD **(1 LG DEM)**	CD	1.731	Se 0.84 to 0.97	TP 25 to 29	FP 15 to 40	Moderate
				Sp 0.43 to 0.79	FN 1 to 5	TN 30 to 55	
	1 AD vs FTD	NP	100	Se 0.90	TP 27	FP 12	Moderate
				Sp 0.83	FN 3	TN 58	
	1 AD vs other dem **(1 LG DEM)**	CD	749	Se 0.97	TP 29	FP 28	Moderate
				Sp 0.60	FN 1	TN 42	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis; NP: neuropathology							

Studies: Gabelle 2012, Tariciotti 2018

CSF beta amiloide t-tau/1-42 (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CSF t-tau /beta amiloide 1-42	1 AD vs no AD	CC	1.149	Se 0.85	TP 26	FP 13	High
				Sp 0.82	FN 4	TN 57	
	1 AD vs other dem	CC	124	Se 0.75	TP 22	FP 18	Very Low
				Sp 0.75	FN 8	TN 52	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria							

Studies: Duits 2014, Ibach 2006

CSF beta amiloide 42/40 (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CSF beta amiloide 42/40	3 AD vs no AD	CD	367	Se 0.64 to 0.90	TP 19 a 27	FP 11 a 23	Very Low
				Sp 0.67 to 0.84	FN 3 a 11	TN 47 a 59	

TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis

Studies: Dumurgier 2015 (3 independent datasets from 3 diferent clinics)

Urinary AD7c-NTP (22ug/ml) (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
Urinary AD7c-NTP (22ug/ml)	1 AD vs no AD	CC	168	Se 0.59	TP 18	FP 19	Moderate
				Sp 0.73	FN 12	TN 51	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria							

Studies: Goodman 2007

Apoliprotein E (ApoE) ε4 ≥ 1 allele (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
ApoE ε4 ≥ 1 allele	1 AD vs other dem	NP	2.188	Se 0.65	TP 20	FP 22	Moderate
				Sp 0.68	FN 10	TN 48	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); NP: neuropathology							

Studies: Mayeux 1998

CSF Amyloid β 42/40 and p-Tau (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CSF Amyloid β 42/40 and p-Tau	1 AD vs no AD	CC	303	Se 0.87	TP 26	FP 6	Low
				Sp 0.91	FN 4	TN 64	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria							

Studies: Dumurgier 2015

CSF Amyloid β 1-42 and t-Tau (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CSF Amyloid β 1-42 and t-Tau	1 dem vs no dem	CC	94	Se 0.42	TP 13	FP 15	Moderate
				Sp 0.79	FN 17	TN 55	
	1 AD vs no AD	CC	94	Se 0.71	TP 21	FP 8	Low
				Sp 0.88	FN 9	TN 62	
	1 AD vs other dem	CC	66	Se 0.71	TP 21	FP 3	Low
				Sp 0.96	FN 9	TN 67	
	1 CJD vs no CJD	NP	250	Se 0.87	TP 26	FP 1	High
				Sp 0.98	FN 4	TN 69	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria; NP: neuropathology							

Studies: Van Everbroeck 2003, Frisoni 2009

CSF Amyloid β (Aβ) 1-42, t-Tau, p-Tau (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CSF Aβ 1-42, t-Tau, p-Tau	2 AD vs no AD	CD	225	Se 0.27 to 0.88	TP 8 to 26	FP 1 to 23	Very Low
				Sp 0.67 to 0.99	FN 4 to 22	TN 47 to 69	
CSF Aβ 1-42, t-Tau, p-Tau (≥ 2 of 3)	1 AD vs no AD	CC	1.149	Se 0.86	TP 26	FP 20	High
				Sp 0.72	FN 4	TN 50	
CSF Aβ 1-42 and t-Tau e/o p-Tau	1 AD vs no AD	CC	1.149	Se 0.74	TP 22	FP 10	High
				Sp 0.86	FN 8	TN 60	
CSF Aβ 1-42, t-Tau, p-Tau (2 of 3)	1 AD vs no AD	CC	147	Se 0.42	TP 13	FP 7	High
				Sp 0.90	FN 17	TN 63	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria; CD: clinical diagnosis							

Studies: Boutoleau-Bretonnière 2012, Duits 2014, Brandt 2008, Dumurgier 2015, Jahn 2011

CSF p-Tau (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CSF p-Tau	10 AD vs no AD **(1 LG DEM)**	CD	3.979	Se 0.33 to 0.86	TP 10 to 26	FP 6 to 28	Very Low
				Sp 0.60 to 0.92	FN 4 to 20	TN 42 to 64	
	1 AD vs FTD	NP	100	Se 0.99	TP 30	FP 10	Moderate
				Sp 0.85	FN 0	TN 60	
	5 AD vs other dem **(2 LG DEM)**	4CD 1NP	1.095	Se 0.63 to 0.94	TP 19 to 28	FP 10 to 56	Low
				Sp 0.20 to 0.86	FN 2 to 11	TN 14 to 60	
	1 AD vs no dem	CC	70	Se 0.67	TP 20	FP 26	Low
				Sp 0.23	FN 10	TN 44	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria; CD: clinical diagnosis							

Studies: Boutoleau-Bretonnière 2012, Brandt 2008, Duits 2014, Dumurgier 2015, Gabelle 2012, Knapskgog 2010, Ibach 2006, Maddalena 2003, Mulder 2010, Toledo 2012, Mattsson-Carlgren 2022, Tariciotti 2018

CSF p-Tau/amyloid β (Aβ) 1-42 (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CSF p-Tau/ Aβ 1-42	2 AD vs no AD	CD	1.434	Se 0.85 to 0.90	TP 26 to 27	FP 4 to 11	Very Low
				Sp 0.84 to 0.94	FN 3 to 4	TN 59 to 66	
	3 AD vs other dem **(1 LG DEM)**	2CD 1NP	302	Se 0.78 to 1	TP 23 to 30	FP 12 to 19	Low
				Sp 0.73 to 0.83	FN 0 to 7	TN 51 to 58	
	1 AD vs no dem	CC	70	Se 0.80	TP 24	FP 8	Moderate
				Sp 0.89	FN 6	TN 62	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria; CD: clinical diagnosis; NP: neuropathology							

Studies: Maddalena 2003, Duits 2014, Dumurgier 2015, Mattsson-Carlgren 2022

CSF t-Tau (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CSF t-Tau	10 AD vs no AD **(1 LG DEM)**	CD	3.978	Se 0.52 to 0.95	TP 16 to 28	FP 3 to 20	Very Low
				Sp 0.72 to 0.96	FN 2 to 14	TN 50 to 67	
	5 AD vs other dem **(2 LG DEM)**	3CD 1CC 1NP	1.055	Se 0.54 to 0.89	TP 16 to 27	FP 6 to 46	Low
				Sp 0.34 to 0.92	FN 3 to 14	TN 24 to 64	
	1 AD vs no dem	CC	46	Se 0.46	TP 14	FP 4	Low
				Sp 0.95	FN 16	TN 66	
	12 CJD vs no CJD **(1 LG DEM)**	4CD 1CC 7NP	3.796	Se 0.78 to 0.97	TP 23 to 29	FP 1 to 23	Low
				Sp 0.67 to 0.98	FN 1 to 7	TN 47 to 69	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria; CD: clinical diagnosis; NP: neuropathology							

Studies: Bahl 2009, Brandt 2008, Chohan 2010, Coulthart 2011, Duits 2014, Dumurgier 2015, Foutz 2017, Gabelle 2012, Hamlin 2010, Knapskgog 2016, Lattanzio 2017, Leitão 2016, Mulder 2010, Rohan 2015, Tagliapietra 2013, Van Everbroeck 2003, 2004, Yakushev 2010, Mattsson-Carlgren 2022, Tariciotti 2018, Fiorini 2020

CSF P-Tau/t-Tau (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CSF P-Tau/t-Tau	2 CJD vs no CJD	1CD 1NP	282	Se 0.86 to 0.97	TP 26 to 29	FP 7 to 8	Moderate
				Sp 0.88 to 0.90	FN 1 to 4	TN 62 to 63	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria							

Studies: Bahl 2009, Leitão 2016

CSF 14-3-3 (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CSF 14-3-3 ELISA	2 CJD vs no CJD	1CD 1NP	292	Se 0.89 to 0.97	TP 27 to 29	FP 1 to 4	Low
				Sp 0.95 to 0.98	FN 1 to 3	TN 66 to 69	

CSF 14-3-3 Immunoblotting	18 CJD vs no CJD **(1 LG DEM)**	12CD 1CC 5NP	6266	Se 0.81 to 1 Sp 0.28 to 1	TP 24 to 30 FN 0 to 6	FP 0 to 50 TN 20 to 70	Low
CSF 14-3-3 ACWA^	1 CJD vs no CJD	CD	268	Se 0.94 Sp 0.95	TP 28 FN 2	FP 4 TN 66	High
CSF 14-3-3 Multiple method	1 CJD vs no CJD	NP/CD	60 (NP) 84 (CD)	Se 0.91 Sp 0.44	TP 27 FN 3	FP 39 TN 31	Moderate
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria; CD: clinical diagnosis; NP: neuropathology							

Studies: Bahl 2009, Beaudry 1999, Burkhard 2001, Chohan 2011, Cuadro-Corrales 2006, Fourier 2017, Foutz 2017, Hamlin 2012, Kenney 2000, Lattanzio 2017, Lemstra 2000, Leitão 2016, Rohan 2015, Tagliapetra 2013, Tschampa 2005, Van Everbroeck 2003, Zerr 2000, Fiorini 2020

CSF 14-3-3 e amyloid β (Aβ) 1-42 (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested** **Pre-test probability of 30%**		**Certainty of evidence (GRADE)**
CSF 14-3-3 and Aβ 1-42	1 CJD vs no CJD	NP	250	Se 0.99 Sp 0.98	TP 30 FN 0	FP 1 TN 69	High
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); NP: neuropathology							

Studies: Van Everbroeck 2003

CSF 14-3-3 e T-tau (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested** **Pre-test probability of 30%**		**Certainty of evidence (GRADE)**
CSF 14-3-3 e T-tau	1 CJD vs no CJD	NP	351	Se 0.75 Sp 0.88	TP 22 FN 8	FP 8 TN 62	Moderate
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); NP: neuropathology							

Studies: Chohan 2010

CSF 14-3-3 e S100B (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CSF 14-3-3 e S100B	1 CJD vs non CJD	NP	411	Se 0.62	TP 19	FP 4	Moderate
				Sp 0.95	FN 11	TN 66	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); NP: neuropathology							

Studies: Chohan 2010

CSF T-tau e S100B (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CSF T-tau e S100B	1 CJD vs no CJD	NP	351	Se 0.59	TP 18	FP 4	Low
				Sp 0.95	FN 12	TN 66	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); NP: neuropathology							

Studies: Chohan 2010

CSF 14-3-3, T-tau e p-tau (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CSF 14-3-3, T-tau e p-tau	1 AD vs other dem	CD	44	Se 0.97	TP 29	FP 22	Very Low
				Sp 0.69	FN 1	TN 48	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis							

Studies: Boutoleau-Bretonnière 2012

CSF 14-3-3, T-tau e S100B (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CSF 14-3-3, T-tau e S100B	1 CJD vs CJD	NP	351	Se 0.57	TP 17	FP 3	Low
				Sp 0.96	FN 13	TN 67	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); NP: neuropathology							

Studies: Chohan 2010

Electroencephalography (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
EEG	1 AD vs no AD	CD	372	Se 0.70	TP 21	FP 42	High
				Sp 0.40	FN 9	TN 28	
	2 CJD vs no CJD	CD	202	Se 0.32 to 1	TP 10 to 30	FP 4 to 67	Very Low
				Sp 0.04 to 0.94	FN 0 to 20	TN 3 to 66	
	1 DLB vs no DLB	CD	387	Se 0.87	TP 26	FP 8	Moderate
				Sp 0.48	FN 4	TN 62	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis							

Studies: Engedal 2015, Tagliapietra 2013, Tschampa 2005

Creutzfeldt Jacobs Disease Criteria (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CJD Criteria European	1 CJD vs no CJD	NP	236	Se 0.91	TP 27	FP 50	Moderate
				Sp 0.28	FN 3	TN 20	
CJD Criteria	1	NP	236	Se 0.88	TP 26	FP 35	Low

French	CJD vs no CJD			Sp 0.50	FN 4	TN 35	
CJD Criteria Master 's	1 CJD vs no CJD	NP	236	Se 0.98	TP 29	FP 63	Low
				Sp 0.10	FN 1	TN 7	
New Criteria for sporadic CJD	1 CJD vs no CJD	NP/CD	74	Se 0.98	TP 29	FP 20	Low
				Sp 0.71	FN 1	TN 50	
WHO CJD Criteria	2 CJD vs no CJD	1CC 1NP	306	Se 0.89 to 0.92	TP 27 to 28	FP 20 to 20	Moderate
				Sp 0.71 to 0.71	FN 2 to 3	TN 50 to 50	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria; CD: clinical diagnosis; NP: neuropathology							

Studies: Brandel 2000, Heath 2010, Zerr 2009

Neuron-specific enolase (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
Neuron-specific enolase	2 CJD vs CJD	CD	295	Se 0.73 to 0.80	TP 22 to 24	FP 6 to 7	Moderate
				Sp 0.90 to 0.91	FN 6 to 8	TN 63 to 64	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis							

Studies: Bahl 2009, Beaudry 1999

RT-QuIC (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
RT-QuIC	3 CJD vs no CJD **(1 LG DEM)**	1CC 2NP	961	Se 0.82 to 0.96	TP 25 to 29	FP 0 to 1	Moderate
				Sp 0.99 to 1	FN 1 to 5	TN 69 to 70	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); NP: neuropathology; CC: clinical criteria							

Studies: Foutz 2017, Lattanzio 2017, Fiorini 2020

CSF S100B (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
S100B 1 ng/mL	1 CJD vs no CJD	NP	412	Se 0.65 Sp 0.90	TP 20 FN 10	FP 7 TN 63	Moderate
S100B 2.5 ng/mL	2 CJD vs no CJD	CD	1.053	Se 0.87 to 0.88 Sp 0.85 to 0.87	TP 26 to 26 FN 4 to 4	FP 9 to 10 TN 60 to 61	Moderate
S100B 4.2 ng/mL	1 CJD vs no CJD	NP	924	Se 0.52 Sp 0.97	TP 16 FN 14	FP 2 TN 68	Moderate
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis; NP: neuropathology							

Studies: Chohan 2010, Beaudry 1998, Coulthart 2011

^{123}I-FP-CIT-SPECT (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
Single camera							
^{123}I-FP-CIT-SPECT	1 DLB vs no DLB	NP	23	Se 1 Sp 0.92	TP 30 FN 0	FP 6 TN 64	Low
	1 DLB vs other dem	CC	31	Se 0.90 Sp 0.91	TP 27 FN 3	FP 6 TN 64	Moderate
Multiple camera							
^{123}I-FP-CIT-SPECT	4 DLB vs no DLB **(1 LG DEM)**	2CC 2NP	179	Se 0.63 to 0.92 Sp 0.83 to 1	TP 19 to 28 FN 2 to 11	FP 0 to 12 TN 58 to 70	Low
	1 DLB vs other dem	NP	20	Se 0.88 Sp 1	TP 26 FN 4	FP 0 TN 70	Moderate
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria; NP: neuropathology							

Studies: Walker 2007, Walker 2009, Thomas 2017, O'Brien 2009, Kemp 2011, Treglia 2012, Jung 2018

^{123}I-IMP-SPECT (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
^{123}I-IMP-SPECT	1 DLB vs no DLB	CC	101	Se 0.62	TP 19	FP 18	Low
				Sp 0.75	FN 11	TN 52	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria							

Studies: Sakamoto 2014

^{123}I-IMP-SPECT and ^{123}I-MIBG myocardial scintigraphy (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
^{123}I-IMP-SPECT and ^{123}I-MIBG myocardial scintigraphy	1 DLB vs no DLB	CC	100	Se 0.88	TP 26	FP 10	Moderate
				Sp 0.86	FN 4	TN 60	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria							

Studies: Sakamoto 2014

^{123}I-MIBG myocardial scintigraphy (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
^{123}I-MIBG myocardial scintigraphy	6 DLB vs no DLB **(1 LG DEM)**	2CD 4NP	663	Se 0.67 to 1	TP 20 to 30	FP 0 to 18	Low
				Sp 0.75 to 1	FN 0 to 10	TN 52 to 70	
	1 DLB vs other dem	Non specificato	31	Se 0.90	TP 27	FP 7	Moderate
				Sp 0.91	FN 3	TN 63	
	1 PDD+DLB vs other dem	CD	96	Se 0.95	TP 28	FP 9	Moderate
				Sp 0.87	FN 2	TN 61	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis; NP: neuropathology							

Studies: Estorch 2008, Hanyu 2006, Manabe 2017, Treglia 2012, Sakamoto 2014, Sakamoto 2017, Slaets 2015, Matsubara 2022

Biomarker formulas (specialist care setting)

Outcomes	No. of Studies	Reference standard	No. of participants	Accuracy: range	Effect per 100 patients tested		Certainty of evidence (GRADE)
					Pre-test probability of 30%		
BF Hulstaert	1 AD vs no AD	CC	1.149	Se 0.93	TP 28	FP 18	High
				Sp 0.74	FN 2	TN 52	
BF Mattson	1 AD vs no AD	CC	1.149	Se 0.80	TP 24	FP 10	High
				Sp 0.85	FN 6	TN 60	
BF Mulder	1 AD vs no AD	CC	1.149	Se 0.93	TP 28	FP 19	High
				Sp 0.73	FN 2	TN 51	
BF Schoonenboom	1 AD vs no AD	CC	1.149	Se 0.91	TP 27	FP 15	High
				Sp 0.78	FN 3	TN 55	

TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria

Studies: Duits 2014

Mass spectrometry (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
Mass spectrometry	1 AD vs no AD	CC	86	Se 0.87	TP 26	FP 12	Moderate
				Sp 0.83	FN 4	TN 58	

TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria

Studies: Jahn 2011

Skin biopsy (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
Skin biopsy	1 CADASIL vs CADASIL-like	CD	90	Se 0.96	TP 29	FP 48	High
				Sp 0.68	FN 1	TN 22	

TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis

Studies: Ampuero 2009

Corticobasal Degeneration Consensus Criteria (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CDCC	1 CBD vs CBD	NP	33	Se 0.93	TP 28	FP 68	Low
				Sp 0.03	FN 2	TN 2	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); NP: neuropathology							

Studies: Alexander 2014

Lewy body Composite Risk Score (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
LBCRS ≥ 3	1 DLB vs AD	CC	153	Se 0.94	TP 28	FP 15	Moderate
				Sp 0.78	FN 2	TN 55	
	1 DLB vs other dem	CC	177	Se 0.98	TP 29	FP 10	Moderate
				Sp 0.86	FN 1	TN 60	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria							

Studies: Skogseth 2017

REM Sleep Behavior Disorder (RBD), visual hallucinations (VH), Parkinsonism (P), fluctuating attention and concentration (FAC) (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
RBD o ≥ 2 of VH, P, FAC	1 DLB vs no DLB	CC	234	Se 0.90	TP 27	FP 19	High
				Sp 0.73	FN 3	TN 51	
≥ 2 di VH, P, FAC	1 DLB vs no DLB	CC	234	Se 0.85	TP 26	FP 19	High
				Sp 0.73	FN 4	TN 51	
≥ 2 di VH, P, RBD	1 DLB vs no DLB	CC	234	Se 0.83	TP 25	FP 10	High
				Sp 0.85	FN 5	TN 60	
≥ 2 of VH, P, FAC, RBD	1 DLB vs no DLB	CC	234	Se 0.88	TP 26	FP 19	High
				Sp 0.73	FN 4	TN 51	

TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CC: clinical criteria

Studies: Ferman 2011

DLB Consensus Criteria (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
DLB CC	1 DLB vs other dem	NP	55	Se 0.80	TP 24	FP 8	Low
				Sp 0.89	FN 6	TN 62	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); NP: neuropathology							

Studies: Skogseth 2017

Movement Disorders Criteria for PDD (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
MDCPD ≤ 120	1 PDD vs no PDD	CD	40	Se 0.80	TP 24	FP 4	Low
				Sp 0.95	FN 6	TN 66	
MDCPD ≤ 123	1 PDD vs no PDD	CD	40	Se 0.94	TP 28	FP 15	Low
				Sp 0.78	FN 2	TN 55	
MDCPD ≤ 132	1 PDD vs no PDD	CD	40	Se 0.98	TP 29	FP 38	Low
				Sp 0.45	FN 1	TN 32	
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis							

Studies: Kiesmann 2013

Hachinski ischemic score (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
HIS ≥ 5	1 VaD+MD vs AD	CD	214	Se 0.86	TP 26	FP 19	Low
				Sp 0.73	FN 4	TN 51	

HIS ≥ 7	1 VaD vs AD+MD	CC	110	Se 0.56 Sp 0.66	TP 17 FN 13	FP 24 TN 46	Low
	1 VaD vs other dem	NP	190	Se 0.69 Sp 0.92	TP 21 FN 9	FP 6 TN 64	Moderate
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); CD: clinical diagnosis; CC: clinical criteria; NP: neuropathology							

Studies: Siritho 2006, Bacchetta 2007

Alzheimer's disease diagnostic and treatment centers criteria (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested** **Pre-test probability of 30%**		**Certainty of evidence (GRADE)**
ADDTCC possible	1 VaD vs AD+MD	NP	89	Se 0.70 Sp 0.78	TP 21 FN 9	FP 15 TN 55	Moderate
ADDTCC probable	1 VaD vs AD+MD	NP	89	Se 0.25 Sp 0.91	TP 8 FN 22	FP 6 TN 64	Moderate
ADDTCC	1 VaD vs AD+MD	NP	110	Se 0.58 Sp 0.74	TP 17 FN 13	FP 18 TN 52	Low
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); NP: neuropathology							

Studies: Gold 2002

National Institute of Neurological Disorders and Stroke (NINDS) and the Association Internationale pour la Recherche et l'Enseignement en Neurosciences (AIREN) (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested** **Pre-test probability of 30%**		**Certainty of evidence (GRADE)**
NINDS-AIREN possible	1 VaD vs AD+MD	NP	89	Se 0.55 Sp 0.84	TP 17 FN 13	FP 11 TN 59	Moderate
NINDS-AIREN probable	1 VaD vs AD+MD	NP	89	Se 0.20 Sp 0.93	TP 6 FN 24	FP 5 TN 65	Moderate
NINDS-AIREN	1 VaD vs AD+MD	NP	110	Se 0.56 Sp 0.73	TP 17 FN 13	FP 19 TN 51	Low
TP (people with dementia, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without dementia, **true negatives**); FP (people incorrectly classified with dementia, **false positives**); NP: neuropathology							

Studies: Gold 2002

MILD COGNITIVE IMPAIRMENT (MCI) IN PRIMARY AND SPECIALIST CARE SETTINGS

Mini-Mental State Examination (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
MMSE 24-25	4 MCI vs no MCI	3CD 1CC	574	Se 0.17 to 0.76 Sp 0.75 to 0.96	TP 5 to 23 FN 7 to 25	FP 3 to 18 TN 52 to 67	Low
MMSE 25-26	6 MCI vs no MCI	4CD 2CC	2.805	Se 0.06 to 0.87 Sp 0.74 to 1	TP 2 to 26 FN 4 to 28	FP 0 to 18 TN 52 to 70	Very Low
MMSE 26-27	1 MCI vs no MCI	CD	89	Se 0.53 Sp 0.78	TP 16 FN 14	FP 15 TN 55	Moderate
MMSE 27-28	3 MCI vs no MCI	2CD 1CC	701	Se 0.29 to 0.85 Sp 0.45 to 0.92	TP 9 to 26 FN 4 to 21	FP 6 to 38 TN 32 to 64	Low
TP (people with MCI, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without MCI, **true negatives**); FP (people incorrectly classified with MCI, **false positives**); CC: clinical criteria; CD: clinical diagnosis							

Studies: Dong 2013, Larner 2015, Luis 2009, Ravaglia 2005, Biundo 2013, Mellor 2016, Saxton 2009, Smith 2007, Yu 2012

Montreal Cognitive Assessment (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
MoCA 19-20	1 MCI vs no MCI	CD	211	Se 0.80 Sp 0.92	TP 24 FN 6	FP 6 TN 64	Low
MoCA < 21	1 MCI vs no MCI	CD	693	Se 0.37 Sp 0.78	TP 11 FN 19	FP 15 TN 55	Very Low
MoCA 21-22	1 MCI vs no MCI	CD	980	Se 0.69 Sp 0.64	TP 21 FN 9	FP 25 TN 45	Moderate
MoCA 22-23	2 MCI vs no MCI	2CC	1.064	Se 0.87 to 0.96 Sp 0.73 to 0.95	TP 26 to 29 FN 1 to 4	FP 4 to 19 TN 51 to 66	Low
MoCA 26	6 MCI vs no MCI **(1 LG DEM)**	4CD 2CC	9.994	Se 0.80 to 1 Sp 0.31 to 0.82	TP 24 to 30 FN 0 to 6	FP 13 to 48 TN 22 to 57	Low
TP (people with MCI, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without MCI, **true negatives**); FP (people incorrectly classified with MCI, **false positives**); CC: clinical criteria; CD: clinical diagnosis							

Studies: Dong 2011, Yu 2012, Luis 2009, Mellor 2016, Larner 2017, Lu 2011, Smith 2007, Dautzenberg 2022

Clinical Dementia Rating (specialist care setting setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CDR 0,5	1 MCI vs no MCI	CD	697	Se 0.24	TP 7	FP 4	Moderate
				Sp 0.95	FN 23	TN 66	
TP (people with MCI, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without MCI, **true negatives**); FP (people incorrectly classified with MCI, **false positives**); CD: clinical diagnosis							

Studies: Woolf 2016

Clock Drawing Test (specialist care setting setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CDT Sunderland 5	2 MCI vs no MCI	CD	257	Se 0.06 to 0.40	TP 2 to 12	FP 4 to 10	Low
				Sp 0.85 to 0.95	FN 18 to 28	TN 60 to 66	
CDT Sunderland 7	1 MCI vs no MCI	CD	89	Se 0.60	TP 18	FP 4	Moderate
				Sp 0.95	FN 12	TN 66	
CDT Sunderland 8	1 MCI vs no MCI	CD	89	Se 0.67	TP 20	FP 7	Moderate
				Sp 0.90	FN 10	TN 63	
CDT Rouleau 5	1 MCI vs no MCI	CC	108	Se 0.43	TP 13	FP 6	Low
				Sp 0.92	FN 17	TN 64	
CDT Rouleau 7-8	3 * MCI vs no MCI	CD	643	Se 0.56 to 0.79	TP 17 to 24	FP 5 to 23	Low
				Sp 0.66 to 0.93	FN 6 to 13	TN 46 to 65	
CDT Shulman 1	1 MCI vs no MCI	CC	105	Se 0.40	TP 12	FP 28	Low
				Sp 0.60	FN 18	TN 42	
CDT Cahn 6	1 MCI vs no MCI	CD	89	Se 0.60	TP 18	FP 5	Low
				Sp 0.93	FN 12	TN 65	
CDT Cahn 7	1 MCI vs no MCI	CD	89	Se 0.75	TP 22	FP 17	Low
				Sp 0.76	FN 8	TN 53	
CDT Cahn 8	1 MCI vs no MCI	CD	89	Se 0.83	TP 25	FP 24	Low
				Sp 0.66	FN 5	TN 46	
CDT Wolf-Klein 6	1 MCI vs no MCI	CD	168	Se 0.23	TP 7	FP 8	Low
				Sp 0.89	FN 23	TN 62	

CDT Todd 6-6.5	1 MCI vs no MCI	CD	465	Se 0.44 Sp 0.81	TP 13 FN 17	FP 13 TN 57	Moderate
CDT Freedman 9-10	1 MCI vs no MCI	CD	465	Se 0.41 Sp 0.83	TP 12 FN 18	FP 12 TN 58	Moderate
TP (people with MCI, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without MCI, **true negatives**); FP (people incorrectly classified with MCI, **false positives**); CC: clinical criteria; CD: clinical diagnosis							

Studies: Ravaglia 2005, Yamamoto 2004, Ramlall 2014, Lee 2008, Beinhoff 2005

AD8 (specialist care setting setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested** **Pre-test probability of 30%**		**Certainty of evidence (GRADE)**
AD8 ≥ 8	2 MCI vs no MCI	1CD 1CC	200	Se 0.97 to 1 Sp 0.17 to 0.77	TP 29 to 30 FN 0 to 1	FP 16 to 58 TN 12 to 54	Low
TP (people with MCI, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without MCI, **true negatives**); FP (people incorrectly classified with MCI, **false positives**); CC: clinical criteria; CD: clinical diagnosis							

Studies: Larner 2015, Razavi 2014

Informant Questionnaire on Cognitive Decline in the Elderly (specialist care setting setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested** **Pre-test probability of 30%**		**Certainty of evidence (GRADE)**
IQCODE ≥3.4	1 MCI vs no MCI	CC	57	Se 0.46 Sp 0.89	TP 14 FN 16	FP 8 TN 62	Low
TP (people with MCI, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without MCI, **true negatives**); FP (people incorrectly classified with MCI, **false positives**); CC: clinical criteria							

Studies: Razavi 2014

Mini-Addenbrooke's Cognitive Examination (specialist care setting setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested** **Pre-test probability of 30%**		**Certainty of evidence (GRADE)**
Mini-ACE 25	2	2CD	717	Se 0.95 to 0.97	TP 28 to 29	FP 34 to 36	Moderate

	MCI vs no MCI			Sp 0.49 to 0.51	FN 1 to 2	TN 34 to 36	
TP (people with MCI, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without MCI, **true negatives**); FP (people incorrectly classified with MCI, **false positives**); CD: clinical diagnosis							

Studies: Larner 2017, Williamson 2018

Trail Making Test-A (specialist care setting setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
TMT-A 72-72,5	2 MCI vs no MCI	2CC	717	Se 0.48 to 0.77	TP 14 to 23	FP 15 to 26	Low
				Sp 0.63 to 0.78	FN 7 to 16	TN 44 to 55	
TP (people with MCI, **true positives**); FN (people incorrectly classified as healthy, **false negatives**); TN (people without MCI, **true negatives**); FP (people incorrectly classified with MCI, **false positives**); CC: clinical criteria							

Studies: Ramlall 2014, Wei 2018

Review question 3a (RQ NICE). What drugs that may worsen cognitive decline are commonly prescribed in people diagnosed with dementia?

No systematic literature reviwe was conducted for this review question

Review question 3b (RQ NICE). What are the most effective tools to identify drugs that may be causing cognitive decline?

Risk of dementia in population exposed to differente levels of anticholinergic burden, measured with the Anticholinergic Risk Scale (ARS)					
Population: older adults **Setting:** specialist care setting **Intervention:** anticholinergic burden (ARS ≥ 1) **Comparator:** no anticholinergic burden (ARS = 0)					
Outcomes	**Anticipated absolute effect (95% CI)**		**Risk Ratio (95% CI)**	**No. of participants (studies)**	**Certainty of evidence (GRADE)**
	Risk with no ARS	**Risk with ARS**			
Dementia-ARS≥1	116 per 1,000	149 per 1,000 (145 to 153)	**RR 1.28** **(1.25 a 1.32)**	117,166 (2 cohorts)	Low[a]
CI: confidence interval; **RR**: risk ratio a: I2>75% Studies: Brombo 2018, Hsu 2021					
Studies	**Population**	**ARS 1**	**ARS 2**	**ARS 3**	**ARS 4**
Brombo[1] 2018	1,123	**ARS≥1** M1 2.43 (1.26-4.69) M2 2.19 (1.09-4.40) M3 1.49 (0.60-3.70)	-	-	-
Hsu 2021[2]	116,043	**Age 65-74** 10.32 (9.56-11. 14) **Age 75-84** 8.22 (7.52-8.98) **Age 85+** 6.61 (5.10-8.56)	**Age 65-74** 3.41 (3.06-3.80) **Age 75-84** 3.22 (2.82-3.68) **Age 85+** 2.72 (1.85-4.01)	**Age 65-74** 2.38 (2.10-2.70) **Age 75-84** 2.20 (1.89-2.56) **Age 85+** 1.39 (0.84-2.29)	**Age 65-74** 7.16 (6.36-8.06) **Age 75-84** 5.27 (4.51-6.16) **Age 85+** 4.63 (2.90-7.40)

[1] Odds Ratio; Model 1: unadjusted. Model 2: adjusted for age, gender and education. Model 3: adjusted for age, gender, education, smoke, MMSE score at discharge, change in MMSE score during follow-up, ACB/ARS scores at first follow-up, hypertension, coronary artery disease, renal failure, anemia, and infectious diseases.

[2] Odds Ratio; models were adjusted for gender and comorbidities over time (measured with Charlson Comorbidity Index) and for the average daily dose of drugs with anticholinergic properties (calculated on the basis of the defined daily dose).

Risk of dementia in population exposed to differente levels of anticholinergic burden, measured with Anticholinergic Cognitive Burden Scale (ACB)						
Population: older adults assessed by ACB **Setting:** specialist care setting **Intervention:** anticholinergic burden (ACB ≥ 1) **Comparator:** no anticholinergic burden (ACB = 0)						
Outcomes	**Anticipated absolute effect (95% CI)**			**Risk Ratio (95% CI)**	**No. of participants (studies)**	**Certainty of evidence (GRADE)**
	Risk with no ACB	**Risk with ACB**				
Dementia in ACB=1	171 per 1,000	**170 per 1.000** (134 to 216)		**RR 0.99 (0.78 to 1.26)**	1360 (2 cohorts)	Low[b,c]
Dementia in ACB≥1	123 per 1,000	**126 per 1.000** (122 to 129)		**RR 1.02 (0.99 to 1.05)**	119,496 (2 cohorts)	Low[b]
Dementia in ACB=1-2	58 per 1,000	**54 per 1.000** (52 to 57)		**RR 0.94 (0.90 to 0.98)**	675,160 (2 cohorts)	Low[d]
Dementia in ACB≥2	58 per 1,000	**63 per 1.000** (62 to 64)		**RR 1.08 (1.06 to 1.11)**	748,739 (3 cohorts)	Low[d]
Dementia in ACB=3	69 per 1,000	**129 per 1.000** (85 to 196)		**RR 1.88 (1.24 to 2.84)**	3,045 (1 cohort)	Low [c]
Dementia in ACB≥2 in PD	195 per 1,000	**177 per 1.000** (140 to 224)		**RR 0.91 (0.72 to 1.15)**	1,232 (1 cohort)	Low[b,c]
Dementia in ACB low (≤2) vs high (≥3)	89 per 1,000	**368 per 1.000** (152 to 893)		**RR 4.14 (1.71 to 10.05)**	109 (1 cohort)	Low[c]
CI: confidence interval; **RR**: risk ratio a. I^2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; Studies: Brombo 2018, Chuang 2017, Grossi 2019, Hafdi 2020, Hsu 2021, Liu 2020						
Studies	**Population**	**ACB 1**	**ACB 2**	**ACB 3**	**ACB ≥ 4**	**ACB ≥ 5**
Brombo 2018[1]	1,123	**ACB≥1** M1 2.38 (1.37-4.13) M2 2.27 (1.28-4.02) M3 2.77 (1.39-5.54)	-	-	-	-
Chuang 2017[2]	585	**ACB≥1** **M1** 1.65 (1.05-2.61) **M2** 1.67 (1.06-2.66) **M3** 1.63 (1.02-2.60)	**ACB≥2** **M1** 0.91 (0.54-1.54) **M2** 0.91 (0.54-1.53) **M3** 0.90 (0.53-1.52)	-	-	-
Grossi 2019[3]	13,004	**ACB 1-2** **unadj** 1.26 (0.95-1.67) **adj** 0.89 (0.68-1.17)		**unadj** 1.70 (1.09-2.65) **adj** 1.28 (0.82-2.00)	-	-
Hafdi 2020[4]	3,526	**< 3 vs no ACB** **unadj** 1.08 (0.81-1.44) **adj** 0.92 (0.68-1.26)		**≥3 vs no ACB** **unadj** 1.76 (1.21-2.75) **adj** 1.41 (0.88-2.25)		
Hsu 2021[5]	116,043	**65-74** 2.88 (2.66-3.12) **75-84** 2.01	**65-74** 6.23 (5.18-7.48) **75-84** 2.98	**65-74** 9.15 (8.38-9.99) **75-84** 6.18	**65-74** 9.20 (8.42-10.05) **75-84** 5.44 (4.24-6.97) **85+** 4.76	-

		(1.55-2.61) **85+** 2.31 (1.80-2.97)	(2.14-4.15) **85+** 4.07 (1.99-8.33)	(5.11-7.48) **85+** 6.31 (4.65-8.58)	(3.54-6.39)	
Liu 2020[6]	790,240	**ACB 1-2** 1.042 (0.848-1.084)	**2-3** 1.13 (0.94-1.29)	**3-5** 0.99 (0.99-1.36)	**≥5** 1.32 (1.04-1.53)	**ACB 1-2** 1.042 (0.848-1.084)

1. OR. Model 1: unadjusted. Model 2: adjusted for age, gender and education. Model 3: adjusted for age, gender, education, smoke, MMSE score at discharge, change in MMSE score during follow-up, ACB/ARS scores at first follow-up, hypertension, Coronary artery disease, renal failure, anemia, and infectious diseases.
2. HR. Model 1: adjusted for gender, ethnicity, education (years) and time to follow-up. Model 2: adjusted for smoke and alcohol. Model 3: adjusted for number of cardiovascular comorbidities.
3. IRR. Adjusted for gender, age, education, social class; accomodation, recruitment center, study arm; health condition at Y0 or Y2, self-reported health condition at Y2, disability at Y2, MMSE at Y2, MMSE orientation score at Y2, MMSE score reduction between Y0 and Y2, and self-reported change in memory function between Y0 and Y2.
4. HR. Adjusted for age, history of cardiovascular disease and/or stroke, education, MMSE at baseline, and Geriatric Depression Scale at baseline.
5. OR. The models were adjusted for sex and time-varying comorbidities (Charlson comorbidity index) and for the average daily dose of drugs with anticholinergic properties (calculated from the defined daily dose).
6. HR. Models were adjusted for gender, age, education, insurance premium, comorbidity, location, level of urbanization, and level of care.

Studies	**Population**	**ACB law (≤2) versus high (≥3)**
Naharci 2017[1]	109	**unadj** 4.17 (1.51-11.52) **adj** 4.18 (1.43-12.21)

1. Adjusted through backward stepwise elimination of variables including age, gender, smoke, hyoertension, diabetes, ACB total score ≥3 e polypharmacy.

Studies	**Population**	**ACB≥2 in Parkinson Disease**
Sheu 2019[1]	1,232	**adj HR:** 0.97 (0.72-1.27) **Cumulative minimum doses: 91-365** aHR: 1.34 (0.51-3.49); **366-730** aHR: 2.28 (0.94-5.54); **731-1095** aHR: 2.50 (1.01-6.22); **>1095** aHR: 3.06 (1.35-6.97)
		SAA in Parkinson Disease
Ehrt 2010[2]	235 76 8y FU	Dementia at baseline: non-users 21% (29/133) vs users 32.4% (33/102) Dementia at 8 years FU: non-users 30% (6/20) vs users 64.3% (36/56)

1. Adjusted variables included age, sex, duration of Parkinson's disease before the index date, conditions (hypertension, stroke, hypercholesterolemia, diabetes mellitus, depression, anxiety, psychotic disorders, alcohol-related disorders, sleep disorders, and head injury), and medications (antihypertensives, antidiabetics, anticoagulants, antihyperlipidemics, antidepressants, benzodiazepines, and antipsychotics).
SAA: serum anticholinergic activity

Studies	Population	serum anticholinergic activity
Ancelin 2006[1]	327	**MCI:** users 80% (66%-94%) vs non-users 35% (CI 30%-41%); AR 19%; adj OR 5.12 (1.94-13.51) **Demenza:** users 16% vs non-users 14%

AR: Attributable risk; Adjusted for age, sex, education level, untreated depression, and treated hypertension.

[1] primary care setting

Studies	Population	Clinician's rated Anticholinergic Scale
Han 2008[1]	544	"Cumulative anticholinergic exposure was associated with poorer performance on short term verbal memory and executive function"

[1] Only men.

Studies	Population	Clinician's rated Anticholinergic Scale
Sittironnarit 2011	768 sani 133 MCI 211 AD	"MCI and AD: no differences between users and non-users in MMSE, CDR and other cognitive measures HC: modest negative impact of ACL drugs on cognitive measures"

Review question 4 (RQ NICE). What are the most effective methods of differentiating dementia or dementia with delirium from delirium alone?

Prevalence of dementia: 30% based on Carpenter et al. 2019 "Accuracy of Dementia Screening Instruments in Emergency Medicine: A Diagnostic Meta-analysis"

Modified Richmond Agitation Sedation Scale (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
mRASS	1 dem vs no dem	CC	285	Se 0.27 (0.14. 0.43)	TP 8	FP 6	Moderate
				Sp 0.91 (0.87. 0.95)	FN 22	TN 64	
	1 del vs no del	CC	285	Se 0.70 (0.46. 0.88)	TP 21	FP 5	Moderate
				Sp 0.93 (0.89. 0.96)	FN 9	TN 65	
TP (people with dementia or delirium, **true positives**); FN (people uncorrectly classified healthy, **false negatives**); TN (people without dementia or without delirium, **true negatives**); FP (people correctly classified with dementia or with delirium, **false positives**); CC: clinical criteria							

Studies: Grossman 2017 (consecutive patients aged ≥65 attending the emergency department)

Prevalence of dementia: 30% based on Carpenter et al. 2019 "Accuracy of Dementia Screening Instruments in Emergency Medicine: A Diagnostic Meta-analysis"

4A's Test (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
4AT	1 dem vs no dem	CD	378	Se 0.84 (0.74. 0.91)	TP 25	FP 26	Moderate
				Sp 0.63 (0.57. 0.69)	FN 5	TN 44	
	1 del vs no del	CD	350	Se 0.93 (0.83. 0.98)	TP 28	FP 6	Moderate
				Sp 0.91 (0.88. 0.94)	FN 2	TN 64	
TP (people with dementia or delirium, **true positives**); FN (people uncorrectly classified healthy, **false negatives**); TN (people without dementia or without delirium, **true negatives**); FP (people correctly classified with dementia or with delirium, **false positives**); CD: clinical diagnosis							

Studies: O'Sullivan 2017 (consecutive patients aged ≥65 attending the emergency department)

Prevalence of dementia: 30% based on Carpenter et al. 2019 "Accuracy of Dementia Screening Instruments in Emergency Medicine: A Diagnostic Meta-analysis"

6-item Cognitive Impairment Test (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
6-CIT 8-9 (post-hoc optimal)	1 dem vs no dem	CD	368	Se 0.84 (0.73–0.91)	TP 25	FP 17	Moderate
				Sp 0.76 (0.71–0.81)	FN 5	TN 53	
6-CIT 9-10	1	CD	368	Se 0.81 (0.70–0.89)	TP 24	FP 17	Moderate

(pre specified)	dem vs no dem			Sp 0.76 (0.71–0.81)	FN 6	TN 53	
6-CIT 9-10 (pre specified)	1 del vs no del	CD	378	Se 0.89 (0.77–0.96)	TP 27	FP 18	Moderate
				Sp 0.74 (0.68–0.78)	FN 3	TN 52	
6-CIT 13-14 (post-hoc optimal)	1 del vs no del	CD	378	Se 0.83 (0.70–0.92)	TP 25	FP 9	Moderate
				Sp 0.87 (0.83–0.91)	FN 5	TN 61	
TP (people with dementia or delirium, **true positives**); FN (people uncorrectly classified healthy, **false negatives**); TN (people without dementia or without delirium, **true negatives**); FP (people correctly classified with dementia or with delirium, **false positives**); CD: clinical diagnosis							

Studies: O'Sullivan 2017 (consecutive patients aged ≥65 attending the emergency department)

Prevalence of dementia: 30% based on Carpenter et al. 2019 "Accuracy of Dementia Screening Instruments in Emergency Medicine: A Diagnostic Meta-analysis"

Confusion Assessment Method (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CAM≥7 symptoms	1 dem vs no dem or del	CC	154	Se 0.27 (0.18. 0.38)	TP 8	FP 12	Low
				Sp 0.83 (0.71. 0.92)	FN 22	TN 58	
	1 del vs no dem or del	CC	100	Se 0.95 (0.83. 0.99)	TP 28	FP 12	Low
				Sp 0.83 (0.71. 0.92)	FN 2	TN 58	
	1 del+dem vs no dem or del	CC	168	Se 0.98 (0.94. 1)	TP 29	FP 12	Low
				Sp 0.83 (0.71. 0.92)	FN 1	TN 58	
TP (people with dementia or delirium, **true positives**); FN (people uncorrectly classified healthy, **false negatives**); TN (people without dementia or without delirium, **true negatives**); FP (people correctly classified with dementia or with delirium, **false positives**); CC: clinical criteria							

Studies: Cole 2002 (people admitted to a medical department from the emergency department).
Patients with dementia were diagnosed using the IQCODE with a cut-off of 3.51 after admission.

Prevalence of dementia: 30% based on Carpenter et al. 2019 "Accuracy of Dementia Screening Instruments in Emergency Medicine: A Diagnostic Meta-analysis"

Short Portable Mental Status Questionnaire (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
SPMSQ>5	1 dem[1] vs no OBS	CD	215	Se 0.67 (0.22. 0.96)	TP 20	FP 0	Very Low
				Sp 1 (0.98. 1)	FN 10	TN 70	
	1 del[2] vs no OBS	CD	233	Se 0.17 (0.07. 0.32)	TP 5	FP 0	Very Low
				Sp 1 (0.98. 1)	FN 25	TN 70	
	1 del+dem vs no OBS	CD	198	Se 0.78 (0.56. 0.93)	TP 23	FP 0	Very Low
				Sp 1 (0.98. 1)	FN 7	TN 70	

TP (TP (people with dementia or delirium, **true positives**); FN (people uncorrectly classified healthy, **false negatives**); TN (people without dementia or without delirium, **true negatives**); FP (people correctly classified with dementia or with delirium, **false positives**); CD: clinical diagnosis; OBS: organic brain syndrome; [1]dementia without delirium; [2]delirium without dementia

Studies: Erkinjuntti 1987 (patients hospitalized)

Prevalence of dementia: 30% based on Carpenter et al. 2019 "Accuracy of Dementia Screening Instruments in Emergency Medicine: A Diagnostic Meta-analysis"

Cognitive Test for Delirium – Spatial Span Forward (CTD-SSF) (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
CTD-SSF	1 dem vs no dem	CD	215	Se 0.15 (0.03. 0.38)	TP 5	FP 2	Very Low
				Sp 0.97 (0.87. 1)	FN 25	TN 68	
	1 del vs no del	CD	233	Se 0.65 (0.48. 0.79)	TP 20	FP 2	Very Low
				Sp 0.97 (0.87. 1)	FN 10	TN 68	
	1 del+dem vs no dem+del	CD	198	Se 0.63 (0.46. 0.77)	TP 19	FP 2	Very Low
				Sp 0.97 (0.87. 1)	FN 11	TN 68	
TP (people with dementia or delirium, **true positives**); FN (people uncorrectly classified healthy, **false negatives**); TN (people without dementia or without delirium, **true negatives**); FP (people correctly classified with dementia or with delirium, **false positives**); CD: clinical diagnosis							

Studies: Leonard 2016

Prevalence of dementia: 30% based on Carpenter et al. 2019 "Accuracy of Dementia Screening Instruments in Emergency Medicine: A Diagnostic Meta-analysis"

Observational Scale of Level of Arousal (OSLA) (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
OSLA cutoff 3-4	1 del vs no del[1]	CC*	114	Se 0.85 (0.72. 0.93)	TP 26	FP 13	Very Low
				Sp 0.82 (0.70. 0.91)	FN 4	TN 57	
	1 dem+del vs dem	CC*	59	Se 0.74 (0.55. 0.88)	TP 22	FP 3	Very Low
				Sp 0.96 (0.82. 1)	FN 8	TN 67	
TP (people with dementia or delirium, **true positives**); FN (people uncorrectly classified healthy, **false negatives**); TN (people without dementia or without delirium, **true negatives**); FP (people correctly classified with dementia or with delirium, **false positives**); CC: clinical criteria; [1] Delirium (including del+dem) vs no delirium (dementia alone and no dementia); * DSM-5 for delirium and IQCODE or MMSE for dementia.							

Studies: Richardson 2017 (people admitted to five acute or rehabilitation hospitals)

Prevalence of dementia: 30% based on Carpenter et al. 2019 "Accuracy of Dementia Screening Instruments in Emergency Medicine: A Diagnostic Meta-analysis"

Attention Test (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
AT cutoff 3-4	1 del vs no del[1]	CC*	114	Se 0.90 (0.77. 0.97)	TP 27	FP 25	Very Low
				Sp 0.65 (0.51. 0.76)	FN 3	TN 45	
	1 dem+del vs dem	CC*	59	Se 0.84 (0.66. 0.95)	TP 25	FP 19	Very Low
				Sp 0.73 (0.51. 0.87)	FN 5	TN 51	
TP (people with dementia or delirium, **true positives**); FN (people uncorrectly classified healthy, **false negatives**); TN (people without dementia or without delirium, **true negatives**); FP (people correctly classified with dementia or with delirium, **false positives**); CC: clinical criteria; [1] Delirium (including del+dem) vs no delirium (dementia alone and no dementia); * DSM-5 for delirium and IQCODE or MMSE for dementia.							

Studies: Richardson 2017 (people admitted to five acute or rehabilitation hospitals)

Prevalence of dementia: 30% based on Carpenter et al. 2019 "Accuracy of Dementia Screening Instruments in Emergency Medicine: A Diagnostic Meta-analysis"

Observational Scale of Level of Arousal + Attention Test (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
OSLA+AT cutoff 9-10	1 del vs no del[1]	CC*	114	Se 0.85 (0.72. 0.93)	TP 26	FP 2	Very Low
				Sp 0.97 (0.89. 1)	FN 4	TN 68	
	1 dem+del vs dem	CC*	114	Se 0.94 (0.79. 0.99)	TP 28	FP 5	Very Low
				Sp 0.93 (0.76. 0.99)	FN 2	TN 65	
TP (people with dementia or delirium, **true positives**); FN (people uncorrectly classified healthy, **false negatives**); TN (people without dementia or without delirium, **true negatives**); FP (people correctly classified with dementia or with delirium, **false positives**); CC: clinical criteria; [1] Delirium (including del+dem) vs no delirium (dementia alone and no dementia); * DSM-5 for delirium and IQCODE or MMSE for dementia							

Studies: Richardson 2017 (people admitted to five acute or rehabilitation hospitals)

Prevalence of dementia: 30% based on Carpenter et al. 2019 "Accuracy of Dementia Screening Instruments in Emergency Medicine: A Diagnostic Meta-analysis"

Cognitive Test for Delirium – Spatial Span Forward (CTD-SSF) (specialist care setting)							
Outcomes	**No. of Studies**	**Reference standard**	**No. of participants**	**Accuracy: range**	**Effect per 100 patients tested**		**Certainty of evidence (GRADE)**
					Pre-test probability of 30%		
DRS-R98 17.75	1 del vs dem	CC*	37	Se 1 (0.86. 0.1)	TP 30	FP 10	Very Low
				Sp 0.85 (0.55. 0.98)	FN 0	TN 60	

DRS-R98 21.5	1 dem vs dem	CC*	37	Se 0.92 (0.73. 0.99) Sp 0.85 (0.55. 0.98)	TP 28 FN 2	FP 10 TN 60	Very Low
DRS-R98 22.5	1 dem vs dem	CC*	37	Se 0.92 (0.73. 0.99) Sp 1 (0.75. 1)	TP 28 FN 2	FP 0 TN 70	Very Low
TP (people with dementia or delirium, **true positives**); FN (people uncorrectly classified healthy, **false negatives**); TN (people without dementia or without delirium, **true negatives**); FP (people correctly classified with dementia or with delirium, **false positives**); CC: clinical criteria; *DSM-5							

Studies: Trzepacz 2001 (Patients with dementia or delirium, schizophrenia, depression, or other psychiatric disorders from a range of medical and nursing home settings).

		DRS-R98, IQCODE, NPI-Q, CTD-SSF
Leonard 2016	50 delirium 32 dementia 62 dementia + delirium 32 controls	**DRS tot**: del 22.0±8.4; dem 14.0±6.8; dem+del 18.9±6.9; ctrl 6.1±5.2 **s-IQCODE**: del 3.1±0.3; dem 4.10±0.7; dem+del 4.2±1.4; ctrl 2.9±0.6 **NPI distress**: del 8.4±6.4; dem 6.7±6.1; dem+del 9.9±7.2; ctrl 1.5±2.1 **NPI severity**: del 11.9±10.6; dem 10.2±9.5; dem+del 12.3±10.6; ctrl 1.6±2.7
Meagher 2010	40 delirium 20 dementia 40 dementia + delirium 40 controls	**DRS tot:** del 22.0±6.6; dem 11.2±3.5; dem+del 21.0±5.1; ctrl 4.1±1.8
Trzepacz 2001	24 delirium 13 dementia	**DRS tot:** del 26.9±6.7; dem 13.9±4.2

Studies: Leonard 2016: Patients ≥60 years old with altered mental status referred to a psychiatry for later life consultationliaison service.
Meagher 2010: Patients ≥60 years old with altered mental status identified on daily rounds

Review question 5 (RQ NICE). How effective are pre-, peri- and post-diagnostic counselling and support on outcomes for people living with dementia and their caregivers?

Pre-, peri- and post-diagnostic counselling versus no counselling				
Outcomes	**No. of Studies**	**Observed effect (95% IC), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Outcomes for people with dementia				
ADCS-ADL	2 RCT (Koivisto 2016, Phung 2013)	**MD -5.09 (-8.92. -1.27), I^2 0%**	436	Low[c]
ADL	2 RCT (Kim 2017, Villars 2021)	SMD -0.05 (-0.30. 0.19), I^2 0%	257	Low[b]
BDI	1 RCT (Kim 2017)	MD -1.37 (-3.10. 0.35), I^2 n.a.	236	Low[b]
CDR-SB	2 RCT (Koivisto 2016, Laakkonen 2016)	MD 0.30 (-1.48. 2.09), I^2 85%	372	Very Low[b,c,d]
CSDD	1 RCT (Phung 2013)	MD 0.55 (-0.78. 1.88), I^2 n.a.	194	Low[b]
GDS	1 RCT (Kim 2017)	**MD -2.55 (-3.91. -1.19), I^2 n.a.**	62	Moderate
MMSE	3 RCT (Koivisto 2016, Phung 2013, Villars 2021)	MD −0.47 (−1.31. 0.37), I^2 0%	609	Low[b]
NPI	3 RCT (Koivisto 2016, Phung 2013, Villars 2021)	MD 0.27 (−0.94. 1.47), I^2 55%	631	Low[a,b]
QoL-AD	3 RCT (Koivisto 2016, Phung 2013, Villars 2021)	MD 0.15 (-1.46. 1.76), I^2 63%	630	Low[b,c]
HR-QoL	1 RCT (Laakkonen 2016)	MD 0.01 (-0.00. 0.02), I^2 n.a.	136	Low[b]
Suicidal Ideation Scale	1 RCT (Kim 2017)	**MD -2.35 (-3.46. -1.24), I^2 n.a.**	62	Low[c]
Perceived Health Status	1 RCT (Kim 2017)	**MD 1.33 (0.37. 2.29), I^2 n.a.**	62	Low[c]
Outcomes caregivers				
HADS-tot[1]	1 RCT (Livingston 2020)	MD −1.45 (−2.80. −0.10)*, I^2 n.a.	222	Moderate
HADS-D[2]	1 RCT (Livingston 2020)	MD −0.93 (−1.63. −0.24)*, I^2 n.a.	222	Moderate
Zarit Burden Inventory	1 RCT (Villars 2021)	MD -0.49 (-4.54. 3.57), I^2 n.a.	195 dyads	Very Low[b,c]
Burden Scale for Family Caregivers	1 RCT (Metcalfe 2019)	MD -0.70 (-5.78. 4.38), I^2 n.a.	61 caregivers	Very Low[b,c]
Caregiver Perceived Stress Scale	1 RCT (Metcalfe 2019)	MD -3.30 (-7.95. 1.35), I^2 n.a.	61 caregivers	Very Low[b,c]
Nottingham Health Profile	1 RCT (Villars 2021)	MD -7.12 (-35.48. 21.23), I^2 n.a.	196 dyads	Very Low[b,c]
QoL 15D	1 RCT (Koivisto 2016)	MD 0.00 (-0.03. 0.02), I^2 n.a.	236 dyads	Low[b]
General Health Questionnaire	1 RCT (Koivisto 2016)	MD -0.92 (-2.51. 0.67), I^2 n.a.	236 dyads	Low[b]
EQ - 5D - 5L	1 RCT (Metcalfe 2019)	MD 0.03 (-0.09. 0.15), I^2 n.a.	61 caregivers	Low[b]
Health Related QoL	1 RCT (Laakkonen 2016)	MD 1.70 (-0.38. 3.78), I^2 n.a.	136 dyads	Low[b]
Caregiver Geriatric Depression Scale	1 RCT (Phung 2013)	MD 0.67 (-0.64. 1.98), I^2 n.a.	197 dyads	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference

a. I^2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; *adjusted for setting, score at baseline and time; [§] informal caregivers

Review question 6 (RQ NICE). What are the specific needs of younger people living with dementia?

Themes identified for experiences and coping in employment			
No. of Studies	**Study design**	**Description**	**Confidence (CERQual)**
PWD: An awareness of changes in their functioning in the work place as they developed dementia			
1 (Chaplin 2016)	Interviews	For three participants, the Engineer, the Businessman and the Schools Meals Assistant, the first signs were poor short-term memory and a difficulty in remembering names and adjusting to new tasks.	Low
PWD: Shock at losing their expected future			
1 (Clemerson 2014)	Semi-structured interviews	For many, this included loss of employment as they were forced to take early retirement.	Low
PWD: A reluctance to acknowledge the signs			
1 (Chaplin 2016)	Interviews	All of the participants described how they did not initially think that these difficulties in specific areas of functioning were the first signs of something more serious. At this stage, they tended to ascribe the changes to pressure of work, new work roles, life-long traits, such as poor memory or declining physical skills such as poor eyesight.	Low
PWD: Sharing the fears			
1 (Chaplin 2016)	Interviews	They then began to suspect it was something more serious and all discussed their difficulties with their partners and were encouraged to seek further help.	Low
PWD: Self-management			
1 (Chaplin 2016)	Interviews	Three of the participants were able to discuss strategies for managing the symptoms of their illness in the workplace. They all spent more time and effort in planning and organising tasks and acknowledged how difficult it could be even with these strategies in place.	Low
PWD: Feeling under scrutiny			
1 (Chaplin 2016)	Interviews	The three participants who worked more closely with others described how their managers or colleagues had noticed that they were having difficulties in some tasks. They mainly tried to manage this by increased observation of the employee but did not discuss this with the employee. Consequently, the participants felt that they were being watched covertly and they would have preferred to have been consulted about this.	Low
PWD: A lack of consultation about management decisions			
1 (Chaplin 2016)	Interviews	Though two of the participants were given some adjusted duties when their employers became aware that they were having difficulties, none of the participants said that they were offered any 'reasonable adjustments' to their work role under the Equality Act (2010) after diagnosis. None of the participants were referred to a Disability Employment Advisor by their workplace. The HGV Driver and the School Meals Assistant were advised to take sickness leave when their employers became aware of the extent of their difficulties at work. They were advised to seek further assessment of their difficulties from their GP. Both of their GP's did make referrals on, one to a Neurologist and one to a Psychiatrist. Both these participants were then on sickness leave for the full six months and never returned to work.	Low
PWD: A belief in continued competence despite the realisation of impairment			

1 (Chaplin 2016)	Interviews	Three of the participants felt that they would have been able to carry on with an adjusted work role when they were diagnosed with dementia, while the School meals Assistant and the Businessman believed that they were no longer competent.	Low
PWD: Feeling abandoned by the workplace and consequent feelings of resentment towards the workplace			
1 (Chaplin 2016)	Interviews	Three of the participants expressed feelings of abandonment in how their employment situation was managed by their workplace. They felt that when they received their diagnosis and informed their workplace, no real attempt was made to find any adjusted work role for them.	Low
PWD: An acceptance of the final outcome			
1 (Chaplin 2016)	Interviews	Two of the participants are now on Employment Support Allowance, one has taken early retirement and two classed themselves as semi-retired. Four of the participants said that their work was a big part of their life and that they had enjoyed it and taken a pride in doing it well.	Low
PWD: Financial hardship and consequent worry			
1 (Chaplin 2016)	Interviews	All of the participants said that leaving work had affected their family and their relationships. The Nursing Assistant and the HGV Driver both had partners who are still working and they had taken on more domestic roles to help them. For the HGV Driver and the School Meals Assistant, leaving work had meant some financial hardship and consequent worry.	Low
PWD: A positive outlook for the future			
1 (Chaplin 2016)	Interviews	Despite their difficult experiences all of the participants were determined to be positive about their future. All of the participants said that they had taken up new hobbies or restarted old ones since leaving or reducing their work. The three participants who are under the age of 65 had been referred to the Young Onset Dementia Service in their local area and had become involved in the various social and leisure activities facilitated by this service.	Low
PWD: people with dementia			

Themes identified for general experiences and coping			
No. of Studies	**Study design**	**Description**	**Confidence (CERQual)**
PWD: Relief at getting the diagnosis confirmed			
1 (Clayton-Turner 2015)	Interviews	Relief at getting the diagnosis confirmed.	Low
PWD: Feelings of shock and a sense of loss at receiving the diagnosis			
2 (Pipon-Young 2012, Rabanal 2018)	Interviews, group discussion, semi-	Feelings of shock and a sense of loss at receiving the diagnosis.	Low

	structured interviews		
PWD: Experiences of feeling 'too young'			
3 (Clemerson 2014, Pipon- Young 2012, Rabanal 2018)	Interviews, group discussion, semi-structured interviews	What surprised people was their age at diagnosis, with the general assumption that dementia was something affecting older people.	High
PWD: Ambiguity of the term 'younger people with dementia'			
1 (Pipon-Young 2012)	Interviews, group discussion	Ambiguity of the term 'younger people with dementia', and people being unsure whether the label applied to them.	Low
PWD: Younger people living with dementia often have responsibility for children, a mortgage or a business to run			
1 (Pipon-Young 2012)	Interviews, group discussion	Younger people living with dementia often have responsibility for children, a mortgage or a business to run.	Low
PWD: People coped by normalising the situation			
1 (Clemerson 2014)	Semi-structured interviews	Creating an identity as an older person, even transiently, allowed people to make sense of developing AD by normalising the life-cycle.	Very Low
PWD: Telling children about the diagnosis is difficult			
1 (Clayton-Turner 2015)	Interviews	Telling children about the diagnosis is difficult, particularly at an age when they will not have been expecting it.	Low
PWD: Developing dementia forced people to contemplate death			
1 (Clemerson 2014)	Semi-structured interviews	Developing dementia forced people to contemplate death.	Very Low
PWD: Shock at losing their expected future			
1 (Clemerson 2014)	Semi-structured interviews	For many, this included loss of employment as they were forced to take early retirement.	Very Low
PWD: Loss of adult competency			
1 (Clemerson 2014)	Semi-structured interviews	Loss of adult competency represents another subtheme in the disruption to the life-cycle. This emerged through people's experience of either feeling more 'childlike' due to a loss of skills or being treated this way by others.	Very Low
PWD: Some people tried to prevent themselves from thinking about the future			

1 (Clemerson 2014)	Semi-structured interviews	Some people tried to prevent themselves from thinking about the future.	Very Low
PWD: Some people tried to stay positive, which for a few meant denying further significant decline			
1 (Clemerson 2014)	Semi-structured interviews	Some people tried to stay positive, which for a few meant denying further significant decline.	Very Low
PWD: With further reflection it seemed that some participants were working towards resolving concerns through comparing their situation to others who were more impaired or died younger than themselves			
1 (Clemerson 2014)	Semi-structured interviews	With further reflection it seemed that some participants were working towards resolving concerns through comparing their situation to others who were more impaired or died younger than themselves.	Very Low
PWD: Redefining self			
2 (Clemerson 2014, Pipon-Young 2012)	Interviews, group discussion, semi-structured interviews	Acknowledging change. Descriptions of the experience of dementia often related to changes people experienced, particularly in relation to what they could no longer do, a loss of independence or how their life had changed. This included a loss in social status and an inability to carry out everyday tasks.	High
PWD: All participants referred to their concerns of what may happen as their dementia progresses. This concern arose in response to meeting others with more advanced dementia			
1 (Pipon-Young 2012)	Interviews, group discussion	This concern arose in response to meeting others with more advanced dementia. It was also frightening for people to imagine a time when they may not realize their memory was deteriorating.	Low
PWD: Often raised was the negative impact of others' perceptions			
1 (Pipon-Young 2012)	Interviews, group discussion	Typically described were the negative perceptions of the word 'dementia', resulting in a lack of understanding about dementia and a loss as to how to be with people with dementia. A number of misconceptions were described regarding others' understanding of dementia. There seemed to be a sense that there was an avoidance of a true understanding in order to prevent painful truths.	Low
PWD: A reduced sense of self-worth also contributed to the threat to self			
1 (Clemerson 2014)	Semi-structured interviews	Simply having the disease made some individuals question their worth.	Very Low
PWD: Most participants who disclosed their condition had positive responses from others, which helped them to accept their diagnosis as part of who they were			
1 (Clemerson 2014)	Semi-structured interviews	Most participants who disclosed their condition had positive responses from others, which helped them to accept their diagnosis as part of who they were.	Very Low
PWD: Holding on to their existing self-concept			
2 (Clemerson 2014, Pipon-Young 2012)	Interviews, group discussion, semi-structured interviews	Nearly all participants raised the importance of acknowledging that although they have dementia, there were many aspects of their lives that remained the same.	High
PWD: Many participants described ways in which they covered up their dementia			

1 (Pipon-Young 2012)	Interviews, group discussion	Reasons for this surrounded the uncertainty of others' reactions and perceptions of them. Participants described wishing others would keep seeing them as the person they always were and 'normal'.	Low
PWD: Other people saw it as better to tell others that they had dementia, so they could understand their difficulties.			
1 (Pipon-Young 2012)	Interviews, group discussion	Other people saw it as better to tell others that they had dementia, so they could understand their difficulties.	Low
PWD: Participants spoke of the importance of remaining independent, active and involved			
1 (Pipon-Young 2012)	Interviews, group discussion	This could be achieved by finding a reason to keep fighting and not only focusing on deficits.	Low
1 (Rabanal 2018)	Semi-structured interviews	Need to engage in meaningful activity in order to maintain their well-being and to remain active.	Low
PWD: Many participants spoke of the importance of knowing other people with dementia and being able to share understandings through similar experiences			
2 (Pipon-Young 2012, Rabanal 2018)	Interviews, group discussion, semi-structured interviews	Many participants spoke of the importance of knowing other people with dementia and being able to share understandings through similar experiences.	Low
PWD: Participants described support from partners, friends, family, services, professionals, and through faith and spirituality			
2 (Pipon-Young 2012, Rabanal 2018)	Interviews, group discussion	Participants described support from partners, friends, family, services, professionals, and through faith and spirituality.	Low
PWD: Resilience			
1 (Pipon-Young 2012)	Interviews, group discussion	There was a sense from participants that being diagnosed with dementia was not a helpless situation. There were still things they could do for themselves.	Low
PWD: Participants discussed keeping their brains stimulated			
1 (Pipon-Young 2012)	Interviews, group discussion	Participants discussed keeping their brains stimulated.	Low
PWD: Disconnection and isolation			
1 (Clemerson 2014)	Semi-structured interviews	A shared phenomenon of feeling isolated or disconnected from others emerged, which is heightened by a lack of age-appropriate services.	Very Low
Theme: PWD: Re-engaging in life following people's initial experience of disconnection and isolation			
1 (Clemerson 2014)	Semi-structured interviews	Although disconnection was identified as a way of managing the sense of difference to others, it was recognised that this could not be sustained long term.	Very Low
PWD: As people began to reconnect with others, their focus shifted			
1 (Clemerson 2014)	Semi-structured interviews	Their focus shifted from concern with how they cope to concern with how their loved ones cope. Others focussed their attentions on contributing to the community and helping other people with dementia.	Very Low
PWD: The intention to regain control emerged as a common coping strategy in response to the experience of loss of agency			

1 (Clemerson 2014)	Semi-structured interviews	The intention to regain control emerged as a common coping strategy in response to the experience of loss of agency.	Very Low
PWD: Dementia Service User Network (otherwise known as the 'Forget-Me-Nots') provide social comradeship and are a useful resource			
1 (Clayton-Turner 2015)	Interviews	Dementia Service User Network (otherwise known as the 'Forget-Me-Nots') provide social comradeship and are a useful resource.	Low
PWD: Making the most of life			
1 (Clayton-Turner 2015)	Interviews	Receiving a diagnosis of a life-limiting condition tends to concentrate the mind. It helps you recognise what is important, clarifying life goals and helping you identify things you want to do. Dementia forces you to make the most of every day, to live in the moment and cherish times of fun, intimacy and discovery. You find a new strength within and a depth to some relationships which become closer through the hard times.	Low
PWD: Younger people living with dementia find YoungDementia UK very helpful			
1 (Clayton-Turner 2015)	Interviews	Younger people living with dementia find YoungDementia UK very helpful.	Low
Caregiver and PWD: Having dementia is frustrating, concerning and induces fear			
1 (Clayton-Turner 2015)	Interviews	Having dementia is frustrating, concerning and induces fear, and caring for a young person with dementia is stressful.	Low
Caregiver: There is a lack of support for younger people living with dementia and their carers			
1 (Clayton-Turner 2015)	Interviews	There is a lack of support for younger people living with dementia and their carers.	Low
Caregiver: When caring for a younger person living with dementia, key to coping and staying well is to carve out time for self			
1 (Clayton-Turner 2015)	Interviews	When caring for a younger person living with dementia, key to coping and staying well is to carve out time for self.	Low
Caregiver: Carers can receive support online at Talking Point, a peer support community run by Alzheimer's Society			
1 (Clayton-Turner 2015)	Interviews	Carers can receive support online at Talking Point, a peer support community run by Alzheimer's Society.	Low
Caregiver: A diagnosis of dementia should be made before stopping work			
1 (Clayton-Turner 2015)	Interviews	Otherwise, a person may not get their full pension. If a person stops working because of sickness, they may get their full pension. In addition, a diagnosis might enable the person to continue working at a reduced role or with support.	Low
Caregiver: Driving should be discussed			
1 (Clayton-Turner 2015)	Interviews	Driving should be discussed.	Low
Caregiver: Becoming involved with research is advantageous for younger people living with dementia and their carers			
1 (Clayton-Turner 2015)	Interviews	Becoming involved with research is advantageous for younger people living with dementia and their carers.	Low

Caregiver: Younger people living with dementia benefit from having relationships that are allowed to develop			
1 (Clayton-Turner 2015)	Interviews	Younger people living with dementia benefit from having relationships that are allowed to develop.	Low
PWD: people with dementia.			

Themes idetified for a walking group for youger people with dementia and their caregivers			
No. of Studies	**Study design**	**Description**	**Confidence (CERQual)**
PWD: The walking group created supportive and positive relationships, bringing closeness, friendship and compassion			
1 (Hegarty 2014)	Focus groups, interviews, questionnaire	The walking group created supportive and positive relationships, bringing closeness, friendship and compassion.	Low
PWD: Group members were clear about the benefits to partners			
1 (Hegarty 2014)	Focus groups, interviews, questionnaire	Group members were clear about the benefits to partners.	Low
PWD: Some talked about the disadvantages of having a large walking group			
1 (Hegarty 2014)	Focus groups, interviews, questionnaire	Some talked about the disadvantages of having a large walking group.	Low
***Caregiver*: Through the spouses' questionnaire, partners reported some positive impact on physical health and communication skills, and a substantial positive impact on mood**			
1 (Hegarty 2014)	Focus groups, interviews, questionnaire	Through the spouses' questionnaire, partners reported some positive impact on physical health and communication skills, and a substantial positive impact on mood.	Low
PWD: people with dementia.			

Themes idetified for a day service for younger people with dementia (ACE club)			
No. of Studies	**Study design**	**Description**	**Confidence (CERQual)**
A sense of belonging			
1 (Davies ‐ Quarrell 2010)	Interviews	To feel part of a valued group, to maintain or form important relationships. An opportunity to simply 'be myself' and 'not pretend' are important to evaluative outcomes of a successful service.	Low
ACE club provided a sense of achievement			

1 (Davies-Quarrell 2010)	Interviews	It enabled members to reach valued goals to the satisfaction of self and/or others. In considering this sense and its place in their life, ACE club members took a broad viewpoint on inclusion, which included a focus on physical rehabilitation to promote health and wellbeing, and supported practical strategies for daily living to promote confidence and reaffirm roles within the home.	Low
ACE club enabled members to talk through their problems			
1 (Davies-Quarrell 2010)	Interviews	ACE club enabled members to talk through their problems.	Low
ACE club provides a sense of purpose			
1 (Davies-Quarrell 2010)	Interviews	ACE club provides a sense of purpose.	Low
A sense of security			
1 (Davies - Quarrell 2010)	Interviews	To feel safe physically, psychologically, existentially. Many of the responses shared by members in the evaluation reinforce a sense of security on many levels. However, the inclusive nature of the membership of the ACE club strengthened the sense of security for the wider family and this was seen as a vital part of the service and the meaning that it held for members. The evaluation process demonstrated that group cohesion provided a sense of security for its membership where 'permission' to be vulnerable within a supportive environment was essential to human growth. Without this sense of security, some members feared that they would simply have to return to smaller family networks where their role and status may not be so well supported.	Low
A sense of significance			
1 (Davies - Quarrell 2010)	Interviews	To feel that you 'matter' and are accorded value and status. Interestingly, this was the 'sense' that was evaluated by the ACE club members as being the most important. Significance was experienced on a number of levels and with multiple meanings. The ACE club members valued the opportunities to speak at local, regional and national conferences with their campaigning voice for younger people with dementia, helping to spark and inform the development of a number of service philosophies and initiatives across the country, as well as inspire similar clubs in Australia, namely CALM and ConnexUS in Adelaide, South Australia. Additionally, members saw the significance of being involved in teaching clinical psychology students and student nurses. This sense of significance cascaded through their lives both at home and within the wider community and enhanced their experience of living and reaffirmed their sense of self.	Low
ACE club was felt to slow down the progression of dementia			
1 (Davies-Quarrell 2010)	Interviews	ACE club was felt to slow down the progression of dementia.	Low

Themes identified for a lunchtime social group for younger women with dementia ("Ladies who lunch")			
No. of Studies	**Study design**	**Description**	**Confidence (CERQual)**
PWD: Ladies who Lunch provided value to those attending it			

1 (Johnson 2008)	Written and oral feedback	Ladies who Lunch provided companionship, a relaxing atmosphere, was enjoyable and was valued by bot the women and their carers.	Low
Caregvier: Ladies who Lunch gives younger women living with dementia greater confidence			
1 (Higgins 2010)	Written and oral feedback	Ladies who Lunch gives younger women living with dementia greater confidence.	Low
PWD: people with dementia.			

Themes identified for different support groups			
No. of Studies	**Study design**	**Description**	**Confidence (CERQual)**
Specialist Advice and Information on Young Onset Dementia			
1 (Stamou 2020)	Survey with open-ended questions	Participants valued opportunities to receive in-depth information through education courses on young onset dementia, in order to understand future challenges and prepare accordingly.	Moderate
Access to Age-appropriate Services			
1 (Stamou 2020)	Survey with open-ended questions	Referrals that led YPD to care provided by specialist teams appeared to be highly valued, as the latter provided a sense of security.	Moderate
1 (Stamou 2020)	Survey with open-ended questions	Participants stressed the significance of having a professional who coordinated their care and access to services, according to their emerging needs.	Moderate
Interventions for Physical and Mental Health			
1 (Stamou 2020)	Survey with open-ended questions	Positive experiences to services that aimed to enable YPD to maintain their physical and mental health. This was achieved through offering opportunities to address challenges with cognitive functions and physical health.	Moderate
Opportunities for Social Participation			
1 (Stamou 2020)	Survey with open-ended questions	The accepting social environment of peer support forums generated new social relationships and met social needs, including those that were gender-specific.	Moderate
Enablement of Financial Stability			
1 (Stamou 2020)	Survey with open-ended questions	Some of these services enabled YPD to continue working while living with the diagnosis.	Moderate
1 (Stamou 2020)	Survey with open-ended questions	Participants also reported positive experiences with services which helped them to locate additional financial support for external care. At the early stages, this was provided through gradually increasing funded home care.	Moderate
Support Interventions for Family Relationships			
1 (Stamou 2020)	Survey with open-ended questions	Participants described the benefits of services, which aimed improve communication and to establish or restore a functional balance of roles and tasks within the family of younger people.	Moderate

Review question 7a. (RQ NICE) What are the most effective methods of care planning, focusing upon improving outcomes for people with dementia and their carers?

Care coordination/management using a protocol/action plan (that involves educating the caregivers) and meeting every 3 months				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Dem-QoL (PwD)	1 RCT (Jansen 2011)	MD 0.40 (-0.14. 0.94), I^2 n.a.	99	Low[b]
SF-36 mental (QoL *caregiver*)	1 RCT (Jansen 2011)	MD -2.90 (-8.10. 2.30), I^2 n.a.	99	Very Low[b,c]
SF-36 physical (QoL *caregiver*)	1 RCT (Jansen 2011)	MD 1.90 (-4.06. 7.86), I^2 n.a.	99	Very Low[b,c]
Burden (SPPIC)	1 RCT (Jansen 2011)	MD 0.30 (-1.14. 1.74), I^2 n.a.	99	Low[b]
Depression (CES-D)	1 RCT (Jansen 2011)	MD -0.30 (-4.12. 3.52), I^2 n.a.	99	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; a. I^2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I^2>75%; *adjusted for setting, score at baseline and time; [§] informal caregivers				

Care coordination/management with monthly follow-up calls and visits every 3 months				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Depression (BDI) >9	1 RCT (Schoenmakers 2010)	**OR 0.16 (0.03–0.86), I^2 n.a.**	46	Very Low[,e]
Burden (ZBI) >9	1 RCT (Schoenmakers 2010)	OR 0.09 (0.007–1.1), I^2 n.a.	46	Very Low[a,b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; a. I^2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; *adjusted for setting, score at baseline and time; [§] informal caregivers				

Care coordination/management using a protocol/action plan (that involves educating the caregivers) and monthly meetings				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Cognitive symptoms	2 RCT (Bass 2015, Callahan 2006)	SMD 0.03 (-0.15. 0.22), I^2 0%	481	Very Low[b,c]
CSDD	1 RCT (Callahan 2006)	MD -0.20 (-2.36. 1.96), I^2 n.a.	153	Very Low[b,c]
Mean N° hospital admissions	2 RCT (Bass 2003, Bass 2015)	MD -0.05 (-0.20. 0.10), I^2 0%	510	Low[b]
% of hospital admissions	1 RCT (Bass 2015)	RR 1.25 (0.91. 1.72), I^2 n.a.	328	Low[b]
% participants with ER admission	1 RCT (Bass 2015)	RR 0.94 (0.77. 1.15), I^2 n.a.	328	Very Low[b,c]
Mean N° ED visits	2 RCT (Bass 2003, Bass 2015)	MD -0.18 (-0.42. 0.05), I^2 0%	510	Low[b]
Institutionalization rate	3 RCT (Callahan 2006, Eloniemi-Sulkava 2001, Fortinsky 2009)	RR 0.74 (0.49. 1.12), I^2 12%	337	Low[b]
Caregivers' unmeet needs (at 12 months)	1 RCT (Bass 2013)	**MD -4.30 (-7.29. -1.31), I^2 n.a.**	486	Low[c]
NPI	1 RCT (Callahan 2006)	MD -4.80 (-12.33. 2.73), I^2 n.a.	153	Very Low[b,c]
Behavioural symptoms (0-14)	1 RCT (Bass 2015)	MD -0.22 (-1.01. 0.57), I^2 n.a.	328	Very Low[b,c]
Caregiver satisfaction with quality of services	2 RCT (Bass 2003, Vickrey 2006)	SMD 0.10 (-0.07. 0.26), I^2 0%	590	Very Low[b,c]
ZBI	1 RCT (Fortinsky 2009)	MD 1.21 (-7.87. 10.29), I^2 n.a.	84	Very Low[b,c]
Caregiver depression	2 RCT (Bass 2003, Fortinsky 2009)	SMD -0.17 (-0.42. 0.08), I^2 0%	266	Very Low[b,c]
EuroQol-5D	1 RCT (Vickrey 2006)	MD 0.01 (-0.05. 0.07), I^2 n.a.	408	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; a. I^2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I^2>75%				

Care coordination/management using a protocol/action plan (that involves educating the caregivers) and approx 10-14 meetings over 4 months vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
CSDD	1 RCT (Lam 2010)	MD -0.50 (-3.49. 2.49), I^2 n.a.	92	Very Low[b,c]
MMSE	1 RCT (Lam 2010)	MD 0.50 (-2.94. 3.94), I^2 n.a.	92	Very Low[b,c]
NPI	1 RCT (Lam 2010)	MD 5.00 (-14.87. 24.87), I^2 n.a.	92	Very Low[b,c]
ZBI	1 RCT (Lam 2010)	MD 1.50 (-18.06. 21.06), I^2 n.a.	92	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; a. I^2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I^2>75%				

Care coordination/management using a protocol/action plan (that involves educating the caregivers) and 1 meeting per month for 18 months with additional meetings as required				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
CSDD	1 RCT (Samus 2014)	MD 0.10 (-1.76. 1.96), I^2 n.a.	188	Low[b]
QoL-AD self-reported	1 RCT (Samus 2014)	MD 1.90 (-0.66. 4.46), I^2 n.a.	188	Very Low[b,c]
NPI	1 RCT (Samus 2014)	MD 0.90 (-1.25. 3.05), I^2 n.a.	188	Low[b]
Caregiver QoL – mental (SF-12)	1 RCT (Tanner 2015)	MD 0.66 (-3.37. 4.69), I^2 n.a.	289	Very Low[b,c]
Caregiver QoL – physical (SF-12)	1 RCT (Tanner 2015)	MD 1.54 (-2.58. 5.66), I^2 n.a.	289	Very Low[b,c]
ZBI	1 RCT (Tanner 2015)	MD -1.91 (-5.18. 1.36), I^2 n.a.	289	Very Low[b,c]
Caregiver depression	1 RCT (Tanner 2015)	MD -0.39 (-1.53. 0.75), I^2 n.a.	289	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%				

Care coordination/management using a protocol/action plan (that involves educating the carers) and approx 2 meetings per month for 6 months				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
MMSE	1 RCT (Chien 2008)	MD -0.30 (-3.34, 2.74), I^2 n.a.	88	Very Low[,c]
Institutional rate	1 RCT (Chien 2008)	**MD -3.10 (-3.90, -2.30), I^2 n.a.**	88	Moderate
Caregiver burden (CBI)	1 RCT (Chien 2008)	**MD -17.90 (-26.65, -9.15), I^2 n.a.**	88	Moderate
Caregiver burden (ZBI)	1 RCT (Dias 2008)	MD -5.50 (-13.17, 2.17), I^2 n.a.	81	Very Low[b,c,d]
Caregiver WHO-QoL	1 RCT (Chien 2008)	**MD 18.40 (9.19, 27.61), I^2 n.a.**	88	Low[c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%				

Care coordination/management using a protocol/action plan (that involves educating the caregivers) and weekly meetings for a month, followed by a meeting every 2 weeks for 5 months				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
MMSE	1 RCT (Chien 2011)	MD -0.20 (-2.46. 2.06), I^2 n.a.	92	Very Low[c]
NPI	1 RCT (Chien 2011)	**MD -6.80 (-12.23. -1.37), I^2 n.a.**	92	Low[c]
Mean N° of institutionalitation	1 RCT (Chien 2011)	**MD -3.00 (-4.21. -1.79), I^2 n.a.**	92	Moderate
Caregiver WHO-QoL	1 RCT (Chien 2011)	**MD 20.50 (12.73. 28.27), I^2 n.a.**	92	Moderate
Caregiver Burden (FCBI)	1 RCT (Chien 2011)	**MD -19.70 (-26.76. -12.64), I^2 n.a.**	92	Moderate
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%				

Follow-up organised by memory clinic vs GPs				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
QoL-AD self-rated	1 RCT (Meeuwsen 2012)	MD 0.25 (−0.73, 1.23), I^2 n.a.	175	Low[b]
GDS	1 RCT (Meeuwsen 2012)	MD 0.25 (−0.36, 0.86), I^2 n.a.	175	Low[b]
NPI	1 RCT (Meeuwsen 2012)	MD 1.13 (−0.51, 2.77), I^2 n.a.	175	Low[b]
Caregiver QoL-AD	1 RCT (Meeuwsen 2012)	MD 0.17 (−0.70, 1.04), I^2 n.a.	175	Low[b]
Caregiver CES-D	1 RCT (Meeuwsen 2012)	**MD 2.09 (0.16, 4.02), I^2 n.a.**	175	Low*
STAI trait	1 RCT (Meeuwsen 2012)	**MD 2.14 (0.25, 4.03), I^2 n.a.**	175	Low*
STAI state	1 RCT (Meeuwsen 2012)	**MD 2.35 (0.34, 4.36), I^2 n.a.**	175	Low*
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%				

Medicare Alzheimer's Disease Demonstration (care coordination/management with unspecified follow-up frequency)				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Caregiver Depression (GDS)	1 RCT (Newcomer 1999)	**MD -0.32 (-0.58, -0.06), I^2 n.a.**	5303	Moderate
Caregiver Burden	1 RCT (Newcomer 1999)	MD -0.50 (-1.11, 0.11), I^2 n.a.	5301	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%				

Personalised carer support for minority groups				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I²**	**No. of participants**	**Certainty of evidence (GRADE)**
Caregiver QoL – mental (SF-36)	1 RCT (Xiao 2016)	**MD 12.70 (7.09, 18.31), I^2 n.a.**	61	Low[c]
Caregiver QoL – physical (SF-36)	1 RCT (Xiao 2016)	MD 2.20 (-3.28, 7.68), I^2 n.a.	61	Very Low[b,c]
Behavioural symptoms	1 RCT (Xiao 2016)	MD -3.30 (-7.35, 0.75), I^2 n.a.	61	Very Low[b,c]
Caregiver Distress	1 RCT (Xiao 2016)	MD -6.40 (-12.87, 0.07), I^2 n.a.	61	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%				

Care coordination/management within the DEM-DISC model				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I²**	**No. of participants**	**Certainty of evidence (GRADE)**
Caregiver Depression (GDS)	1 RCT (Van Mierlo 2015)	RR 1.48 (0.87, 2.51), I^2 n.a.	49	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%				

Multidisciplinary group				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I²**	**No. of participants**	**Certainty of evidence (GRADE)**
MMSE	1 RCT (Chen 2019)	MD -0.17 (-3.75, 3.41), I^2 n.a.	129	Very Low[b,c]
NPI	1 RCT (Chen 2019)	MD -2.65 (-7.75, 2.45), I^2 n.a.	129	Very Low[b,c]
Caregiver QoL	1 RCT (Chen 2019)	MD 0.68 (-1.97, 3.33), I^2 n.a.	129	Low[b]
Caregiver Burden (ZBI)	1 RCT (Chen 2019)	MD -3.39 (-10.33, 3.55), I^2 n.a.	129	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%				

Review and optimization of pharmacological treatments using the Care Ecosystem model				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Lower mean number of potentially inappropriate prescriptions	1 RCT (Liu 2023)	**MD -0.35 (-0.49, -0.20), I^2 n.a.**	490	Low[b]
Mean N° drugs prescribed	1 RCT (Liu 2023)	**MD -0.53 (-0.92,-0.14), I^2 n.a.**	490	Low[b]
Lower number of people with at least one potentially inappropriate prescription	1 RCT (Liu 2023)	-1 person on CE +13 people on control	490	Moderate
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%				

Case management: combined, by frequency of follow-up				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Weekly follow-up				
MMSE	1 RCT (Chien 2011)	MD -0.20 (-2.46, 2.06), I^2 n.a.	92	Very Low[b,c]
NPI	1 RCT (Chien 2011)	**MD -6.80 (-12.23, -1.37), I^2 n.a.**	92	Low[c]
Caregiver Burden (FCBI)	1 RCT (Chien 2011)	**MD -19.70 (-26.76, -12.64), I^2 n.a.**	92	Moderate
Caregiver WHO-QoL	1 RCT (Chien 2011)	**MD 20.50 (12.73, 28.27), I^2 n.a.**	92	Moderate
Mean N° of institutionalization	1 RCT (Chien 2011)	**MD -3.00 (-4.21, -1.79), I^2 n.a.**	92	Moderate
Monthly follow-up				
Cognitive symptoms	2 RCT (Bass 2015, Callahan 2006)	SMD 0.03 (-0.15, 0.22), I^2 0%	481	Very Low[b,c]
CSDD	2 RCT (Samus 2014, Callahan 2006)	MD -0.03 (-1.44, 1.38), I^2 0%	456	Very Low[b,c]
QoL	2 RCT (Samus 2014, Vickrey 2006)	**SMD 0.16 (0.01, 0.31), I^2 0%**	711	Low[c]
BPSD	3 RCT (Samus 2014, Callahan 2006, Bass 2015)	SMD -0.04 (-0.20, 0.13), I^2 18%	456	Very Low[b,c]
Caregiver depression	1 RCT (Bass 2003, Tanner 2015)	SMD -0.12 (-0.31, 0.06), I^2 0%	471	Very Low[b,c]
Caregiver Burden (ZBI)	1 RCT (Tanner 2015)	MD -1.91 (-5.18, 1.36), I^2 n.a.	289	Very Low[b,c]
EuroQol-5D	1 RCT (Vickrey 2006)	MD 0.01 (-0.05, 0.07), I^2 n.a.	408	Low[b]
Institutionalization risk	2 RCT (Callahan 2006, Samus 2014)	RR 1.23 (0.72, 2.11), I^2 0%	456	Low[b]
Follow-up every two months				
MMSE	1 RCT (Chien 2008)	MD -0.30 (-3.34, 2.74), I^2 n.a.	88	Very low[b,c]
NPI	2 RCT (Chien 2008, Dias 2008)	SMD -0.74 (-1,70, 0,22), I^2 89%	169	Very low[b,c,d]
Caregiver Burden (FCBI)	1 RCT (Chien 2008)	**MD -17.90 (-26.65, -9.15), I^2 n.a.**	88	Moderate

Caregiver Burden (ZBI)	1 RCT (Dias 2008)	MD -5.50 (-13.17, 2.17), I^2 n.a.	81	Very Low[c,d]
Caregiver WHO-QoL	1 RCT (Chien 2008)	**MD 18.40 (9.19, 27.1), I^2 n.a.**	88	Low[c]
Institutionalization rate	1 RCT (Chien 2008)	**MD -3.10 (-3.90, -2.30), I^2 n.a.**	88	Moderate
% of institutionalization	1 RCT (Eloniemi-Sulkava 2001)	RR 0.82 (0.46, 1.48), I^2 n.a.	125	Very Low[b,c]
10/14 follow-up nell'arco di quattro mesi				
MMSE	1 RCT (Lam 2010)	MD 0.50 (-2.94, 3.94), I^2 n.a.	92	Very Low[b,c]
CSDD (depression)	1 RCT (Lam 2010)	MD -0.50 (-3.49, 2.49), I^2 n.a.	92	Very Low[b,c]
NPI	1 RCT (Lam 2010)	MD 5.00 (-14.87, 24.87), I^2 n.a.	92	Very Low[b,c]
Caregiver Burden (ZBI)	1 RCT (Lam 2010)	MD 1.50 (-18.06, 21.06), I^2 n.a.	92	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%				

Case management: combined, by contact method at follow-up				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Follow-up visits in clinics				
Cognitive outcomes (range 0-41)	1 RCT (Callahan 2006)	MD –0.10 (-3.83, 3.63), I^2 n.a.	153	Very Low[b,c]
CSDD	1 RCT (Callahan 2006)	MD -0.20 (-2.36, 1.96), I^2 n.a.	153	Low[b]
NPI	2 RCT (Callahan 2006, Dias 2008)	MD -2.37 (-5.37, 0.64), I^2 0%	234	Low[b]
Caregiver Burden (ZBI)	1 RCT (Dias 2008)	MD -5.50 (-13.17, 2.17), I^2 n.a.	81	Very Low[b,c]
Follow-up visits at home				
MMSE	2 RCT (Chien 2008, Chien 2011)	MD -0.24 (-2.05, 1.58), I^2 0%	180	Very Low[b,c]
CSDD	1 RCT (Lam 2010)	MD -0.50 (-3.49, 2.49), I^2 0%	92	Very Low[b,c]
NPI	3 RCT (Chien 2008, Chien 2011, Lam 2010)	MD -9.34 (-20.04, 1.37), I^2 80%	272	Very Low[b,c]
Caregiver depression (GDS)	1 RCT (Newcomer 1999)	**MD -0.32 (-0.58, -0.06), I^2 n.a.**	5307	Very Low[b,c]
Caregiver Burden (FCBI)	2 RCT (Chien 2008, Chien 2011)	**MD -18.99 (-24.48, -13.50), I^2 0%**	180	Low[c]
Caregiver Burden (ZBI)	2 RCT (Lam 2010, Newcomer 1999)	MD -0.50 (-1.11, 0.11), I^2 0%	5396	Low[b]
Caregiver WHO-QoL	2 RCT (Chien 2008, Chien 2011)	**MD 19.63 (13.69, 25.56), I^2 0%**	180	Low
Institutionalization rate	2 RCT (Chien 2008, Chien 2011)	**MD -3.07 (-3.73, -2.41), I^2 0%**	180	Moderate
Telephone follow-up				
Cognitive outcomes (range 0-14)	1 RCT (Bass 2015)	MD 0.03 (-1.13, 1.19), I^2 n.a.	328	Very Low[b,c]

HUIM-3 (QoL PwD)	1 RCT (Vickrey 2006)	MD 0.06 (-0.02, 0.14), I^2 0%	408	Low[b]
BPSD (range 0-12)	1 RCT (Bass 2015)	MD -0.22 (-1.01, 0.57), I^2 0%	328	Very Low[b,c,d]
Caregiver cognitive symptoms (CDS)	1 RCT (Bass 2003)	MD -0.11 (-0.29, 0.07), I^2 n.a.	182	Low[b]
EuroQol-5D	1 RCT (Vickrey 2006)	MD 0.01 (-0.05, 0.07), I^2 n.a.	408	Low[b]
Mixed-method follow-up				
CSDD	1 RCT (Samus 2014)	MD 0.10 (-1.76, 1.96), I^2 n.a.	303	Low[b]
QoL-AD self-rated	1 RCT (Samus 2014)	MD 1.90 (-0.66, 4.46), I^2 n.a.	303	Very Low[b,c]
BPSD	1 RCT (Samus 2014)	MD 0.90 (-1.25, 3.05), I^2 n.a.	303	Very Low[b,c]
Caregiver cognitive symptoms (GDS)	1 RCT (Tanner 2015)	MD -0.39 (-1.53, 0.75), I^2 n.a.	289	Very Low[b,c]
Caregiver Burden (ZBI)	1 RCT (Tanner 2015)	MD -1.91 (-5.18, 1.36), I^2 n.a.	289	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%

Review question 7c (RQ NICE) How should health and social care be co-ordinated for people living with dementia?

Themes identified for the self-management intervention for people living with dementia and their carers			
No. of Studies	**Study design**	**Description**	**Confidence (CERQual)**
The program training was enjoyable			
1 (Martin 2015)	Focus group, interviews	Although people living with dementia said that they could not recall all of the activities, they had enjoyed the program.	Low
The participants felt empowered			
2 (Martin 2015, Moore 2011)	Focus group, interviews	The training program encouraged people living with dementia to continue with their hobbies and goals (Faith 2015). Access to a budget provided a sense of empowerment (Moore 2011).	Moderate
***Caregivers* felt burdened and people living with dementia felt disempowered**			
1 (Toms 2015)	Semi-structured interviews	The caregivers felt responsible and burdened. This left the person with dementia feeling disempowered.	Low
Support groups were considered valuable			
1 (Toms 2015)	Semi-structured interviews	Peer support, such as support groups, was considered valuable by participants.	Low
***Caregivers* and people with dementia questioned what would happen once time-limited support ended**			
1 (Toms 2015)	Semi-structured interviews	Additional support, such as a support group, was available, but these were often time-limited, which led both *caregivers* and people with dementia to the question of what happened when such support ended.	Low
There was a lack of support			
1 (Toms 2015)	Semi-structured interviews	People living with dementia and their *caregivers* felt that there was a lack of support.	Low
Respondents thought that professional support was important for effective self-management			
1 (Toms 2015)	Semi-structured interviews	Respondents thought that professional support was important for effective self-management and valued this resource. They thought that this help was necessary because not everything could be self-managed within the family.	Low
Many respondents were unsure how to access the services and reported finding them limited and poorly integrated			
1 (Toms 2015)	Semi-structured interviews	Many respondents were unsure how to access the services that were available and reported finding them limited and poorly integrated. This made it harder to self manage the condition.	Low
Some people living with dementia used practical aids to support their memory			
1 (Toms 2015)	Semi-structured interviews	Some people living with dementia used practical aids to support their memory.	Low

What was most pertinent to carers was the diminished ability of the person living with dementia to complete daily tasks			
1 (Toms 2015)	Semi-structured interviews	What was most pertinent to carers was the diminished ability of the person living with dementia to complete daily tasks.	Low
The approach of normalising difficulties was evident in many interviews			
1 (Toms 2015)	Semi-structured interviews	The approach of normalising difficulties was evident in many interviews.	Low
People living with dementia and their carers endured hardship without showing their feelings or complaining			
1 (Toms 2015)	Semi-structured interviews	A sense of stoicism, often expressed when respondents gave their ideas about self-management, was evident in many interviews, and this seemed to be a form of psychological management.	Low
People with dementia were uncertain about the future. This led to lack of confidence and a diminished belief that they could self-manage			
1 (Toms 2015)	Semi-structured interviews	Some people with dementia discussed losing confidence. It was implied that this loss of confidence could diminish people's belief that they could self-manage. In some cases, this loss of confidence seemed to relate to uncertainty about the future and how the illness would progress.	Low
Diaphragmatic breathing was relaxing			
1 (Martin 2015)	Focus group, semi-structured interviews	Participants found the relaxation activity of diaphragmatic breathing relaxing.	Low
Funding for respite was useful for carers			
1 (Moore 2011)	Interviews	Funding for respite was useful for carers.	Very Low
Finding personal assistants was difficult			
1 (Moore 2011)	Interviews	Finding suitable individuals to become personal assistants was difficult for some people.	Very Low
When suitable individuals became personal assistants, there were positive results			
1 (Moore 2011)	Interviews	When suitable individuals became personal assistants, there were positive results.	Very Low

Themes identified for outcome-focussed/needs-led care vs standard care			
No. of Studies	**Study design**	**Description**	**Confidence (CERQual)**
Standard care: Familial carers often feel not able to cope			
1 (Gethin-Jones 2014)	Semi-structured interviews	The most common concern of familial carers is the feeling of not being able to cope.	Moderate
Standard care: Carers felt isolated			
1 (Gethin-Jones 2014)	Semi-structured interviews	The sense of isolation expressed by the participants came over very strongly. This isolation appeared to come from their sense that they were on the outside with little control because the care was planned by	Mdoerata

		the other professionals. Family carers felt that they were isolated as they had all the responsibility and in their eyes and potentially all the blame when things went wrong.	
Outcome-focussed care: Carers' self-reported well-being improved after the outcome-focused intervention had been implemented			
2 (Gethin-Jones 2014, Rothera 2008)	Semi-structured interviews	There was an improvement in the carers' self-reported subjective well-being, after the outcome-focused homecare intervention had been implemented.	High
Outcome-focussed care: Carers felt the subjective well-being of their relative had improved after the outcome-focused care intervention			
1 (Gethin-Jones 2014)	Semi-structured interviews	All the carers felt the subjective well-being of their relative had improved after the six-month outcome-focused care intervention.	Moderate

Themes identified for community-based case management			
No. of Studies	**Study design**	**Description**	**Confidence (CERQual)**
Meeting health and social care professionals at home was more relaxing and less stressful			
1 (Gibson 2007)	Interviews	Meeting health and social care professionals at home was more relaxing and less stressful compared to using the memory service.	Moderate
Being at home facilitated communication			
1 (Gibson 2007)	Interviews	Being at home facilitated communication with health and social care professionals.	Moderate
The case manager was good at identifying needs and providing the right support			
1 (Iliffe 2014)	Interviews	The case manager was good at identifying needs and providing the right support.	Moderate
Carers expected case managers to provide information about dementia and services			
1 (Iliffe 2014)	Interviews	Carers expected case managers to provide information about dementia and services.	Moderate
Case managers should be proactive in asking carers and people living with dementia if they feel they need assistance			
1 (Iliffe 2014)	Interviews	Case managers should be proactive in asking carers and people living with dementia if they feel they need assistance. This is because participants frequently expressed a reluctance to initiate contact with the case manager, which undermines the concept that they could ask for help when needed.	Moderate
A common reason why people living with dementia and their carers do not initiate contact with case managers is because they do not associate case managers with assisting with day-to-day issues			
1 (Iliffe 2014)	Interviews	A common reason why people living with dementia and their carers do not initiate contact with case managers is because they associate case managers with assisting with 'major' problems such as arranging residential care homes. They do not associate case managers with assisting with day-to-day issues.	Moderate
People living with dementia and their carers preferred to have their case manager based at their GP's surgery			

1 (Iliffe 2014)	Interviews	People living with dementia and their carers preferred to have their case manager based at their GP's surgery. This is because there was the perception that their GP's surgery would then be a 'one-stop shop'. In addition, having the case manager at the GP's surgery provided an additional opportunity to talk to the case manager while visiting the GP's surgery.	Moderate
Appointments at clinics were more anxiety provoking compared to home appointments			
1 (Gibson 2007)	Interviews	For some, exposure to others at more severe stages of the illness within the clinic was a potent contributor towards anxiety, illustrating what could be expected as the disease progresses. Appointments at home removed this exposure.	Moderate
Nurses as case managers were perceived as providing a more direct link to the GP for advice and support			
1 (Iliffe 2014)	Interviews	From the perspectives of some people living with dementia and their carers, nurses as case managers were perceived as providing a more direct link to the GP for advice and support for comorbidities and minor ailments.	Low
A direct link to the GP was not a priority because they preferred their case manager to have expertise in social services			
1 (Iliffe 2014)	Interviews	From the perspectives of some people living with dementia and their carers, a direct link to the GP was not a priority because they preferred their case manager to have expertise in social services. The inference is that they would prefer a social worker to be the case manager.	Low
People living with dementia and their carers emphasised interpersonal skills			
1 (Iliffe 2014)	Interviews	People living with dementia and their carers emphasised interpersonal skills such as empathy.	Moderate
Case management made access to services easier			
1 (Iliffe 2014)	Interviews	Case management made access to services easier including GPs, benefit checks and links to other services.	Moderate
Case managers should respond as quickly as possible to questions			
1 (Iliffe 2014)	Interviews	Case managers should respond as quickly as possible to questions from people living with dementia or their carers.	Moderate
The idea of background support was valued by people living with dementia and their carers			
1 (Iliffe 2014)	Interviews	A key aspect of case management valued by people living with dementia and their carers was the idea of background support that could easily be called on at a time of need.	Moderate
There needed to be time and opportunities to develop a deeper relationship			
1 (Iliffe 2014)	Interviews	For people living with dementia and their carers to feel comfortable about contacting the case manager in the event of difficulties, there needed to be time and opportunities to develop a deeper relationship.	Moderate
Face-to-face contact was preferred			
1 (Iliffe 2014)	Interviews	Face-to-face and telephone contact were both considered acceptable, although face-to-face contact was often preferred as it facilitated relationship building better than telephone contact.	Moderate
Some people living with dementia and their carers do not mind contact by telephone			
1 (Iliffe 2014)	Interviews	Some people living with dementia and their carers appreciate the service that case managers provide and also appreciate how hard they work. Therefore, they do not mind contact by telephone.	Moderate
Case managers should explain what support they can provide			

1 (Iliffe 2014)	Interviews	Case managers should explain to carers, and where appropriate to people living with dementia, what support they can provide.	Moderate
Participants found case management more useful than dementia advisors			
1 (Iliffe 2014)	Interviews	Participants found case management more useful than dementia advisors. This is because case management offers continuity of care but dementia advisors do not.	Moderate

Themes identified for memory-clinic case management			
No. of Studies	**Study design**	**Description**	**Confidence (CERQual)**
The memory service was well received			
1 (Hean 2011)	Interviews	The memory service was well received.	Very Low
People living with dementia experienced an increase in their quality of life			
1 (Sonola 2013)	Focus group, survey	People living with dementia generally experienced an increase in their quality of life.	Low
Familial carers' stress scores improved or remained stable			
1 (Sonola 2013)	Focus group, survey	Familial carers' stress scores improved or remained stable for all the carers measured.	Low
There was difficulty and effort in accessing treatment			
1 (Gibson 2007)	Interviews	There was difficulty and effort in accessing treatment.	Moderate
For memory services that do not have post-diagnostic support, participants expressed feelings of abandonment			
1 (Kelly 2016)	Semi-structured interviews	For memory services that do not have post-diagnostic support, many participants expressed feelings of abandonment or 'being sent away' by professionals on receipt of diagnosis.	Moderate
For memory services that do have post-diagnostic support, participants explained the value of having support as soon after diagnosis as possible			
1 (Kelly 2016)	Semi-structured interviews	For memory services that do have post-diagnostic support, people with dementia and their carers explained the value of having support as soon after diagnosis as possible and the importance of skilled, knowledgeable, sensitive project workers to deliver support.	Moderate
Carers frequently reported positively on the help received from the project workers with claiming benefits			
1 (Kelly 2016)	Semi-structured interviews	Carers frequently reported positively on the help received from the project workers with claiming benefits.	Moderate
Carers spoke of receiving support with arranging Power of Attorney			
1 (Kelly 2016)	Semi-structured interviews	Carers spoke of receiving support with arranging Power of Attorney and valued the input from project workers in negotiating the process.	Moderate

Participants found the information they received useful			
1 (Kelly 2016)	Semi-structured interviews	Family members and one person newly diagnosed with dementia found the information they received (books and leaflets) along with general advice useful.	Moderate
Exposure to others at more severe stages of the illness within the clinic was a potent contributor towards anxiety			
1 (Gibson 2007)	Interviews	For some, exposure to others at more severe stages of the illness within the clinic was a potent contributor towards anxiety, illustrating what could be expected as the disease progresses. Appointments at home removed this exposure.	Moderate
The coordination of care was valued			
2 (Hean 2011, Sonola 2013)	Interviews, focus group, survey	The coordination of care was valued.	High
The service made carers and people living with dementia feel supported and reassured			
2 (Hean 2011, Sonola 2013)	Interviews, focus group, survey	The service and nature of the staff made carers and people living with dementia feel supported and reassured. (Having a named person to contact in times of crisis, and the security that they would not left to manage alone).	High
The language used was not quite right			
1 (Hean 2011)	Interviews	The language used was not quite right.	Very Low
People living with dementia felt pressure of time because the psychiatrist was busy			
1 (Hean 2011)	Interviews	People living with dementia felt pressure of time because the psychiatrist was busy.	Very Low
Some found it difficult to get to the right people and get the answers needed			
1 (Hean 2011)	Interviews	Some found it difficult to get to the right people and get the answers needed.	Very Low
There were accounts of receiving insufficient information			
1 (Kelly 2016)	Semi-structured interviews	There were accounts of receiving no information, or insufficient or inappropriate information following diagnosis.	Moderate
Some carers expressed discomfort with some of the information they received			
1 (Kelly 2016)	Semi-structured interviews	Some carers expressed discomfort with some of the information they received. Some felt that it was too much to face too soon. Many participants stated that a 'one size fits all' approach was not what they wanted.	Moderate
Participants valued information that was delivered on a one-to-one basis and targeted to individual needs and wishes			
1 (Kelly 2016)	Semi-structured interviews	Participants valued that information was delivered by the project workers on a one-to-one basis and specifically targeted to individual needs and wishes.	Moderate
People living with dementia and their carers liked seeing the same person throughout treatment			
2 (Hean 2011, Willis 2011)	Semi-structured interviews	People living with dementia and their carers liked seeing the same person throughout treatment.	High
People living with dementia and their carers recognised the one stop shop aspect of the memory service			

1 (Willis 2011)	Semi-structured interviews	Convenience. People living with dementia and their carers recognised the one stop shop aspect of the memory service. Ten participants described the memory service as a central point of access to all necessary services.	Low
People living with dementia and their carers thought that home visits were very good			
1 (Hean 2011)	Semi-structured interviews	People living with dementia and their carers thought that home visits were very good.	Very Low
People living with dementia and their carers valued transport that was arranged by case managers/project workers			
1 (Kelly 2016)	Semi-structured interviews	People living with dementia and their carers valued transport that was arranged by case managers/project workers.	High
Care management does not promote advance care planning			
1 (Kelly 2016)	Semi-structured interviews	Care management does not promote advance care planning.	Moderate
Memory service post-diagnostic support when individualised and one-to-one, causes people with dementia to re-engage			
1 (Kelly 2016)	Semi-structured interviews	Memory service post-diagnostic support when individualised and one-to-one, causes people with dementia to re-engage socially or with old hobbies.	Moderate

Themes identified for Daisy Chain: a commercial person-centred dementia service that seems to have some elements of case management			
No. of Studies	**Study design**	**Description**	**Confidence (CERQual)**
The person-centred community-based dementia service was well received			
1 (Gladman 2007)	Observations, semi-structured interviews	The person-centred community-based dementia service was well received.	Low
The person-centred community-based dementia service provides a personalised service			
1 (Gladman 2007)	Observations, semi-structured interviews	The person-centred community-based dementia service provides a personalised service.	Low
The person-centred community-based dementia service helped carers to cope			
1 (Gladman 2007)	Observations, semi-structured interviews	The person-centred community-based dementia service helped carers to cope.	Low
The person-centred community-based dementia service kept the people living with dementia and their accommodation clean			
1 (Gladman 2007)	Observations, semi-structured interviews	The person-centred community-based dementia service kept the people living with dementia and their accommodation clean.	Low
The person-centred community-based dementia service enabled people living with dementia to stay at home			

1 (Gladman 2007)	Observations, semi-structured interviews	The person-centred community-based dementia service enabled people living with dementia to stay at home.	Low
The person-centred community-based dementia service had good communication			
1 (Gladman 2007)	Observations, semi-structured interviews	The person-centred community-based dementia service had good communication.	Low
There is a 'right time' for someone living with dementia to move to a residential care home			
1 (Gladman 2007)	Observations, semi-structured interviews	There is a 'right time' for someone living with dementia to move to a residential care home.	Low
Some carers would prefer the person living with dementia to remain in their own home			
1 (Gladman 2007)	Observations, semi-structured interviews	Some carers would prefer the person living with dementia to remain in their own home.	Low
There are sometimes differences of opinion			
1 (Gladman 2007)	Observations, semi-structured interviews	There are sometimes differences of opinion between people living with dementia, paid carers and familial carers.	Low

Themes identified for non-specified case management style(s) in predominantly remote and rural areas in Scotland			
No. of Studies	**Study design**	**Description**	**Confidence (CERQual)**
Carers said they required more help			
1 (Innes 2014)	Semi-structured interviews	Carers generally expressed satisfaction with support received but said they required more help.	Very Low
The lack of alternative options sometimes led to provision of no support at all			
1 (Innes 2014)	Semi-structured interviews	The lack of alternative options sometimes led to provision of no support at all.	Very Low
Poor coordination of services			
2 (Górska 2013, Innes 2014)	Semi-structured interviews	Poor coordination of services. The participants particularly emphasized poor communication between existing services, which results in unsatisfactory case management and delays in service provision. The need for a single point of access to information and service coordination was expressed as a means to manage these challenges and to facilitate more efficient and effective service delivery. Participant reports also highlighted inconsistencies in care provision and suggested the need for well-defined care pathways.	High
Some experienced lack of continuity of care			
2 (Górska 2013, Innes 2014)	Semi-structured interviews	Some experienced lack of continuity of care. This can lead to poor communication and is confusing.	High

Lack of mental stimulation			
1 (Górska 2013)	Semi-structured interviews	Lack of mental stimulation.	Low
Some people living with dementia do not want to make use of day centres			
1 (Innes 2014)	Semi-structured interviews	Some people living with dementia do not want to make use of day centres.	Very Low
Some GPs have a specific interest in dementia and this improves communication			
1 (Innes 2014)	Semi-structured interviews	One interviewee pointed out that some GPs have a specific interest in dementia and this improves communication.	Very Low
There were high satisfaction levels with the support received from the Community Mental Health Team			
1 (Innes 2014)	Semi-structured interviews	There were high satisfaction levels with the support received from the Community Mental Health Team.	Moderate
Participants discussed the importance of staff building a rapport with the person with dementia			
1 (Innes 2014)	Semi-structured interviews	Participants discussed the importance of staff building a rapport with the person with dementia. This facilitates communication.	Very Low
When it was available, a carers' group was appreciated			
1 (Innes 2014)	Semi-structured interviews	When it was available, a carers' group (caregiver support) was appreciated.	Very Low
Practical support was important to carers who received help from services regularly			
1 (Innes 2014)	Semi-structured interviews	Practical support was important to most carers who received help from private or voluntary services regularly. Carers perceived this type of support as an opportunity to take a respite from caregiving responsibilities. Many used the respite time to rest, run errands which required getting out, or to attend carers meetings.	Very Low
Other sources of post-diagnostic support were from family, friends, and neighbours			
1 (Innes 2014)	Semi-structured interviews	Other sources of post-diagnostic support were from family, friends, and neighbours.	Moderate
Some carers have difficulty leaving their relative with someone else			
1 (Innes 2014)	Semi-structured interviews	Some carers have difficulty leaving their relative with someone else.	Very Low
Information was not always in a format appropriate for the person with dementia or carers			
1 (Innes 2014)	Semi-structured interviews	Information was not always in a format appropriate for the person with dementia or carers.	Moderate
Participants preferred a direct approach when receiving information with the opportunity to ask questions			
1 (Innes 2014)	Semi-structured interviews	The way information was delivered was important. Participants preferred a direct approach with the opportunity to ask questions.	Moderate
Care managers should be proactive in anticipating the needs of people living with dementia and their carers			
1 (Innes 2014)	Semi-structured interviews	Care managers should be proactive in anticipating the needs of people living with dementia and their carers and provide relevant information.	Very Low

Themes identified for case management in residential care homes			
No. of Studies	**Study design**	**Description**	**Confidence (CERQual)**
The need for activities, interaction and outings was the most prevalent theme overall			
1 (Popham 2012)	Focus group, interviews	The need for activities, interaction and outings was the most prevalent theme overall.	Moderate
Participants valued freedom to carry out normal everyday activities and domestic chores			
1 (Popham 2012)	Focus group, interviews	Participants spoke about having the freedom to be able to carry out normal everyday activities and domestic chores.	Moderate
Rooms with views were highly valued			
1 (Popham 2012)	Focus group, interviews	Rooms with views were highly valued.	Moderate

Themes identified for Case planning – the Adaption-Coping Model			
No. of Studies	**Study design**	**Description**	**Confidence (CERQual)**
Family carers also valued having the opportunity to learn more about dementia and see other people in the same situation			
1 (Brooker 2017)	Focus group, interviews	It enabled some carers to gain a broader perspective on their own experiences, and facilitate adjustment. By seeing how their relatives were treated at the Meeting Centre and responded to the interactions, some carers were able to reflect on the difficulties faced in their everyday lives.	Moderate
Participants liked the warmth and friendliness of the staff			
1 (Brooker 2017)	Focus group, interviews	Participants liked the warmth and friendliness of the staff. It gave them confidence.	Moderate
The Meeting Centre provides a supportive space for feelings to be aired			
1 (Brooker 2017)	Focus group, interviews	Some carers felt that they were unable to share their true feelings or experiences with family members for fear of judgement, and again the Meeting Centre provides a supportive space for those feelings to be aired.	Moderate
The experience enabled some people to reflect upon their own emotional adjustment			
1 (Brooker 2017)	Focus group, interviews	The experience enabled some people to reflect upon their own emotional adjustment.	Moderate
The planned activity provided a useful structure			
1 (Brooker 2017)	Focus group, interviews	The planned activity provided a useful structure.	Moderate
The participants felt that they were not alone			
1 (Brooker 2017)	Focus group, interviews	The participants felt that they were not alone.	Moderate
Carers were able to get a different perspective			

1 (Brooker 2017)	Focus group, interviews	Seeing other people in similar situations and getting outside perceptions helped one carer to reassess how he views his wife's situation.	Moderate
Attendance was good			
1 (Brooker 2017)	Focus group, interviews	The participants enjoyed attending and therefore the attendance was good.	Moderate

Themes identified for Case planning – Rotherham Carers Resilience Service			
No. of Studies	**Study design**	**Description**	**Confidence (CERQual)**
***Caregiver*: Often people suggested that they felt unsure and extremely anxious about the person they were caring for**			
1 Dayson (2016)	Interviews	Often people suggested that they felt unsure and extremely anxious about the person they were caring for	Moderate
***Caregiver*: Carers felt that the service provided them with a great deal of reassurance, both in practical terms but also emotional**			
1 Dayson (2016)	Interviews	Carers felt that the service provided them with a great deal of reassurance, both in practical terms but also emotional.	Moderate
***Caregiver*: The relief people felt moving forwards**			
1 Dayson (2016)	Interviews	Understanding that the situation will change in the future, beneficiaries of the service described how their knowledge of the service helped them to feel more positive about the future.	Moderate
***Caregiver*: Participants felt supported**			
1 Dayson (2016)	Interviews	People now felt 'in the system' and felt reassured knowing where they could go for support should anything occur in the future.	Moderate
***Caregiver*: Carers reported that the knowledge and experience of the staff was key**			
1 Dayson (2016)	Interviews	Carers were reassured by the expertise of the staff.	Moderate
***Caregiver*: Carers found that they had benefited from the information provided**			
1 Dayson (2016)	Interviews	This is because they had learnt something new or had been reassured that what they were experiencing was not an isolated case.	Moderate
***Caregiver*: Carers received practical assistance**			
1 Dayson (2016)	Interviews	Examples of help ranged from assessments of homes, recommending alarms and safety devices, through to benefits advice and information about community transport and the provision of a home based support service, whereby a care support worker can come to sit with someone for support and reassurance whilst their carer/partner is away.	Moderate

Themes identified for Coordination – for people living with dementia who have comorbidity			
No. of Studies	**Study design**	**Description**	**Confidence (CERQual)**
Family members were often proactive in facilitating continuity and negotiating access to services for their relatives with dementia			
1 Bunn (2017)	Semi-structured interviews	This included acting as an advocate for their family member with dementia, noticing when something was wrong and seeking help.	Moderate
Family members were often proactive in helping clinicians make treatment decisions, such as whether to thrombolyse a PLWD after a stroke			
1 Bunn (2017)	Semi-structured interviews	Family carers also had a significant role in coordinating their relative's care, navigating healthcare systems and facilitating continuity of care; for example, managing appointments, organising transport, keeping records of test results and medication.	Moderate
Family members were often proactive in actively transferring information between HCPs and different services			
1 Bunn (2017)	Semi-structured interviews	Family members were often proactive in actively transferring information between HCPs and different services.	Moderate
The availability of a family carer to act as a proxy, and provide consent, information and post-discharge support impacted on a PLWD's access to care			
1 Bunn (2017)	Semi-structured interviews	HCPs recognised that PLWD who lived alone, or did not have support from a family carer or advocate, were particularly vulnerable and may have poorer access to care.	Moderate
Although HCPs in our study valued the role family carers played, there was little formal recognition of the carers' role, and no systems for negotiating how or when carers' views could be incorporated into care planning			
1 Bunn (2017)	Semi-structured interviews	This was reflected in the many examples provided by their interviews where carers felt undervalued or excluded from decision-making about their relative's care.	Moderate
There were many challenges for family carers			
1 Bunn (2017)	Semi-structured interviews	These included difficulty in understanding how health systems worked and who to contact, their own health problems, emotional and practical challenges of changing roles.	Moderate
Living at a distance and/or with work and family commitments that made taking on responsibilities for day-to-day care difficult			
1 Bunn (2017)	Semi-structured interviews	Caring at a distance may be particularly problematic for carers of PLWD as it is difficult for them to offer support or to monitor adherence to medication over the phone.	Moderate
Support from social networks, such as extended family, friends and religious groups, and from third sector providers were clearly important to PLWD and their carers			
1 Bunn (2017)	Semi-structured interviews	Support from social networks, such as extended family, friends and religious groups, and from third sector providers were clearly important to PLWD and their carers.	Moderate
Formal support from health and social care was often seen as inadequate			
1 Bunn (2017)	Semi-structured interviews	Formal support from health and social care was often seen as inadequate.	Moderate
PWD and family carers valued continuity, in terms of relationships with practitioners but also in terms of encounters that factored in the impact of dementia, that built on earlier conversations and appointments and that included people with dementia and their carers in decision-making			

1 Bunn (2017)	Semi-structured interviews	Many PWD and carers reported positive relationships with their GPs and recognised the role that GPs played in coordinating care.	Moderate
How PWD managed their care, for example, either independently, in tandem with a family carer or with external health and social care support, was linked to where they were on the dementia trajectory			
1 Bunn (2017)	Semi-structured interviews	Some people with early stage dementia were still able to self-manage their care. As the dementia got worse, the PLWD's ability to self-manage declined and responsibility moved, either partly or totally, from the PLWD to a carer. These transitions often happened when strategies to facilitate self-management, for example, memory aids, diaries and dosette boxes, ceased to be effective.	Moderate
Current infrastructure did not support the sharing of information across different specialities			
1 Bunn (2017)	Semi-structured interviews	Current infrastructure did not support the sharing of information across different specialities.	Moderate
For many participants, their comorbid health condition predated the diagnosis of dementia			
1 Bunn (2017)	Semi-structured interviews	Despite this, there appeared to be inadequate consideration by some services of the implications of a diagnosis of dementia on the management of existing conditions.	Moderate
PWD: persona con demenza (person with dementia); HCPs: professionisti sanitari (healthcare professionals).			

Review question 7d (New RQ). How should health and social care be co-ordinated for people with *Mild Cognitive Impairment* (MCI)?

No evidence was found for this review question

Review question 8a (RQ NICE). How should people living with dementia be reviewed post diagnosis?

Post diagnosis review for people living with dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Flexible, multicomponent, care consultation intervention delivered via telephone in partnership with Alzheimer's Associations services				
Mean use of care consultation services	1 RCT (Bass 2003) *	**MD -0.16 (-0.29, -0.03), I^2 n.a.**	157	Moderate
Use of direct care community services	1 RCT (Bass 2003) *	MD 0.02 (-0.47, 0.51), I^2 n.a.	157	Low[b]
Use of non-Association information and support services	1 RCT (Bass 2003) *	MD -0.10 (-0.50, 0.30), I^2 n.a.	157	Low[b]
Number of emergency department visits	1 RCT (Bass 2003) *	MD -0.17 (-0.51, 0.17), I^2 n.a.	157	Low[b]
Number of hospital admissions	1 RCT (Bass 2003) *	MD -0.08 (-0.26, 0.10), I^2 n.a.	157	Low[b]
Number of physician visits	1 RCT (Bass 2003) *	MD -0.01 (-1.36, 1.38), I^2 n.a.	157	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I^2>75%; e: methodological limitations *intervention on dyads				

Post diagnosis review for people living with dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Multidisciplinary case conferences with the involvement of GPs for improving the appropriateness of the management of persons with dementia admitted to residential facilities				
MAI	1 RCT (Crotty 2004) *	**MD 3.69 (1.53, 5.85), I^2 n.a.**	104	Low
Mean number of drugs prescriptions	1 RCT (Crotty 2004) *	MD 0.39 (-0.55, 1.33), I^2 n.a.	104	Low[b]
NHBPS	1 RCT (Crotty 2004) *	MD -2.70 (14.97, 9.57), I^2 n.a.	104	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I^2>75%; e: methodological limitations * intervention on dyads MAI: Medication Appropriateness Index; NHBPS: Nursing Home Behaviour Problem Scale				

Post diagnosis review for people living with dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Network multidisciplinary care including different healthcare professionals				
MMSE	1 RCT (Köhler 2014)	MD 0.70 (-1.70, 3.10), I^2 n.a.	203	Low[b,c]

IADL	1 RCT (Köhler 2014)	MD 0.10 (-0.72, 0.92), I^2 n.a.	203	Low[b]
QoL-AD	1 RCT (Köhler 2014)	MD -0,40 (-2,43, 1,63), I^2 n.a.	203	Low[b]
SF-36 caregiver physical quality of life	1 RCT (Köhler 2014)	MD 0,80 (-3,88, 5,48), I^2 n.a.	203	Low[b]
SF-36 caregiver mental quality of life	1 RCT (Köhler 2014)	MD 2,60 (-3,88, 5,48), I^2 n.a.	203	Low[b]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I^2>75%; e: methodological limitations
* intervention on dyads

Post diagnosis review for people living with dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Care coordination intervention				
STAI – state	1 RCT (Meeuwsen 2012) *	**MD 2.35 (0.35, 4.36), I^2 n.a.**	175	Low
STAI – trait	1 RCT (Meeuwsen 2012) *	**MD 2.14 (0.24, 4.03), I^2 n.a.**	175	Low
CES-D	1 RCT (Meeuwsen 2012) *	**MD 2.09 (0.15, 4.02), I^2 n.a.**	175	Low
Depressive symptoms – GDS	1 RCT (Meeuwsen 2012) *	MD 0.25 (-0.36, 0.86), I^2 n.a.	175	Low[b]
NPI	1 RCT (Meeuwsen 2012) *	MD 1.13 (-0.51, 2.77), I^2 n.a.	175	Low[b]
QoL-AD	1 RCT (Meeuwsen 2012) *	MD 0.25 (-0.76, 1.23), I^2 n.a.	175	Low[b]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
* intervention on dyads

Post diagnosis review for people living with dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Multidimensional assessment				
Mortality	1 RCT (Nourhashemi 2010) *	**RR 1.65 (1.09, 2.49), I^2 n.a.**	1.131	Low
Risk of institutionalisation	1 RCT (Nourhashemi 2010) *	RR 0.52 (0.22, 1.21), I^2 n.a.	1.131	Low[b]
Dropping out of the study	1 RCT (Nourhashemi 2010) *	RR 1.08 (0.90, 1.26), I^2 n.a.	1.131	Low[b]
ADCS-ADL	1 RCT (Nourhashemi 2010) *	MD -0.50 (-2.28, 1.28), I^2 n.a.	1.131	Low[b]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
* intervention on dyads

Post diagnosis review for people living with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
UCLA-ADC Programme - Integrated management of people with dementia by specialist services and GPs based on a structured assessment of people with dementia and their caregivers and implementation of individualised interventions accompanied by continuous monitoring				
Hospice admissions during the last six months of life	1 study* (Jennings 2020)	**RR 1.35 (1.10, 1.65), I^2 n.a.**	3.995	Moderate
Mortality at 7 days after admission to hospice	1 study* (Jennings 2020)	RR 0.53 (0.28, 1.00), I^2 n.a.	3.995	Low[b]
Hospital admissions	1 study* (Jennings 2020)	MD -8.50 (-17.50, 0.50), I^2 n.a.	3.995	Very Low[b]
Number of emergency department access	1 study* (Jennings 2020)	MD -9.40 (-18.97, 0.17), I^2 n.a.	3.995	Very Low[b]
Mean time spent in intensive care unit	1 study* (Jennings 2020)	**MD -8.80 (-16.30, -1.30), I^2 n.a.**	3.995	Low
Mean number of inpatient days	1 study* (Jennings 2020)	**MD -160.10 (-215.74, -104.46), I^2 n.a.**	3.995	Low
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations *Quasi-experimental controlled before-and-after study				

Post diagnosis review for people living with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Integrated care management defined as a complex intervention aimed at the optimal treatment of people with dementia and support of their caregivers through individualised interventions				
Antidementia drug treatment (frequency)	1 RCT (Thyrian 2017) *	**RR 1.47 (1.05, 2.05), I^2 n.a.**	407	Moderate
Potentially inappropriate medication (frequency)	1 RCT (Thyrian 2017) *	**RR 2.31 (1.45, 3.68), I^2 n.a.**	407	Moderate
NPI	1 RCT (Thyrian 2017) *	MD -7.4 (-11.60, -3.20), I^2 n.a.	407	Moderate
MMSE	1 RCT (Thyrian 2017) *	MD -0.80 (-2.45, 0.85), I^2 n.a.	407	Very Low[b,c]
QoL-AD	1 RCT (Thyrian 2017) *	MD 0.10 (-0.01, 0.21), I^2 n.a.	407	Low[b]
BADL	1 RCT (Thyrian 2017) *	MD -0.10 (-0.92, 0.72), I^2 n.a.	407	Low[b]
BIZA-D**	1 RCT (Thyrian 2017) *	MD -0.46 (-1.25, 0.33), I^2 n.a.	407	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations * intervention on dyads ** Berlin Inventory of *Caregivers*' Burden with Dementia Patients				

Post diagnosis review for people living with dementia

Outcomes	No. of Studies	Observed effect, (95% CI), I^2	No. of participants	Certainty of evidence (GRADE)
Multi-component intervention of training and support, with a focus on monitoring and optimising pharmacological treatment with psychotropic drugs in collaboration with the GP				
Drugs prescriptions (mean frequency)	1 RCT (Gedde 2022) *	MD 0.03 (-0.57, -0.63), I^2 n.a.	237	Low[b]
Psychotropic drugs prescriptions (mean frequency)	1 RCT (Gedde 2022) *	MD -0.04 (-0.26, 0.18), I^2 n.a.	237	Low[b]
NPI	1 RCT (Gedde 2022) *	MD -0.07 (-5.18, 5.04), I^2 n.a.	237	Low[b]
CSDD	1 RCT (Gedde 2022) *	MD 1.22 (-0.46, 2.90), I^2 n.a.	237	Low[b]
CGIC	1 RCT (Gedde 2022) *	**MD 0.54 (0.09, 0.99), I^2 n.a.**	237	Moderate

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

* intervention on dyads

** Berlin Inventory of *Caregivers*' Burden with Dementia Patients

Review question 8b (RQ NICE). How should people living with Mild Cognitive Impariment (MCI) be reviewed post diagnosis?

No evidence was found for this review question

Review question 9 (RQ NICE). What effect does training for staff working with people living with dementia have upon the experiences of people living with dementia in their care?

Training for staff working with people living with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Training intervention aimed at improving communication, management of pain and behavioural and psychological disorders, and collaboration between staff from different facilities				
Residential care staff training				
Documented pain assessments (frequency)	1 RCT (Beer 2011)	**aOR 3.75 (1.26, 11.14), I^2 n.a.**	351	Very Low
Structured pain scales (%) at 6 months	1 RCT (Beer 2011)	aOR 1.98 (0.81, 4.83), I^2 n.a.	351	Very Low[b,c]
Frequency of case conferencing at 4 weeks	1 RCT (Beer 2011)	**aOR 4.08 (1.42, 11.67), I^2 n.a.**	351	Very Low
Frequency of case conferencing at 6 months	1 RCT (Beer 2011)	aOR 3.23 (0.95, 11.01), I^2 n.a.	351	Very Low[b,c]
Quality of life	1 RCT (Beer 2011)	aMD 0.97 (-1.55, 3.50), I^2 n.a.	351	Very Low[b,c]
Use of physical restraint observed	1 RCT (Beer 2011)	aOR 1.06 (0.39, 2.94), I^2 n.a.	351	Very Low
Documented restraint at 6 months	1 RCT (Beer 2011)	aOR 1.53 (0.33, 7.14), I^2 n.a.	351	Very Low[b,c]
GPs training				
Documented pain assessments (frequency)	1 RCT (Beer 2011)	**aOR 0.36 (0.14, 0.89), I^2 n.a.**	351	Very Low
Structured pain scales (%) at 6 months	1 RCT (Beer 2011)	aOR 0.60 (0.25, 1.47), I^2 n.a.	351	Very Low[b,c]
Frequency of case conferencing at 4 weeks	1 RCT (Beer 2011)	aOR 1.59 (0.64, 3.95), I^2 n.a.	351	Very Low[b,c]
Frequency of case conferencing at 6 months	1 RCT (Beer 2011)	aOR 1.02 (0.34, 3.02), I^2 n.a.	351	Very Low[b,c]
Documented restraint at 6 months	1 RCT (Beer 2011)	**aOR 0.13 (0.03, 0.47), I^2 n.a.**	351	Very Low
Observed restraint at 6 months	1 RCT (Beer 2011)	aOR 0.44 (0.17, 1.11), I^2 n.a.	351	Very Low[b,c]
Quality of life	1 RCT (Beer 2011)	aMD -0.61 (-3.07, 1.85), I^2 n.a.	351	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations aOR: Odd Ratio aggiustato				

Training for staff working with people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Residential staff training provided by specially trained occupational therapists aimed at improving organizational space, communication and sharing between patients and staff to promote residents' participation in the activities				
MMSE	1 RCT (Wenborn 2013)	aMD -0.36 (-2.22, 1.51), I^2 n.a.	210	Very Low[b,c]
CBS	1 RCT (Wenborn 2013)	aMD 4.13 (-21.10, 29.36), I^2 n.a.	210	Very Low[b,c]
CSDD	1 RCT (Wenborn 2013)	aMD -0.09 (-1.33, 1.16), I^2 n.a.	210	Low[b]
RAID	1 RCT (Wenborn 2013)	aMD 0.57 (-1.52, 2.66), I^2 n.a.	210	Low[b]

QoL-AD	1 RCT (Wenborn 2013)	aMD 0.26 (-3.04, 3.56), I^2 n.a.	210	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
aMD: adjusted mean difference

Training for staff working with people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Residential care staff training: multi-sensory stimulation (snoezelen)				
Frequency of residents' smiling during the morning	1 RCT (van Weert 2005)	**MD 2.87 (0.81, 4.93), I^2 n.a.**	117	Moderate
Aumento della durata media della routine di cure mattutina	1 RCT (van Weert 2005)	**MD 3.98 (1.27, 6.69), I^2 n.a.**	117	Moderate
Nonverbal communication affective positive	1 RCT (van Weert 2005)	MD 7.19 (-5.21, 19.59), I^2 n.a.	117	Very Low[b,c]
Nonverbal communication affective negative	1 RCT (van Weert 2005)	MD 5.36 (-9.39, 1.33), I^2 n.a.	117	Very Low[b,c]
Instrumental communication affettive positive	1 RCT (van Weert 2005)	MD 5.04 (-1.67, 11.75), I^2 n.a.	117	Very Low[b,c]
Instrumental communication affettive negative	1 RCT (van Weert 2005)	MD -0.46 (-1.61, 0.69), I^2 n.a.	117	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Training for staff working with people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Training intervention for nursing home staff aimed at improving their skills in managing behavioral symptoms				
Resident agitation during care interactions	1 RCT (Burgio 2002)	MD 3.61 (-8.89, 16.11), I^2 n.a.	79	Very Low[b,c]
Resident agitation maintained at follow-up	1 RCT (Burgio 2002)	MD 0.60 (-6.85, 8.05), I^2 n.a.	79	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
aMD: mean difference aggiustata

Training for staff working with people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Training program for nursing home staff targeted at providing nutritional skills to improve the staff's attitude and behavior towards nutritional disorders in people with dementia				
Mean quantity of consumed food	1 RCT (Chang 2005)	**MD -0.21 (-0.38, -0.04), I^2 n.a.**	67	Very Low

EdFED	1 RCT (Chang 2005)	**MD 2.70 (1.06, 4.34), I^2 n.a.**	67	Very Low
Total time dedicated to eating	1 RCT (Chang 2005)	MD 2.90 (-0.01, 5.81), I^2 n.a.	67	Very Low[b]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
EdFED: Edinburgh Feeding Evaluation in Dementia

Training for staff working with people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Training program for nursing home staff based on education, group supervision, and individual support				
GADS	1 RCT (Clare 2013)	MD -1.27 (-4.79, 2.25), I^2 n.a.	65	Very Low[b,c]
BASOLL-Motor	1 RCT (Clare 2013)	MD -0.09 (-0.77, 0.59), I^2 n.a.	65	Very Low[b,c]
BASOLL-Sensory functions	1 RCT (Clare 2013)	MD 0.02 (-0.69, 0.65), I^2 n.a.	65	Very Low[b,c]
PRS	1 RCT (Clare 2013)	MD 2.42 (-4.92, 9.76), I^2 n.a.	65	Very Low[b,c]
QUALID	1 RCT (Clare 2013)	MD -3.25 (-7.94, 1.44), I^2 n.a.	65	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
BASOLL: The behavioural assessment scale of later life
PRS: Positive Response Schedule
QUALID: Quality of life in late-Stage Dementia

Training for staff working with people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Structured training programs for nursing home staff targeted at providing specific knowledge on the management of behavioural symptoms of dementia				
CMAI	2 RCT (Davison 2007, Deudon 2009)	MD -5.55 (-9.34, -1.76), I^2 0%	384	Moderate
PAB	2 RCT (Deudon 2009, Visser 2008)	MD -0.08 (-0.37, 0.21), I^2 0%	359	Low[b]
VAB	2 RCT (Deudon 2009, Visser 2008)	MD 0.19 (-1.10, 1.49), I^2 0%	359	Low[b]
ADRQoL	1 RCT (Visser 2008)	MD 2.22 (-11.51, 15.95), I^2 n.a.	53	Very Low[b,c]
Mean number of prescriptions of psychotropic drugs	1 RCT (Deudon 2009)	MD -0.14 (-0.61, 0.33), I^2 n.a.	306	Low[b]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
PAB: Physically Aggressive (PA) behaviour (subscale of CMAI); VAB: Verbally Aggressive (VA) behaviour (subscale of CMAI)

Training for staff working with people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Personalized individual- and group-training program for specialized nursing home staff				
CSDD	1 RCT (McCallion 1999)	**MD -1.41 (-2.47, -0.35), I^2 n.a.**	105	Moderate
CMAI	1 RCT (McCallion 1999)	MD -1.72 (-6.03, 2.59), I^2 n.a.	105	Low[b]
Frequency of physical restrain	1 RCT (McCallion 1999)	MD 0.75 (-0.07, 1.57), I^2 n.a.	105	Low[b]
Frequency of pharmacological restrain	1 RCT (McCallion 1999)	MD 0.37 (-0.56, 1.30), I^2 n.a.	105	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Training for staff working with people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Combined training intervention for nursing home staff specifically aimed at the implementation of personalized care plans				
CSDD	1 RCT (Finnema 2005)	MD 0.72 (-1.35, 2.79), I^2 n.a.	146	Low[b]
Verbally aggresive behaviours – CMAI	1 RCT (Finnema 2005)	MD 0.10 (-1.20, 1.40), I^2 n.a.	146	Low[b]
Physically aggressive behaviours – CMAI	1 RCT (Finnema 2005)	MD -0.16 (-2.14, 1.82), I^2 n.a.	146	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Training for staff working with people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Training programs for nursing home staff to provide multicomponent person-centered interventions of care mapping				
NPI	2 RCT (Chenoweth 2009, van de Ven 2013)	**MD 2.58 (0.79, 436), I^2 0%**	383	Low[b]
Anxiety – CMAI	2 RCT (Chenoweth 2009, van de Ven 2013)	MD -4.97 (-15.54, 5.59), I^2 86%	383	Very Low[b,c,d]
Quality of life	2 RCT (Chenoweth 2009, van de Ven 2013)	SMD -0.04 (-0.25, 0.16), I^2 0%	383	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Training for staff working with people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Training programs for nursing home staff based on a person-centered approach				
Neuroleptic drugs	1 RCT (Fossey 2006)	**RR 0.55 (0.39, 0.76), I^2 n.a.**	338	Moderate
Residents treated with other psychotropic drugs	1 RCT (Fossey 2006)	RR 1.10 (0.92, 1.32), I^2 n.a.	338	Low[b]
n. of residents who fell at least one in the 12 months	1 RCT (Fossey 2006)	RR 0.95 (0.78, 1.16), I^2 n.a.	338	Low[b]
CMAI	1 RCT (Fossey 2006)	MD -0.30 (-1.81, 1.01), I^2 n.a.	338	Low[b]
CMAI	2 RCT (Chenoweth 2009, Chenoweth 2014)	**MD -17.68 (-20.87, -14.48), I^2 0%**	477	Moderate
NPI	1 RCT (Chenoweth 2009)	**MD -7.10 (-9.58, -4.62), I^2 n.a.**	477	Moderate
QUALID	1 RCT (Chenoweth 2009)	**MD -3.10 (-3.90, -2.30), I^2 n.a.**	477	Moderate
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Training for staff working with people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Training intervention for nursing home staff specifically focusing on the management of apathy and depression, and more generally on the management of behavioural symptoms				
NPI- apathy	1 RCT (Leone 2013)	MD 0.11 (-1.57, 1.79), I^2 n.a.	230	Low[b]
NPI- hyperactivity	1 RCT (Leone 2013)	MD 0.40 (-2.97, 3.77), I^2 n.a.	230	Very Low[b,c]
NPI- psychosis	1 RCT (Leone 2013)	MD 0.60 (-1.17, 2.37), I^2 n.a.	230	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Training for staff working with people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Training intervention for nursing home staff specifically focusing on non-verbal communication and expressing emotions				
Composite score including behavioural symptoms, anxiety, depression, and expressiveness	1 RCT (Magai 2002)	**MD -39.20 (-63.22, -15.18), I^2 n.a.**	57	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Training for staff working with people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Training interventions for nursing home staff specifically focusing on the management of behavioral symptoms to decrease the use of restraints and promote the use non-pharmacological strategies				
Frequency of physical restraint	2 RCT (Pellfolk 2010, Huizing 2006)	**RR 0.65 (0.45, 0.94), I^2 62%**	432	Low[a]
Frequency of prescriptions of benzodiazepines	1 RCT (Pellfolk 2010)	RR 1.40 (0.94, 2.08), I^2 n.a.	288	Very Low[b,c]
Frequency of prescriptions of neuroleptic drugs	1 RCT (Pellfolk 2010)	RR 1.24 (0.94, 1.64), I^2 n.a.	288	Very Low[b,c]
Frequency of falls	1 RCT (Pellfolk 2010)	RR 1.17 (0.57, 2.40), I^2 n.a.	288	Very Low[b,c]
Agitation – BARS	1 RCT (Testad 2005)	**MD 4.30 (0.72, 7.88), I^2 n.a.**	142	Low
Frequency of use of physical restraint	1 RCT (Testad 2005)	MD -2.40 (-5.20, 0.40), I^2 n.a.	142	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Training for staff working with people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Specific training intervention for nursing home staff aimed at the implementation of guidelines for the management of depressive and behavioural symptoms				
CSDD	1 RCT (Verkaik 2011)	MD 0.09 (-3.21, 3.39), I^2 n.a.	97	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Training for staff working with people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Training intervention for nursing home staff on a person-centered approach for the management of hygiene				
Towel-bath				
Agitation/aggression	1 RCT (Sloane 2004)	MD -11.22 (-27.80, 5.36), I^2 n.a.	73	Low[a]
Agitation/physical aggression	1 RCT (Sloane 2004)	MD -0.59 (-1.36, 0.18), I^2 n.a.	73	Very Low[b,c]
Verbal agitation	1 RCT (Sloane 2004)	MD -0.31 (-1.00, 0.38), I^2 n.a.	73	Very Low[b,c]
Showering				
Agitation/aggression	1 RCT (Sloane 2004)	MD -8.89 (-25.83, 8.05), I^2 n.a.	73	Very Low[b,c]

Agitation/physical aggression	1 RCT (Sloane 2004)	MD -0.39 (-1.19, 0.41), I^2 n.a.	73	Very Low[b,c]
Verbal agitation	1 RCT (Sloane 2004)	MD -0.09 (-0.79, 0.61), I^2 n.a.	73	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Training for staff working with people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Training intervention for OTs aimed at the implementation of an OT program for people with dementia and their caregivers (COTiD, Community Occupational Therapy in Dementia), along with a specific training on an interdisciplinary training with clinicians and managers				
COPM	1 RCT (Döpp 2015)	MD -0.30 (-1.79, 1.19), I^2 n.a.	33	Very Low[b,c]
DemQoL	1 RCT (Döpp 2015)	MD -0.40 (-1.17, 0.37), I^2 n.a.	33	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations OTs: occupational therapists; COPM: Canadian Occupational Performance Measure				

Training for staff working with people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Implementation of the digital version of a training program for nursing home staff aimed at promoting person-centered interventions, personalized activities and interaction, and the optimization of antipsychotics prescriptions				
Wellbeing of residents – WIB	1 RCT (McDermid 2022)	**MD 0.32 (0.10, 0.54), I^2 n.a.**	130	Moderate
time engaged in positive activities (%)	1 RCT (McDermid 2022)	**MD 10.37 (1.71, 19.03), I^2 n.a.**	130	Low
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Training for staff working with people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Training intervention for nursing home staff, based on Relation Related Care (RRC) and specifically aimed at reducing the use of restraints				
Frequency of restraints use	1 RCT (Testad 2016)	RR 2.06 (0.97, 4.36), I^2 n.a.	197	Very Low[b,c]
NPI	1 RCT (Testad 2016)	MD 4,00 (-2.86, 10.86), I^2 n.a.	197	Very Low[b,c]
CMAI	1 RCT (Testad 2016)	MD 0.50 (-4.67, 5.67), I^2 n.a.	197	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Training for staff working with people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Training protocol for nursing home staff aimed at the implementation of psychosocial interventions and personalized activities, and at the optimization of antipsychotics prescriptions				
NPI	1 RCT (Torres-Castro 2022)	MD 5.20 (-4.31, 14.71), I^2 n.a.	96	Very Low[b,c]
QoL-AD	1 RCT (Torres-Castro 2022)	MD 0.20 (-3.49, 3.89), I^2 n.a.	96	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Training for staff working with people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Training intervention for nursing home staff aimed at implementing guidelines for the review and optimization of medicines in people with severe dementia				
CMAI	1 RCT (Kroger 2023)	MD -2.70 (-8.37, 2.97), I^2 n.a.	123	Low[b]
PACSLAC	1 RCT (Kroger 2023)	MD -0.90 (-2.54, 0.74), I^2 n.a.	123	Low[b]
overall number of drug prescriptions	1 RCT (Kroger 2023)	MD 1.17 (-2.17, 4.51), I^2 n.a.	123	Low[b]
mean number of regular prescriptions	1 RCT (Kroger 2023)	MD 1.33 (-0.33, 2.99), I^2 n.a.	123	Low[b]
mean number of regular prescriptions of antipsychotics	1 RCT (Kroger 2023)	MD 0.03 (-0.27, 0.33), I^2 n.a.	123	Low[b]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
PACSLAC: Pain Assessment Checklist for Seniors with Limited Ability to Communicate

Review question 10a (RQ NICE). What barriers and facilitators have an impact on involving people living with dementia in decisions about their present and future care?
Review question 10b (RQ NICE). What barriers and facilitators have an impact on how people living with dementia can make use of advance planning?

Themes identified for barriers to the involvement of people with dementia in decision-making			
No. of Studies	**Study design**	**Description**	**Confidence (CERQual)**
PWD: Denial of problem			
5 (Goodman 2013, Livingston 2010, Poppe 2012, **Ali 2021, Van Rickstal 2019)**	Focus group, interviews	If the person with dementia is unreconciled to the severity of their needs, this is a barrier to accepting care. The main barrier to advance planning on the part of the people with dementia and carers was difficulty for some people with dementia or carers to accept the diagnosis.	High
9 **(Davies 2021, Dekker 2022, Fried 2021, Ingravallo 2018, Sussman 2021, Tetrault 2022, Tilburgs 2018, Van Rickstal 2019, Van Rickstal 2022)**	Pts observations, interviews, focus groups	Persons with dementia tend to refuse to talk about future decision-making due to personal preferences. Focused on the present, person with dementia did not feel the need to discuss such issues before the actual situation arose, or that they did not want to discuss their own death.	High
PWD: Rejection of help			
1 (Livingston 2010, **Sussman 2021**)	Focus group, interviews	People will often reject help, either because they feel they do not need it or because accepting help would involve psychologically acknowledging the severity of their problems.	High
PWD: Deference to authority			
1 (Goodman 2013)	Interviews	Having dementia combined with living in a care home meant the older people often accepted that staff and visiting healthcare professionals would make decisions on their behalf.	Very Low
4 (Goodman 2013, **Sinclar 2019, Ali 2021, Ingravallo 2018)**	Interviews	Knowing that they had dementia affected confidence in expressing opinions, self-esteem and whether they thought their views were worth listening to.	Very Low
3 (**Fried 2021, Ingravallo 2018, Van Rickstal 2019**)	Focus group, interviews	Knowing that their family will take care of it, they delegate to them all the decisions as they arise.	High
PWD: Poor relationship with formal or informal carers			
1 (Goodman 2013)	Interviews	If the person with dementia has a poor relationship with the carer(s), this could be a barrier to expressing a wish regarding care.	Very Low
PWD: One partner more dominant			
1 (Dening 2017)	Semi-strucutred interviews	Often there was one partner more dominant in decision-making.	Moderate
Professional: Not recognising problems			
1 (Livingston 2010)	Focus group, interviews	Healthcare professionals may not recognise people need additional assistance to be involved in decision making particularly when people are not open about difficulties they are having.	High

Professional: Late diagnosis			
1 (Livingston 2010)	Focus group, interviews	If the diagnosis of dementia is delayed, this can make it difficult for all the necessary advance discussions to be had before capacity issues start to occur.	High
Professional: Timing and quantity of information given			
4 (Livingston 2010, Lord 2015, **Van Rickstal 2022, Fried 2021**)	Focus group, interviews	Feelings of guilt and distress for carers were often exacerbated by a perceived lack of support and information.	High
Professional: Confidentiality and data protection			
1 (Livingston 2010)	Focus group, interviews	Carers felt they could not get the necessary information to help support decision-making because of confidentiality issues.	High
Professional: Bureaucracy and rigidity (sticking to protocols)			
1 (Livingston 2010)	Focus group, interviews	People felt discussions were not sufficiently individualised due to a reliance on following prespecified protocols.	High
Caregiver: Role conflict			
2 (Livingston 2010, Lord 2015)	Focus group, interviews	Many carers reported the decision was against the care recipient's wishes and signalled a major carer role transition. Carers report a shift in the dynamic to a "mother/child" type relationship. They struggled with being expected to relinquish their *caregiver* role and that friends and family perceived the dyadic relationship to be over.	High
Caregiver: Relationship to person living with dementia			
1 (Samsi 2013)	Interviews	Friend carers often felt they were less able to make decisions on behalf of individuals than family carers.	Low
Caregiver: Carer guilt			
2 (Livingston 2010, Lord 2015)	Focus group, interviews	Feelings of anguish and guilt over decisions made. Journey towards a decision was directed by a mixture of fatigue and a lack of obvious or available alternatives. Feelings of guilt and failure were particularly strong for people obliged to cope alone.	High
Caregiver: Family conflict			
2 (Livingston 2010, Samsi 2013)	Focus group, interviews	When the person with dementia was involved in decision-making, they usually expressed reluctance to move to a care home. This often led the carer either to delay the decision or exclude the person with dementia from decision-making.	High
1 (**Davies 2021**)	Semi-structured interviews	A lack of coherence, unclear roles and need for negotiations within families created difficulties in making decisions.	Low
1 (**Sinclar 2019**)	Interviews	Different beliefs, values systems, and "realities" experienced by different people in the person's family and social networks led to conflict around decision-making.	Low
1 (**Sinclar 2019**)	Interviews	Histories of problematic relationships with other family members impacted negatively on establishing collaborative decision-making pro-cesses.	Low

Caregiver: Rigidity of system			
1 (Livingston 2010, **Dekker 2022**)	Focus group, interviews	People felt that once a decision was reached, it was then difficult to change this decision if circumstances changed, and this led to a reluctance to make initial decisions.	High
Caregiver: Cultural issues			
3 (Lord 2015, Mackenzie 2006, **Sinclar 2019)**	Interviews	Cultural issues may place a particular strain on decision-making around the choice of the decision-maker and future places of care. In South Asian communities, there may be a tendency to want to protect the person with dementia from ridicule by keeping them away from other people.	Moderate
1 (**Davies 2021**)	Semi-structured interviews	Societal stigma associated with dementia also contributed to carers' stress and created difficult environments for caring and decision-making	Low
1 (**Ali 2021**)	Interviews	Carers reported that ACP should not be initiated, as such discussions of end-of-life issues were considered taboo and run counter to prevailing Asian cultural values, such as filial piety and respect for the elderly.	Low
Structural: Inability to plan			
2 (Lord 2015, Poppe 2013)	Interviews	Struggle with knowing when to seek care home placement due to dementia being unpredictable and wait lists of institutions. Some patients find discussing the future difficult without knowing what the future will bring.	High
PWD: Capacity, health and well-being			
3 (**Davies 2021, Ali 2021, Ingravallo 2018**)	Semi-structured interviews	Perceptions about physical health, psychological wellbeing, and capacity, affected when and how decisions were made including options available.	High
Professional: Distant behaviour			
1 (**Tilburgs 2018**)	Focus group, interviews	GP was too distant and did not listen to them, too little contact with patients with dementia and their *caregiver*s	Low
Caregiver: Institutional admission (also hospital)			
1 (**Sinclar 2018**)	Interviews	Admission of one partner to hospital or residential care had disrupted usual patterns of joint decision-making, due to institutional processes which excluded the spouse partner and limited their access to information.	Low
Caregiver: Inappropriate Timing of Discussion			
1 (**Ali 2021**)	Interviews	Inertia among *caregiver*s against initiating ACP discussions in the mild stage of dementia, despite acknowledging the benefits of conducting these discussions prior to loss of cognitive functioning, as the patient's condition had not yet sufficiently deteriorated to such an extent as to warrant discussion of such "serious" and taboo matters.	Low
PWD: person with dementia.			

Themes identified for facilitators to the involvement of people with dementia in decision-making			
No. of Studies	**Study design**	**Description**	**Confidence (CERQual)**
PWD: Reconceptualisation and adjustment			
1 (Livingston 2010)	Focus group, interviews	Re-conceptualisation of services as optimising independence. Allowing services to develop slowly.	High
Professional: Providing practical support			
2 (Livingston 2010, Lord 2015)	Focus group, interviews	Suggesting interventions to facilitate agreement, or structured approaches to decision making. Collaboration with staff helped carers with decision making, and this was facilitated by a trusted healthcare professional who consulted them and advocated effectively.	High
1 (Livingston 2010)	Focus group, interviews	Providing high-quality information in a timely fashion.	High
1 (**Sinclar 2019**)	Semi-structured interviews	Taking time to explain concepts, being patient, repeating information as required, and not rushing the person with dementia.	Low
Professional: Initiating conversations			
1 (Lord 2015)	Focus group, interviews	Carers felt that clinician's raising these discussions helped them with decision-making.	High
Professional: Legal and financial issues			
1 (Livingston 2010)	Focus group, interviews	Ensuring the patient is asked to give permission for information to be given to carers. Access to legal and financial advice.	High
Professional: Structured tools			
1 (Poppe 2013)	Interviews	Open-ended, structured tools may be useful to guide discussions around advance planning. Staff who had not yet conducted any advance care planning discussions themselves were unsure how to initiate the discussion with those people with dementia who had not raised the issue themselves, but saw the tool as a potential way of facilitating this.	Low
Caregiver: Participation			
1 (Livingston 2010)	Focus group, interviews	Carer accompanying patient on visits to healthcare professionals. Posing a question to the person at the "right" time, gauging when their relative was likely to be most engaged in conversation, and presenting a limited number of options.	High
Caregiver: Shared decision-making			
2 (Livingston 2010, Lord 2015)	Focus group, interviews	Carers found it helpful to hear the perspectives of other members of the family or professionals when making decision on behalf of the person with dementia – they felt it "gave permission" to make decisions.	High
Caregiver: Family cohesion			
2 (Livingston 2010, Lord 2015)	Focus group, interviews	Not feeling that different members of the family are pulling in different directions. Carers often sought reassurance after decision making from other family members.	High

Intervention: "Talking Mats"			
1 (Murphy 2013)	Interviews	Discussing care was facilitated by using Talking Mats. Talking Mats helped the participants with dementia to be aware of what their family members were doing for them, and were seen an enjoyable activity which improved communication between the person with dementia and his/her family.	Low
Structural: Social support			
2 (Livingston 2010, **Sinclar 2019**)	Focus group, interviews	Extended family, voluntary and community networks.	High
PWD: Validation of fears			
1 (**Sussman 2021**)	Focus group	Validating participants' fears regarding the quality of care that could be expected from formal care providers seemed to offer some opportunities for ACP.	Low
Professional: The relationship with the general practitioner			
1 (**Tilburgs 2018**)	Focus group, interviews	it is important that the GP knows the person with dementia personally, is empathic, supportive and provides information respectfully.	Low
PWD: person with dementia; ACP: Advance Care Planning; GP: General Practitioner.			

Review question 11a (RQ NICE). What are the optimal management strategies (including treatments) for people living with dementia with co-existing physical long-term conditions?

HYPERTENSION

Hypertension treatment in people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Telmisartan vs amlodipine at 6 months of treatment				
MMSE	1 RCT (Kume 2012)	MD 1.30 (-2.27, 4.87), I^2 n.a.	20	Very Low[b,c]
ADAS-Cog	1 RCT (Kume 2012)	MD -4.20 (-10.14, 1.74), I^2 n.a.	20	Very Low[b,c]
Systolic blood pressure	1 RCT (Kume 2012)	MD 5.00 (-6.61, 16.61), I^2 n.a.	20	Very Low[b,c]
Heart rate	1 RCT (Kume 2012)	MD -1.00 (-5.36, 3.36), I^2 n.a.	20	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Hypertension treatment in people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Home blood pressure measurement by people with dementia or their caregivers (HBPM) compared to 24-hour (24h-ABPM) or daily ambulatory blood pressure monitoring (d-ABPM)				
Systolic blood pressure HBPM vs 24h-ABPM	1 RCT (Plichart 2013)	**MD 11.30 (4.61, 17.99), I^2 n.a.**	60	Moderate
Systolic blood pressure HBPM vs d-ABPM	1 RCT (Plichart 2013)	**MD 9.70 (3.08, 16.32), I^2 n.a.**	60	Moderate
Diastolic blood pressure HBPM vs 24h-ABPM	1 RCT (Plichart 2013)	MD 1.00 (-2.76, 4.76), I^2 n.a.	60	Very Low[b,c]
Diastolic blood pressure HBPM vs d-ABPM	1 RCT (Plichart 2013)	MD 0.00 (-3.76, 3.76), I^2 n.a.	60	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Hypertension treatment in people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Thyazides vs not thyazides				
MoCA	1 RCT (Kocyigit 2019)	**MD 2.37 (0.78, 3.96), I^2 n.a.**	62	Very Low
MMSE	1 RCT (Kocyigit 2019)	MD -0.15 (-2.15, 1.85), I^2 n.a.	62	Low[b]
IADL	1 RCT (Kocyigit 2019)	MD -0.03 (-1.21, 1.15), I^2 n.a.	62	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

CARDIOVASCULAR RISK

Cardiovascular risk treatment in people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Multicomponent intervention vs standard care				
Levels of total cholesterol	1 RCT (Richard 2009)	**MD -0.94 (-1.43, -0.45), I^2 n.a.**	94	Low
LDL	1 RCT (Richard 2009)	**MD -0.90 (-1.44, -0.36), I^2 n.a.**	94	Low
HDL	1 RCT (Richard 2009)	MD -0.02 (-0.17, 0.13), I^2 n.a.	94	Low[b]
MMSE	1 RCT (Richard 2009)	MD -0.55 (-3.12, 2.02), I^2 n.a.	94	Very Low[b,c]
Systolic blood pressure	1 RCT (Richard 2009)	MD -4.12 (-14.75, 6.16), I^2 n.a.	94	Very Low[b,c]
Diastolic blood pressure	1 RCT (Richard 2009)	MD -1.97 (-8.21, 4.26), I^2 n.a.	94	Low[b]
Glycated haemoglobin	1 RCT (Richard 2009)	MD 0.20 (-0.08, 0.48), I^2 n.a.	94	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

DIABETES

Diabetes treatment in people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Pioglitazone + standard di cura (sulfaniluree, biguanidi e inibitori dell'α-glucosidasi) vs placebo				
MMSE	1 RCT (Sato 2011)	MD 1.30 (-1.53, 4.14), I^2 n.a.	42	Very Low[b,c]
ADAS-Cog	1 RCT (Sato 2011)	MD -3.50 (-8.02, 1.02), I^2 n.a.	42	Very Low[b,c]
Fasting levels of insulin	1 RCT (Sato 2011)	MD -1.60 (-4.41, 1.21), I^2 n.a.	42	Low[b]
Fasting levels of glucose	1 RCT (Sato 2011)	MD 1.00, (-26.99 – 28.99), I^2 n.a.	42	Very Low[b,c]
Glycated haemoglobin	1 RCT (Sato 2011)	MD 0.00 (-0.84, 0.84), I^2 n.a.	42	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

INCONTINENCY

Incontinency treatment for people with dementia				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Personalized programme				
SPMSQ	1 RCT (Jirovec 2001)	MD -0.37 (-1.81, 1.07), I^2 n.a.	74	Low[b]
Functional abilities	1 RCT (Jirovec 2001)	MD 1.18 (-1.24, 3.60), I^2 n.a.	74	Low[b]
Mean frequency of incontinence	1 RCT (Jirovec 2001)	MD -0.08 (-0.27, -0.11), I^2 n.a.	74	Low[b]
% of participants with an improvement in urinary incontinence	1 RCT (Jirovec 2001)	RR 1.27 (0.83, 1.94), I^2 n.a.	74	Low[b]
Behavioural therapy of prompted voiding				
Mean reduction of incontinent episodes per day	1 RCT (Engberg 2002)	MD 19.8 (-10.49, 50.09), I^2 n.a.	19	Very Low[b,c]
Mean reduction of incontinent episodes in daytime	1 RCT (Engberg 2002)	MD 12.8 (-21.55, 47.15), I^2 n.a.	19	Very Low[b,c]
Mean reduction of urinary incontinence episodes in daytime	1 RCT (Engberg 2002)	MD 8.5 (-28.35, 45.35), I^2 n.a.	19	Very Low[b,c]
Mean reduction of urinary incontinence episodes per day	1 RCT (Engberg 2002)	MD 17.60 (-14.58, 49.78), I^2 n.a.	19	Very Low[b,c]
Number of self-initiated toilets per day	1 RCT (Engberg 2002)	MD 1.20 (-2.20, 4.60), I^2 n.a.	19	Very Low[b,c]
Behavioural therapy on timed voiding (TV)				
Reduction in the number of night-time incontinent episodes (frequency)	1 RCT (Tobin 1986)	**RR 1.80 (1.12, 2.89), I^2 n.a.**	191	Very Low[b,c]
Reduction in the number of daytime incontinent episodes (frequency)	1 RCT (Tobin 1986)	RR 1.34 (0.90, 2.01), I^2 n.a.	191	Very Low[b,c]
N° of people with a lower volume of incontinence	1 RCT (Tobin 1986)	RR 1.01 (0.52, 1.96), I^2 n.a.	191	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

HEARING LOSS

Trattamento dell'ipoacusia in persone con demenza				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Hearing aids				
MMSE	1 RCT (Nguyen 2017, Adrait 2017)	MD -0.40 (-3.05, 2.25), I^2 n.a.	47	Very Low[b,c]
ADAS-Cog	1 RCT (Nguyen 2017, Adrait 2017)	MD 1.50 (-5.71, 8.71), I^2 n.a.	47	Very Low[b,c]
NPI	1 RCT (Nguyen 2017, Adrait 2017)	MD -6.00 (-20.93, 8.93), I^2 n.a.	47	Very Low[b,c]
IADL	1 RCT (Nguyen 2017, Adrait 2017)	MD -0.50 (-2.21, 1.21), I^2 n.a.	47	Very Low[b,c]
ADRQL	1 RCT (Nguyen 2017, Adrait 2017)	MD 21.10 (-39.85, 82.05), I^2 n.a.	47	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Review question 11b (New RQ). What are the optimal management strategies (including treatments) for people with MCI with co-existing physical long-term conditions?

HYPERTENSION

Hypertension treatment in people with MCI				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Candesartan vs lisinopril				
TMT-B	1 RCT (Hajjar 2020)	**aMD -12.0 (-21.70, -2.30), I^2 n.a.**	176	Moderate
TMT-A-B	1 RCT (Hajjar 2020)	**aMD -13.60 (-23.60, -3.70), I^2 n.a.**	176	Moderate
Nilvadipine vs amlodipine				
MMSE	1 RCT (Hanyu 2007)	MD 0.70 (-1.73, 3.13), I^2 n.a.	12	Very Low[b,c]
ADAS-Cog	1 RCT (Hanyu 2007)	MD 0.00 (-2.86, 2.86), I^2 n.a.	12	Very Low[b,c]
Systolic blood pressure	1 RCT (Hanyu 2007)	MD -3.00 (-10.19, 4.19), I^2 n.a.	12	Very Low[b,c]
Diastolic blood pressure	1 RCT (Hanyu 2007)	MD 2.00 (-4.46, 8.46), I^2 n.a.	12	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations aMD: adjusted mean difference				

DIABETES

Diabetes treatment in people with MCI				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Behavioural intervention versus self-management training				
Levels of glycated haemoglobin at 12 months	1 RCT (Rovner 2017)	MD -0.37 (-1,11, 0,37), I^2 n.a.	87	Low[b]
Dapagliflozin and cognitive behavioural training				
MMSE	1 RCT (Zhao 2022)	**MD 2.72 (1.58, 3.86), I^2 n.a.**	96	Moderate
QoL	1 RCT (Zhao 2022)	**MD 9.74 (7.18, 12.30), I^2 n.a.**	96	Moderate
Levels of glycated haemoglobin	1 RCT (Zhao 2022)	**MD -1.78 (-2.47, -1.09), I^2 n.a.**	96	Moderate
Levels of fasting glucose	1 RCT (Zhao 2022)	MD -0.93 (-2.24, 0.38), I^2 n.a.	96	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations aMD: adjusted mean difference				

Review question 12a (RQ NICE). What are the optimal management strategies (including treatments) for people with dementia and an enduring mental health condition?
Review question 12b (New RQ). What are the optimal management strategies (including treatments) for people with Mild Cognitive Impairment and an enduring mental health condition?

No evidence was found for these review questions.

Review question 13 (RQ NICE). What are the most effective ways of managing the transition between different settings (home, care home, hospital, and respite) for people living with dementia?

Intervention for people with dementia

Transition between different settings				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Intervention targeted to people with dementia to improve spatial orientation when moving into a new care environment				
PAS	1 RCT (McGilton 2003)	MD 0.28 (-0.86, 1.42), I^2 n.a.	32	Low[b,e]
SOS	1 RCT (McGilton 2003)	MD 0.90 (-1.15, 2.95), I^2 n.a.	32	Low[b,e]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations; PAS: Pittsburgh Agitation Scale; SOS: spatial orientation				

Intervention for caregivers of people with dementia

Transition between different settings				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Psychosocial intervention aimed at the psychological and emotional support of people with dementia and their caregivers when moving to a care home (Residential Care Transition Module)				
CES-D	1 RCT (Gaugler 2015)	MD -5.00 (-14.38, 4.38), I^2 n.a.	36	Very Low[b,c,e]
PSS	1 RCT (Gaugler 2015)	MD -5.08 (-11.96, 1.80), I^2 n.a.	36	Very Low[b,c,e]
ZBI	1 RCT (Gaugler 2015)	MD -2.85 (-7.93, 2.23), I^2 n.a.	36	Very Low[b,c,e]
Social support intervention for caregivers of people with dementia (New York University Caregiver Intervention, NYUCI) based on family counselling sessions aimed at supporting caregivers of people with dementia who recently moved to a care h				
ZBI	1 RCT (Gaugler 2011)	MD -0.77 (-2.81, 1.27), I^2 n.a.	406	Very Low[b,c,e]
GDS	1 RCT (Gaugler 2011)	**MD -1.71 (-3.02, -0.40), I^2 n.a.**	406	Low[e]
Psychosocial telephone intervention aimed at supporting caregivers of people with dementia who recently moved to a care home				
CES-D	1 RCT (Davis 2011)	MD 0.29 (-8.27, 8.85), I^2 n.a.	46	Very Low[b,c,e]
ZBI	1 RCT (Davis 2011)	MD -5.07 (-15.39, 5.25), I^2 n.a.	46	Very Low[b,c,e]
Facility satisfaction	1 RCT (Davis 2011)	LS MD 0.31 (-0.18, 0.80), I^2 n.a.	46	Very Low[b,c,e]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; LS: least square; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations; PSS: Perceived stress scale; GDS: Geriatric Depression Scale; ZBI: Zarit Burden Inventory; CES-D: Center for Epidemiologic Studies Depression Scale				

Review question 14a (RQ NICE). How effective are caregivers' assessments in identifying the needs of caregivers of people with dementia?

Review question 14b (RQ NICE). What interventions/services are most effective for supporting the wellbeing of informal caregivers of people with dementia?

Psychoeducational -interventions				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Group-based intervention				
Carer burden (ZBI)	5 RCT (Hebert 2003, Hepburn 2005, Seike 2021, Tawfik 2021, Yazdanmanesh 2023)	**MD -6.53 (-11.35, -1.70), I^2 74%**	421	Low[d]
Carer depression (CES-D)	2 RCT (Seike 2021, Sepe-Monti 2016)	MD -6.18 (-18.64, 6.27), I^2 96%	218	Very Low[b,c]
Carer anxiety (STAI)	1 RCT (Hebert 2003)	MD 0.37 (-5.27, 6.01), I^2 n.a.	116	Very Low[b,c]
Carer anxiety (GHQ)	1 RCT (Ghaffari 2019)	**MD -8.66 (-10.54, -6.78), I^2 n.a.**	50	Very Low[b,c]
Carer distress	1 RCT (Hepburn 2005)	MD -1.99 (-7.17, 3.19), I^2 n.a.	131	Very Low[b,c]
Carer depression – MADRS	1 RCT (Kurz 2010)	MD -0.80 (-2.72, 1.12), I^2 n.a.	221	Low[b]
Carer depression (GHQ)	1 RCT (Ghaffari 2019)	**MD -4.38 (-6.62, -2.14), I^2 n.a.**	50	Low[c]
Carer self-efficacy	1 RCT (Hebert 2003)	MD -3.14 (-10.88, 4.60), I^2 n.a.	116	Very Low[b,c]
Carer stress	1 RCT (Done 2001)	MD -0.40 (-7.17, 6.37), I^2 n.a.	41	Very Low[b,c]
Individual intervention				
Carer burden (ZBI)	1 RCT (Caparrol 2021)	MD -2.60 (-14.42, 9.22), I^2 n.a.	37	Very Low[b,c]
Carer self-efficacy	1 RCT (Gitlin 2001)	MD 0.01 (-0.10, 0.12), I^2 n.a.	171	Low[b]
Carer depression (BDI)	1 RCT (Caparrol 2021)	MD -3.60 (-9.47, 2.27), I^2 n.a.	37	Very Low[b,c]
Carer stress	2 RCT (Caparrol 2021, Stirling 2012)	SMD -0.22 (-0.70, 0.26), I^2 0%	68	Very Low[b,c]
Carer anxiety (BAI)	1 RCT (Caparrol 2021)	MD -3.00 (-9.12, 3.12), I^2 n.a.	37	Very Low[b,c]
Technology-based psychoeducational interventions				
Carer burden*	1 RCT (Hattink 2015)	MD 0.04 (-0.77, 0.85), I^2 n.a.	46	Low[b]
Carer burden (ZBI)	3 RCT (Hepburn 2022, Kales 2018, Salehinejad 2022)	**MD -4.12 (-7.50, -0.73), I^2 49%**	256	Low[a]
Carer anxiety (STAI)	1 RCT (Hepburn 2022)	**MD 4.65 (0.90, 8.40), I^2 n.a.**	160	Low[c]
Carer stress	2 RCT (Hepburn 2022, Kales 2018)	SMD 0.37 (-0.37, 1.10), I^2 82%	206	Very Low[b,c]
Carer depression (CES-D)	4 RCT (Brennan 1995, Hepburn 2022, Kales 2018, Eisdorfer 2003)	**MD -3.10 (-4.83, -1.37), I^2 0%**	353	Moderate
Carer depression (BDI)	1 RCT (Steffen 2000)	MD -4.66 (-9.40, 0.08), I^2 n.a.	19	Very Low[b,c]
Carer self-efficacy	2 RCT (Hattink 2015, Steffen 2000)	SMD 0.43 (-0.06, 0.93), I^2 0%	65	Very Low[b,c]

Telephone-based interventions				
Carer depression (CES-D)	2 RCT (Au 2015, Sarabia-Cobo 2021)	MD 1.66 (-11.10, 14.42), I^2 90%	165	Very Low[b,c]
Carer stress (PSS)	1 RCT (Sarabia-Cobo 2021)	MD 2.30 (-1.56, 6,16), I^2 n.a.	106	Very Low[b,c]
Carer self-efficacy (CSES)	1 RCT (Sarabia-Cobo 2021)	**MD 4.40 (4.08, 4.72), I^2 n.a.**	106	Moderate
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; LS: least square; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Skill training interventions				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Group-based intervention				
Carer burden (ZBI)	2 RCT (Hepburn 2001, Zarit 1982)	MD -4.32 (-11.37, 2.74), I^2 17%	115	Very Low[b,c]
Carer depression (CES-D)	3 RCT (Gonzalez 2014, Hepburn 2001, Oken 2010)	MD -2.25 (-4.59, 0.08), I^2 0%	217	Low[b]
Carer depression (ZDS)	1 RCT (Zarit 1982)	MD 5.16 (-3.52, 13.84), I^2 n.a.	21	Very Low[b,c]
Carer Anxiety (STAI)	1 RCT (Gonzalez 2014)	MD 2.37 (-3.93, 8.67), I^2 n.a.	102	Very Low[b,c]
Carer Stress (PSS)	1 RCT (Oken 2010)	MD 1.43 (-4.68, 7.54), I^2 n.a.	21	Very Low[b,c]
Carer self-efficacy (GPSE)	1 RCT (Oken 2010)	MD -1.00 (-6.35, 4.35), I^2 n.a.	21	Very Low[b,c]
Individual interventions				
Carer strain	1 RCT (Horvat 2013)	MD -1.01 (-2.36, 0.34), I^2 n.a.	108	Low[b]
Carer burden (ZBI)	1 RCT (Martin-Carrasco 2009)	**MD -10.20 (-17.52, -2.88), I^2 n.a.**	82	Low[c]
Carer depression (CES-D)	2 RCT (Burgio 2003, Losada 2004)	MD -2.50 (-6.88, 1.88), I^2 0%	137	Very Low[b,c]
Depression (BSI)	1 RCT (Quayhagen 2000)	MD 0.06 (-0.31, 0.43), I^2 n.a.	44	Low[b]
Carer Anxiety (STAI)	1 RCT (Burgio 2003)	MD -0.39 (-3.85, 3.07), I^2 n.a.	118	Very Low[b,c]
Carer Anxiety (BSI)	1 RCT (Quayhagen 2000)	MD -0.02 (-0.39, 0.35), I^2 n.a.	44	Low[b]
Carer Stress	1 RCT (Quayhagen 2000)	MD -1.33 (-14.55, 11.89), I^2 n.a.	44	Very Low[b,c]
Carer self-efficacy (RSCSE)	1 RCT (Horvat 2013)	MD 44.65 (-31.50, 120.80), I^2 n.a.	108	Very Low[b,c]
Technology-based psychoeducational interventions				
Carer burden (ZBI)	1 RCT (Liddle 2012)	MD -3.66 (-10.41, 3.09), I^2 n.a.	29	Very Low[b,c]
Depression	1 RCT (Chang 1999)	MD -0.08 (-0.48, 0.32), I^2 n.a.	65	Very Low[b,c]
Carer anxiety	1 RCT (Chang 1999)	MD -0.05 (-0.43, 0.32), I^2 n.a.	65	Very Low[b,c]
Carer self-efficacy	1 RCT (Chang 1999)	MD 3.04 (-0.71, 6.79), I^2 n.a.	65	Very Low[b,c]

Telephone-based interventions				
Carer burden	1 RCT (Davis 2004)	MD -5.10 (-12.71, 2.51), I^2 n.a.	26	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; LS: least square; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Psychoeducational and skill-training interventions				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Group-based intervention				
Carer Burden (ZBI)	2 RCT (De Rotrou 2011, Ostwald 1999)	MD -3.42 (-9.03, 2.20), I^2 0%	221	Very Low[b,c]
Carer depression (MADRS)	1 RCT (De Rotrou 2011)	MD -1.41 (-5.45, 2.63), I^2 n.a.	141	Very Low[b,c]
Carer depression (CES-D)	2 RCT (Ostwald 1999, Losada 2011)	MD -2.86 (-6.75, 1.03), I^2 0%	199	Very Low[b,c]
Carer Stress	2 RCT (Ulstein 2007, Senanarong 2004)	SMD -0.17 (-0.44, 0.09), I^2 0%	221	Low[b]
Carer ability of coping	2 RCT (De Rotrou 2011, Coon 2003)	SMD 1.04 (-0.37, 2.44), I^2 95%	226	Very Low[b,c]
Carer depression (MAACL)	1 RCT (Coon 2003)	**MD -3.30 (-4.06, -2.54), I^2 n.a.**	85	Moderate
Individual interventions				
Carer Burden (ZBI)	2 RCT (Gavrilova 2009, Guerra 2011)	**MD -4.18 (-5.96, -2.39), I^2 0%**	111	Moderate
Burden (ZBI) – dico.	1 RCT (Belle 2006)	RR 1.14 (0.90, 1.44), I^2 n.a.	518	Low[b]
Carer strain scale	1 RCT (Bourgeois 2002)	MD -11.50 (-27.88, 4.88), I^2 n.a.	33	Very Low[b,c]
Depression (CES-D) – dico.	1 RCT (Belle 2006)	**RR 1.38 (1.11, 1.72), I^2 n.a.**	518	Moderate
Depression (CES-D)	3 RCT (Joling 2012, Burns 2003, Bourgeois 2002)	MD -1.12 (-3.59, 1.35), I^2 0%	306	Low[b]
Depression (CES-D short)	1 RCT (Judge 2013)	MD -0.78 (-2.47, 0.91), I^2 n.a.	118	Very Low[b,c]
Anxiety	1 RCT (Judge 2013)	MD -1.47 (-4.17, 1.23), I^2 n.a.	118	Very Low[b,c]
Depression (HADS)	1 RCT (Livingston 2013)	MD -0.80 (-2.24, 0.64), I^2 n.a.	259	Low[b]
Anxiety (HADS)	2 RCT (Livingston 2013, Joling 2012)	MD -0.35 (-1.30, 0.61), I^2 0%	451	Low[b]
Anxiety (STAI)	1 RCT (Bourgeois 2002)	MD 4.20 (-5.99, 14.39), I^2 n.a.	39	Very Low[b,c]
Carer Stress (RSS)	1 RCT (Nobili 2004)	MD -1.40 (-8.75, 5.95), I^2 n.a.	39	Very Low[b,c]
Carer Stress (PSS)	1 RCT (Bourgeois 2002)	MD -0.50 (-3.30, 2.30), I^2 n.a.	38	Very Low[b,c]
Quality of Life	4 RCT (Burns 2003, Gavrilova 2009, Joling 2012, Judge 2013)	SMD 0.04 (-0.15, 0.23), I^2 0%	433	Low[b]
Carer self-efficacy	3 RCT (Bourgeois 2002, Ducharme 2011, Judge 2013)	SMD 0.16 (-0.10, 0.43), I^2 11%	256	Low[b]
Technology-based psychoeducational interventions				

Carer Burden (ZBI)	1 RCT (Christancho-Lacroix 2015)	MD 1.80 (-9.69, 13.29), I^2 n.a.	49	Very Low[b,c]
Carer strain	1 RCT (Beauchamp 2005)	MD -2.20 (-5.31, 0.91), I^2 n.a.	299	Very Low[b,c]
Carer depression (CES-D)	4 RCT (Beauchamp 2005, Blom 2015, Gallagher-Thompson 2010, Kajiyama 2013)	**MD -2.45 (-4.01, -0.88), I^2 0%**	717	Moderate
Carer depression (BDI)	1 RCT (Christancho-Lacroix 2015)	MD 1.40 (-5.54, 8.34), I^2 n.a.	49	Very Low[b,c]
Carer Anxiety (STAI)	1 RCT (Beauchamp 2005)	MD -1.80 (-3.72, 0.12), I^2 n.a.	299	Low[b]
Carer Anxiety (HADS-A)	1 RCT (Blom 2015)	**MD 2.16 (1.30, 3.02), I^2 n.a.**	245	Moderate
Carer Stress (PSS)	2 RCT (Christancho-Lacroix 2015, Kajiyama 2013)	MD -1.49 (-5.40, 2.41), I^2 32%	152	Very Low[b,c]
Carer Stress	1 RCT (Beauchamp 2005)	**MD -2.70 (-4.87, -0.53), I^2 n.a.**	299	Moderate
Carer self-efficacy	2 RCT (Beauchamp 2005, Christancho-Lacroix 2015)	SMD 0.12 (-0.09, 0.33), I^2 0%	348	Low[b]
Perceived QoL	1 RCT (Kajiyama 2013)	MD 0.43 (-0.52, 1.38), I^2 n.a.	103	Low[b]
Telephone-based interventions				
Carer Burden (ZBI)	3 RCT (Tremont 2008, Tremont 2015, Au 2019)	MD -9.64 (-21.78, 2.49), I^2 84%	394	Very Low[b,c]
Carer depression (CES-D)	2 RCT (Tremont 2015, Au 2019)	**MD -4.37 (-7.19, -1.54), I^2 0%**	361	Moderate
Carer depression (GDS)	1 RCT (Tremont 2008)	MD -2.44 (-7.95, 3.07), I^2 n.a.	33	Very Low[b,c]
Euro-QoL	1 RCT (Tremont 2015)	MD -0.66 (-6.28, 4.96), I^2 n.a.	250	Very Low[b,c]
Carer self-efficacy (SEQ-SM)	1 RCT (Tremont 2015)	MD 2.29 (-1.41, 5.99), I^2 n.a.	250	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; LS: least square; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Supportive interventions				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Group-based interventions				
Carer burden (CBI)	1 RCT (Chu 2011)	MD -2.71 (-15.29, 9.87), I^2 n.a.	60	Very Low[b,c]
Carer distress (NPI-D)	1 RCT (Fung 2002)	MD -5.02 (-13.48, 3.44), I^2 n.a.	52	Very Low[b,c]
Carer depression (BSI)	1 RCT (Quayhagen 2000)	MD 0.20 (-0.17, 0.57), I^2 n.a.	37	Very Low[b,c]
Carer anxiety (BSI)	1 RCT (Quayhagen 2000)	MD 0.00 (-0.37, 0.37), I^2 n.a.	37	Very Low[b,c]
WHO-QoL	1 RCT (Fung 2002)	MD 31.87 (23.66, 40.08), I^2 n.a.	52	Moderate
Individual interventions				
Carer depression (HADS-D)	1 RCT (Charlesworth 2008)	MD 0.10 (-1.37, 1.57), I^2 n.a.	231	Low[b]
Carer anxiety (HADS-A)	1 RCT (Charlesworth 2008)	MD -0.02 (-1.65, 1.61), I^2 n.a.	231	Low[b]

EQ-5D	1 RCT (Charlesworth 2008)	MD 3.50 (-3.15, 10.15), I^2 n.a.	226	Very Low[b,c]
Technology-based psychoeducational interventions				
Carer Burden (ZBI)	1 RCT (Baruah 2021)	MD -3.02 (-12.56, 6.50), I^2 n.a.	55	Very Low[b,c]
Carer depression (CES-D)	1 RCT (Baruah 2021)	MD 0.46 (-3.53, 4.45), I^2 n.a.	55	Very Low[b,c]
EuroQol–VAS	1 RCT (Baruah 2021)	MD -8.13 (-20.64, 4.39), I^2 n.a.	55	Very Low[b,c]
Telephone-based interventions				
Carer Burden (ZBI)	2 RCT (Goodman 1990, Winter 2006)	MD 1.76 (-4.43, 7.95), I^2 0%	169	Very Low[b,c]
Carer depression (CES-D)	2 RCT (Mahoney 2003, Winter 2006)	MD -3.37 (-7.18, 0.45), I^2 0%	203	Low[b]
Carer anxiety (STAI)	1 RCT (Mahoney 2003)	MD -1.70 (-5.42, 2.02), I^2 n.a.	100	Low[b]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; LS: least square; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Cognitive-behavioural therapy				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Group-based interventions				
Carer Anxiety	2 RCT (Akkerman 2004, Losada 2015)	SMD -0.43 (-0.97, 0.12), I^2 49%	125	Very Low[b,c]
Carer depression (CES-D)	4 RCT (Au 2010, Gallagher-Thompson 2008, Losada 2015, Marquez-Gonzalez 2007)	**MD -4.02 (-7.09, -0.94), I^2 0%**	375	Moderate
Carer depression (BDI)	1 RCT (Marriott 2000)	**MD -6.40 (-12.15, -0.65), I^2 n.a.**	40	Low[c]
Carer Self-efficacy (RSCSE)	1 RCT (Au 2010)	MD 104.42 (-8.65, 217.49), I^2 n.a.	27	Very Low[b,c]
Carer Stress (PSS)	1 RCT (Gallagher-Thompson 2008)	MD -1.87 (-4.65, 0.91), I^2 n.a.	184	Low[b]
Individual interventions				
Carer depression (CES-D)	2 RCT (Gallagher-Thompson 2007, Losada 2004)	**MD -6.88 (-13.40, -0.37), I^2 0%**	61	Low[b]
Carer Stress (PSS)	1 RCT (Gallagher-Thompson 2007)	MD -1.25 (-4.70, 2.20), I^2 n.a.	45	Low[b]
Technology-based psychoeducational interventions				
Carer burden (VAS)	1 RCT (Meichsner 2019)	MD 11.83 (-5.98, 29.64), I^2 n.a.	37	⊕◯◯◯ Very low[b,c]
Carer burden (ZBI)	1 RCT (Kwok 2014)	**MD -4.08 (-8.02, -0.14), I^2 n.a.**	38	Low[c]
Carer depression (CES-D)	1 RCT (Meichsner 2019)	MD 5.69 (-2.43, 13.81), I^2 n.a.	37	Very Low[b,c]
Carer Self-efficacy	1 RCT (Kwok 2014)	MD 3.59 (-2.58, 9.76), I^2 n.a.	38	Very Low[b,c]
Telephone-based interventions				
Carer Depression (CES-D)	2 RCT (Topfer 2021, Wilz 2018)	MD 0.12 (-2.89, 3.13), I^2 0%	324	Low[b]

Carer Burden (VAS)	2 RCT (Topfer 2021, Wilz 2018)	MD -6.02 (-18.69, 6.65), I^2 62%	324	Very Low[b,c]
WHO-QoL	1 RCT (Topfer 2021)	MD -2.72 (-16.19, 10.75), I^2 n.a.	51	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; LS: least square; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Case management				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Case consultant				
Carer Burden (ZBI)	1 RCT (Fortinsky 2009)	MD 1.21 (-7.87, 10.29), I^2 n.a.	34	Very Low[b,c]
Carer Depression (CES-D)	1 RCT (Fortinsky 2009)	MD -2.23 (-9.57, 5.11), I^2 n.a.	34	Very Low[b,c]
Symptom management score	1 RCT (Fortinsky 2009)	MD -0.34 (-11.61, 10.93), I^2 n.a.	34	Very Low[b,c]
Case management intervention carried out by district nurses				
Carer Burden (SPPIC)	1 RCT (Jansen 2011)	MD 0.30 (-1.14, 1.74), I^2 n.a.	99	Low[b]
Carer Depression (CES-D)	1 RCT (Jansen 2011)	MD 0.60 (-3.22, 4.42), I^2 n.a.	99	Low[b]
Carer Self-efficacy (SCQ)	1 RCT (Jansen 2011)	MD 0.10 (-3.54, 3.74), I^2 n.a.	99	Very Low[b,c]
Home-based case management intervention led by a care coordinator				
Carer Self-efficacy (Short-SCQ)	1 RCT (Xiao 2016)	**MD 9.00 (5.09, 12.91), I^2 n.a.**	61	Low[c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; LS: least square; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Physical exercise interventions				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Home-based intervention				
Depression (GDS)	1 RCT (Madruga 2021)	MD -0.80 (-2.84, 1.24), I^2 n.a.	48	Low[b]
Burden (ZBI)	1 RCT (Madruga 2021)	MD -8.30 (-18.34, 1.74), I^2 n.a.	48	Very Low[b,c]
Individual intervention				
Depression (VAS)	1 RCT (Hirano 2011)	**MD -4.40 (-6.97, -1.83), I^2 n.a.**	31	Moderate
Burden (ZBI)	1 RCT (Hirano 2011)	**MD -5.90 (-6.93, -4.87), I^2 n.a.**	31	Moderate
Telephone-based interventions				
Burden (RMBPC)	1 RCT (Connell 2009)	MD -0.50 (-5.79, 4.79), I^2 n.a.	137	Very Low[b,c]

Depression (CES-D)	1 RCT (Connell 2009)	MD -0.70 (-2.01, 0.61), I^2 n.a.	137	Low[b]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; LS: least square; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Multicomponent interventions				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Interventions targeted to caregivers				
Carer Burden (ZBI)	9 RCT (Berwig 2017, Davis 2011, Gaugler 2015, Gonyea 2006, Hebert 1994, Newcomer 1999, Martindale-Adams 2013, Shata 2017, Yoo 2018)	MD -4.90 (-10.80, 1.00), I^2 96%*	2491	Very Low[b,c]
Carer Burden (CBI)	1 RCT (Chen 2015)	MD -9.40 (-21.79, 2.99), I^2 n.a.	46	Very Low[b,c]
Carer Depression (CES-D)	6 RCT (Boots 2018, Davis 2011, Finkel 2007, Gaugler 2015, Martindale-Adams 2013, Mohide 1990)	MD -1.15 (-3.37, 1.07), I^2 0%	359	Low[b]
Carer Depression (GDS)	3 RCT (Mittelman 2004, Newcomer 1999, Yoo 2018)	MD -1.26 (-2.59, 0.08), I^2 76%	2354	Very Low[b,c]
Carer Depression (PHQ-4)	1 RCT (Berwig 2017)	MD -0.40 (-1.02, 0.22), I^2 n.a.	81	Low[b]
Carer Depression (HAM-D)	1 RCT (Shata 2017)	**MD -10.20 (-11.28, -9.12), I^2 n.a.**	114	Moderate
Carer Depression (BSI-D)	1 RCT (Hebert 1994)	MD 0.86 (-2.61, 4.33), I^2 n.a.	41	Low[b]
Carer Anxiety (BSI-A)	1 RCT (Hebert 1994)	MD -0.08 (-3.48, 3.32), I^2 n.a.	36	Low[b]
Carer Anxiety (STAI)	1 RCT (Mohide 1990)	MD -3.02 (-14.68, 8.64), I^2 n.a.	42	Very Low[b,c]
Carer Anxiety (HADS)	1 RCT (Boots 2018)	MD 1.46 (-1.19, 4.11), I^2 n.a.	81	Low[b]
Carer Anxiety (PHQ-4)	1 RCT (Berwig 2017)	MD -0.31 (-1.18, 0.56), I^2 n.a.	81	Low[b]
Carer Anxiety (TMAS)	1 RCT (Shata 2017)	**MD -15.05 (-16,56, -13.54), I^2 n.a**.	114	Moderate
HRQoL (SF-12-psy)	1 RCT (Dichter 2020)	MD 1.69 (-3.95, 7.33), I^2 n.a.	35	Very Low[b,c]
Carer CQLI	1 RCT (Mohide 1990)	MD 0.12 (-0.18, 0.42), I^2 n.a.	42	Low[b]
Interventions targeted to dyads				
Carer Burden (ZBI)	8 RCT (Dias 2008, Gaugler 2019, Gitlin 2008, Gitlin 2010, Kwok 2013, Tang 2018, Torkamani 2014, Uyar 2019)	MD -1.58 (-3.81, 0.65), I^2 0%	784	Low[b]
Carer Burden (FCBI)	2 RCT (Chien 2008, Chien 2011)	**MD -18.99 (-24.48, -13.50), I^2 0%**	180	Moderate
Carer Burden (SPPIC)	1 RCT (Prick 2015)	MD 0.08 (-1.12, 1.28), I^2 n.a.	111	Low[b]
Carer Depression (CES-D)	5 RCT (Gaugler 2019, Gitlin 2003, Gitlin 2008, Graff 2006, Prick 2015)	MD -1.41 (-5.03, 2.21), I^2 80%	1541	Very Low[b,c,d]
Carer Depression (GDS)	3 RCT (Bruvik 2013, Martin-Cook 2005, Waldorff 2012)	MD 0.44 (-0.46, 1.33), I^2 0%	607	Low[b]

Carer Depression (MADRS)	1 RCT (Bottino 2005)	MD -1.54 (-8.10, 5.02), I^2 n.a.	13	Very Low[b,c]
Carer Depression (BDI)	1 RCT (Uyar 2019)	**MD -7.35 (-13.05, -1.65), I^2 n.a.**	61	Very Low[b,c]
Carer Anxiety (HAM-A)	1 RCT (Bottino 2005)	MD -4.69 (-9.72, 0.34), I^2 n.a.	13	Very Low[b,c]
Carer Anxiety (BAI)	1 RCT (Uyar 2019)	**MD -7.12 (-12.89, -1.35), I^2 n.a.**	61	Very Low[b,c]
EQ5D-VAS	2 RCT (Torkamani 2014, Waldorff 2012)	MD -0.31 (-4.24, 3.61), I^2 0%	334	Low[b]
WHO-QoL	2 RCT (Chien 2008, Chien 2011)	**MD 19.63 (13.69, 25.57), I^2 0%**	180	Moderate
QoLS	1 RCT (Torkamani 2014)	MD 4.95 (-4.56, 14.46), I^2 n.a.	40	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; LS: least square; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Meditation/mindfulness				
Outcomes	**No. of Studies**	**Observed effect, (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Meditation				
Carer Burden (ZBI)	1 RCT (Pandya 2019)	MD -29.41 (-31.78, -27.04), I^2 n.a.	192	Moderate
Carer Depression (BDI)	1 RCT (Danucalov 2013)	**MD -9.20 (-15.74, -2.66), I^2 n.a.**	46	Low[c]
Carer Depression (HAM-D)	1 RCT (Lavretsky 2013)	MD -2.10 (-4.77, 0.57), I^2 n.a.	39	Low[b]
Carer Depression (CES-D)	1 RCT (Waelde 2017)	MD -5.92 (-14.32, 2.48), I^2 n.a.	31	Very Low[b,c]
Carer Depression (WebNeuro)	1 RCT (Leach 2015)	MD 0.24 (-1.95, 2.43), I^2 n.a.	17	Very Low[b,c]
Carer Anxiety (BAI)	1 RCT (Danucalov 2013)	**MD -10.90 (-18.07, -3.73), I^2 n.a.**	46	Low[c]
Carer Anxiety (WebNeuro test battery)	1 RCT (Leach 2015)	MD -0.48 (-3.07, 2.11), I^2 n.a.	17	Very Low[b,c]
Carer Stress (WebNeuro test battery)	1 RCT (Leach 2015)	MD 0.37 (-1.60. 2.34), I^2 n.a.	17	Very Low[b,c]
Mindfulness				
Carer Depression (CES-D)	4 RCT (Whitebird 2013, Oken 2010, Kor 2019, Kor 2020)	**MD -5.48 (-10.02, -0.93), I^2 20%**	247	Low[c]
Carer Burden (ZBI)	2 RCT (Kor 2019, Kor 2020)	MD -6.83 (-14.20, 0.55), I^2 8%	149	Very Low[b,c]
Carer Anxiety (STAI)	1 RCT (Whitebird 2013)	MD 0.90 (-7.03, 8.83), I^2 n.a.	78	Very Low[b,c]
Carer Anxiety (HADS)	2 RCT (Kor 2019, Kor 2020)	MD -2.21 (-4.59, 0.17), I^2 0%	149	Low[b]
Carer Stress (PSS)	4 RCT (Whitebird 2013, Oken 2010, Kor 2019, Kor 2020)	**MD -3.70 (-6.26, -1.15), I^2 0%**	247	Moderate

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; LS: least square; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Review question 15a (New RQ). How useful (in terms of efficacy and safety) are acetylcholinesterase inhibitors and memantine for the treatment of cognitive symptoms in people with Alzheimer's dementia, and how should they be reviewed?

ACETYLCHOLINESTERASE INHIBITORS AND MEMANTINE IN THE TREATMENT OF ALZHEIMER'S DEMENTIA (NOT STRATIFIED BY SEVERITY)

Donepezil vs placebo for the treatment of Alzheimer's dementia (not stratified by severity)				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
ADAS-Cog	12 RCT (Burns 1999, Frölich 2011, Gault 2015, Gault 2016, Haig 2014, Homma 2000, Johanssen 2006, Maher-Edwards 2011, Moraes 2006, Rogers 1998, Seltzer 2004, Tune 2003)	**SMD -0.38 (-0.49, -0.26), I^2 42%**	2,766	Moderate[a]
MMSE	19 RCT (Courtney 2004, Black 2007, Feldman 2001, Frölich 20011, Gault 2015, Gault 2016, Gauthier 2002, Haig 2014, Holmes 2004, Jia 2017, Johanssen 2006, Maher-Edwards 2011, Mazza 2006, Mohs 2001, Rogers 1998, Seltzer 2004, Tariot 2001, Winblad 2001, Winblad 2006)	**MD 0.99 (0.79, 1.19), I^2 0%**	4,335	High
ADCS-ADL	6 RCT (Black 2007, Gault 2015, Gault 2016, Haig 2014, Homma 2008*, Winblad 2006)	**MD 1.40 (0.69, 2.11), I^2 8%**	1,220	High
CIBIC+	3 RCT (Burns 1999, Gauthier 2002, Rogers 1998)	**MD -0.38 (-0.49, -0.28), I^2 0%**	1,371	High
NPI	9 RCT (Black 2007, Feldman 2001, Gault 2015, Gault 2016, Haig 2014, Johanssen 2006, Tariot 2001, Tune 2003, Winblad 2006)	**MD -2.08 (-3.01, -1.14), I^2 59%**	1,671	Moderate[a]
Discontinuation due to AE	18 RCT (Black 2007, Burns 1999, Feldman 2001, Gault 2015, Gault 2016, Haig 2014, Homma 2000, Homma 2008, Jia 2017, Krishnan 2003, Maher-Edwards 2011, Mazza 2006, Mohs 2001, Rogers 1998, Seltzer 2004, Tariot 2001, Winblad 2001, Winblad 2006)	**RR 1.42 (1.18, 1.72), I^2 0%**	4,818	High
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; RR: risk ratio a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%				

* Homma 2008: two dosages assessed, 5mg and 10mg donepezil

Galantamine vs placebo for the treatment of Alzheimer's dementia (not stratified by severity)				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
ADAS-Cog	8 RCT (Brodaty 2005, Bullock 2004*, Raskind 2000, Rockwood 2001, Rockwood 2006, Tariot 2000, Wilcock 2000, Wilkinson 2001)	**SMD -0.47 (-0.54, -0.41), $I^2$0%**	4,013	High
ADAS-Cog – AD/VD/mix	1 RCT* (Bullock 2004)	**SMD -0.54 (-0.81, -0.27), I^2 n.a.**	230	Moderate
MMSE	1 RCT (Liu 2003)	**MD 1.90 (0.79, 3.01), I^2n.a.**	102	Moderate
ADCS-ADL	4 RCT (Brodaty 2005, Burns 2009, Liu 2003, Tariot 2000 (16 e 24mg))	MD 1.20 (-0.31, 2.71), I^2 79%	1,779	Low[b,c]
CIBIC+	5 RCT (Brodaty 2005, Raskind 2000, Rockwood 2001, Tariot 2000)	**MD -0.26 (-0.34, -0.17), I^2 6%**	2,588	High
NPI	3 RCT (Brodaty 2005, Rockwood 2001, Tariot 2000 (16 e 24mg))	**MD -1.49 (-2.53, -0.46), I^2 0%**	1,656	High

Discontinuation due to AE	8 RCT (Brodaty 2005, Burns 2009, Liu 2003, Raskind 2000, Rockwood 2001, Tariot 2000 (16 e 24mg), Wilcock 2000, Wilkinson 2001)	**RR 2.12 (1.34, 3.36), I^2 76%**	3,953	Moderate

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; RR: risk ratio
a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%

Rivastigmine vs placebo for the treatment of Alzheimer's dementia (not stratified by severity)				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Rivastigmine tablets vs placebo				
ADAS-Cog	4 RCT (Corey-Bloom 1998, Feldman 2007a, Rösler 1999, Winblad 2007)	**SMD -0.28 (-0.43, -0.14), I^2 69%**	2.629	Moderate[a]
MMSE	6 RCT (Agid 1998, Corey-Bloom 1998, Feldman 2007a, Mowla 2007, Rösler 1999, Winblad 2007)	**MD 0.95 (0.55, 1.36), I^2 66%**	3.314	Moderate[a]
ADCS-ADL	1 RCT (Winblad 2007)	**MD 1.80 (0.20, 3.40), I^2 n.a.**	535	Moderate
CIBIC+	3 RCT (Corey-Bloom 1998, Feldman 2007a, Rösler 1999)	**MD -0.35 (-0.50, -0.21), I^2 28%**	2.040	High
NPI	1 RCT (Winblad 2007)	MD -0.50 (-2.68, 1.68), I^2 n.a.	535	Low[b]
Discontinuation due to AE	3 RCT (Feldman 2007a, Rösler 1999, Winblad 2007)	**RR 1.98 (1.16, 3.36), I^2 67%**	1.755	Moderate[a]
Rivastigmine transdermal patch (10cm² o 20cm²) vs placebo				
ADAS-Cog	2 RCT (Nakamura 2011, Winblad 2007 (10cm2 or 20cm2 patch))	**SMD -0.37 (-0.48, -0.26), I^2 1%**	1.324	High
MMSE	2 RCT (Nakamura 2011, Winblad 2007 (10cm2 or 20cm2 patch))	**MD 0.71 (0.20, 1.22), I^2 49%**	1.290	Moderate[a]
ADCS-ADL	1 RCT (Winblad 2007)	**MD 2.25 (0.83, 3.66), I^2 0%**	791	Moderate
NPI	1 RCT (Winblad 2007)	MD -0.29 (-2.23, 1.65), I^2 0%	792	Low[b]
Discontinuation due to AE	2 RCT (Nakamura 2011, Winblad 2007 (10cm2 or 20cm2 patch))	**RR 1.69 (1.18, 2.43), I^2 0%**	1.471	High

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; RR: risk ratio
a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%

Memantina confrontata con placebo for the treatment of Alzheimer's dementia (not stratified by severity)				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
ADAS-Cog	4 RCT (Bakchine 2008, Dysken 2014, Peskind 2006, Porsteinsson 2008)	**SMD -0.12 (-0.23, -0.02), I^2 0%**	1,417	High
MMSE	5 RCT (Fox 2012, Porsteinsson 2008, Reisberg 2003, Wang 2013, Wilkinson 2012)	MD 2.00 (-0.36, 4.35), I^2 93%	1,104	Low[a,c]
ADCS-ADL	9 RCT (Bakchine 2008, Grossberg 2013, Homma 2007, Peskind 2006, Peters 2015, Porsteinsson 2008, Reisberg 2003, Tariot 2004, van Dyck 2007)	**MD 0.65 (0.11, 1.18), I^2 42%**	3,256	Moderate[a]

CIBIC+	6 RCT (Grossberg 2013, Peskind 2006, Porsteinsson 2008, Reisberg 2003, Tariot 2004, van Dyck 2007)	**MD -0.24 (-0.34, -0.15), I^2 16%**	2,445	High
NPI	10 RCT (Bakchine 2008, Dysken 2014, Fox 2012, Grossberg 2013, Herrmann 2013, Peskind 2006, Porsteinsson 2008, Reisberg 2003, Tariot 2004, van Dyck 2007)	**MD -1.19 (-2.16, -0.22), I^2 61%**	3,430	Moderate[a]
Discontinuation due to AE	8 RCT (Bakchine 2008, Grossberg 2013, Herrmann 2013, Peskind 2006, Porsteinsson 2008, Reisberg 2003, Tariot 2004, van Dyck 2007)	RR 1.24 (0.90, 1.72), I^2 49%	3,358	Low[a,b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; RR: risk ratio a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%				

ACETYLCHOLINESTERASE INHIBITORS AND MEMANTINE IN THE TREATMENT OF MILD-MODERATE ALZHEIMER'S DEMENTIA

Donepezil vs placebo for the treatment of mild-moderate Alzheimer's dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
ADAS-Cog	12 RCT (Burns 1999, Frölich 2011, Gault 2015, Gault 2016, Haig 2014, Homma 2000, Johanssen 2006, Maher-Edwards 2011, Moraes 2006, Rogers 1998, Seltzer 2004, Tune 2003)	**SMD -0.37 (-0.49, -0.25), I^2 45%**	2,326	Moderate[a]
MMSE	8 RCT (Frölich 2011, Gault 2015, Gault 2016, Haig 2014, Mazza 2006, Mohs 2001, Rogers 1998, Tariot 2001)	**MD 0.88 (0.53, 1.23), I^2 0%**	1,253	High
ADCS-ADL	3 RCT (Gault 2015, Gault 2016, Haig 2014)	**MD 2.43 (0.83, 4.03), I^2 28%**	391	High
CIBIC+	2 RCT (Burns 1999, Rogers 1998)	**MD -0.36 (-0.48, -0.25), I^2 0%**	1,268	High
NPI	6 RCT (Gault 2015, Gault 2016, Haig 2014, Johanssen 2006, Tariot 2001 (16 e 24mg), Tune 2003)	**MD -1.50 (-2.79, -0.21), I^2 27%**	1,398	High
Discontinuation due to AE	13 RCT (Burns 1999, Gault 2015, Gault 2016, Haig 2014, Homma 2000, Krishnan 2003, Maher-Edwards 2011, Mazza 2006, Mohs 2001, Rogers 1998, Seltzer 2004, Tariot 2001, Winblad 2001)	**RR 1.36 (1.07, 1.72), I^2 0%**	3,322	High
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; RR: risk ratio a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%				

Galantamine vs placebo for the treatment of mild-moderate Alzheimer's dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
ADAS-Cog	7 RCT (Brodaty 2005, Raskind 2000, Rockwood 2001, Rockwood 2006, Tariot 2000-24mg, Wilcock 2000, Wilkinson 2000)	**SMD -0.47 (-0.54, -0.40), I^2 0%**	3,783	High
MMSE	1 RCT (Liu 2003)	**MD 1.90 (0.79, 3.01), I^2 n.a.**	102	Moderate[c]
ADCS-ADL	3 RCT (Brodaty 2005, Liu 2003, Tariot 2000 (16 e 24mg))	**MD 1.86 (0.67, 3.06), I^2 39%**	1,372	High
CIBIC+	5 RCT (Brodaty 2005, Raskind 2000, Rockwood 2001, Rockwood 2006, Wilcock 2000)	**MD -0.26 (-0.34, -0.17), I^2 6%**	2,588	High
NPI	3 RCT (Brodaty 2005, Rockwood 2001, Tariot 2000 (24mg))	**MD -1.41 (-2.51, -0.31), I^2 0%**	1,402	High
Discontinuation due to AE	7 RCT (Brodaty 2005, Liu 2003, Raskind 2000, Rockwood 2001, Tariot 2000, Wilcock 2000, Wilkinson 2001)	**RR 2.43 (1.57, 3.75), I^2 66%**	3,546	Moderate[a]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; RR: risk ratio a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%				

Rivastigmine vs placebo for the treatment of mild-moderate Alzheimer's dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Rivastigmine tablets vs placebo				
ADAS-Cog	4 RCT (Corey-Bloom 1998, Feldman 2007a, Rösler 1999, Winblad 2007)	**SMD -0.32 (-0.42, -0.21), I^2 35%**	2,387	High
MMSE	5 RCT (Agid 1998, Feldman 2007a, Mowla 2007, Rösler 1999, Winblad 2007)	**MD 0.91 (0.42, 1.40), I^2 72%**	2,096	Moderate[a]
ADCS-ADL	1 RCT (Winblad 2007)	**MD 1.80 (0.20, 3.40), I^2 n.a.**	535	Moderate
CIBIC+	3 RCT (Corey-Bloom 1998, Feldman 2007a, Rösler 1999)	**MD -0.35 (-0.50, -0.21), I^2 28%**	2,040	High
NPI	1 RCT (Winblad 2007)	MD -0.50 (-2.68, 1.68), I^2 n.a.	534	Low[b]
Discontinuation due to AE	4 RCT (Feldman 2007a, Nakamura 2011, Rösler 1999, Winblad 2007)	**RR 1.88 (1.28, 2.77), I^2 54%**	2,330	Moderate[a]
Rivastigmine transdermal patch (10cm² or 20cm²) vs placebo				
ADAS-Cog	2 RCT (Nakamura 2011, Winblad 2007 (10cm2, 20cm2))	**SMD -0.28 (-0.40, -0.17), I^2 0%**	1,324	High
MMSE	2 RCT (Nakamura 2011, Winblad 2007 (10cm2, 20cm2))	**MD 0.71 (0.20, 1.22), I^2 49%**	1,290	Moderate[a]
ADCS-ADL	1 RCT (Winblad 2007) *	**MD 2.25 (0.83, 3.66), I^2 0%**	791	High
NPI	1 RCT (Winblad 2007) *	MD -0.29 (-2.23, 1.65), I^2 0%	792	Low[b]
Discontinuation due to AE	2 RCT (Nakamura 2011, Winblad 2007 (10cm2, 20cm2))	**RR 1.69 (1.18, 2.43), I^2 0%**	1,471	High
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; *Winblad 2007 (10cm2, 20cm2)				

Memantine vs placebo for the treatment of mild-moderate Alzheimer's dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
ADAS-Cog	4 RCT (Bakchine 2008, Dysken 2014, Peskind 2006, Porsteinsson 2008)	**SMD -0.12 (-0.23, -0.02), I^2 0%**	1,417	High
MMSE	2 RCT (Porsteinsson 2008, Wilkinson 2012)	MD 0.36 (-0.54, 1.26), I^2 0%	385	Moderate[b]
ADCS-ADL	4 RCT (Bakchine 2008, Peskind 2006, Peters 2015, Porsteinsson 2008)	MD -0.03 (-1.05, 0.99), I^2 0%	1,412	Moderate[b]
CIBIC+	2 RCT (Peskind 2006, Porsteinsson 2008)	MD -0.18 (-0.45, 0.10), I^2 75%	820	Low[a,b]
NPI	5 RCT (Bakchine 2008, Dysken 2014, Herrmann 2013, Peskind 2006, Porsteinsson 2008)	MD -0.04 (-1.72, 1.64), I^2 23%	1,517	Moderate[b]
Discontinuation due to AE	4 RCT (Bakchine 2008, Herrmann 2013, Peskind 2006, Porsteinsson 2008)	RR 1.45 (0.89, 2.35), I^2 38%	1,675	Moderate[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; RR: risk ratio a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%				

ACETYLCHOLINESTERASE INHIBITORS AND MEMANTINE IN THE TREATMENT OF MODERATE-SEVERE ALZHEIMER'S DEMENTIA

Donepezil vs placebo for the treatment of moderate-severe Alzheimer's dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
MMSE	5 RCT (Black 2007, Feldman 2001, Gauthier 2002, Jia 2017, Winblad 2006)	**MD 1.15 (0.64, 1.66), I^2 41%**	1,293	Moderate[a]
ADCS-ADL	3 RCT (Black 2007, Homma 2008 (5 e 10mg), Winblad 2006)	**MD 1.04 (0.26, 1.81), I^2 0%**	829	High
CIBIC+	1 RCT (Gauthier 2002)	**MD -0.55 (-0.86, -0.04), I^2 n.a.**	203	Moderate
NPI	3 RCT (Black 2007, Feldman 2001, Winblad 2006)	MD -2.09 (-5.97, 1.79), I^2 76%	835	Very Low[b,c,d]
Discontinuation due to AE	5 RCT (Black 2007, Feldman 2001, Homma 2008 (5 e 10mg), Jia 2017, Winblad 2006)	**RR 1.54 (1.13, 2.10), I^2 0%**	1,496	High
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; RR: risk ratio a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%				

Galantamine vs placebo for the treatment of moderate-severe Alzheimer's dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
ADCS-ADL	1 RCT (Burns 2009)	MD -0.44 (-1.34, 0.46), I^2 n.a.	407	Low[b]
Discontinuation due to AE	1 RCT (Burns 2009)	RR 0.94 (0.59, 1.49), I^2 n.a.	407	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; RR: risk ratio a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%				

Memantine vs placebo for the treatment of moderate-severe Alzheimer's dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
MMSE	3 RCT (Fox 2012, Reisberg 2003, Wang 2013)	**MD 0.78 (0.15, 1.39), I^2 0%**	419	High
ADCS-ADL	5 RCT (Grossberg 2013, Homma 2007, Reisberg 2003, Tariot 2004, van Dyck 2007)	**MD 0.91 (0.27, 1.55), I^2 3%**	1,844	High
CIBIC+	4 RCT (Grossberg 2013, Reisberg 2003, Tariot 2004, van Dyck 2007)	**MD -0.29 (-0.39, -0.18), I^2 0%**	1,625	High
NPI	5 RCT (Fox 2012, Grossberg 2013, Reisberg 2003, Tariot 2004, van Dyck 2007)	**MD -3.00 (-4.85, -1.14), I^2 32%**	835	High
Discontinuation due to AE	4 RCT (Grossberg 2013, Reisberg 2003, Tariot 2004, van Dyck 2007)	RR 1.10 (0.69, 1.77), I^2 62%	1,683	Low[a,b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; RR: risk ratio a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%				

Review question 15b (New RQ). How useful (in terms of efficacy and safety) are acetylcholinesterase inhibitors and memantine for the treatment of cognitive symptoms in people with Mild Cognitive Impairment, and how should they be reviewed?

Donepezil vs placebo for the treatment of Mild cognitive impairment (MCI)				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
ADAS-Cog	3 RCT (Salloway 2004, Petersen 2005, Doody 2009)	**MD -0.16 (-0.28, -0.03), I^2 30%**	1,531	High
MMSE	3 RCT (Ozenli 2007, Petersen 2005, Doody 2009)	MD 0.14 (-0.22, 0.50), I^2 0%	1,320	Moderate[b]
CDR-SB	2 RCT (Petersen 2005, Doody 2009)	MD -0.08 (-0.31, 0.15), I^2 0%	1,269	Moderate[b]
ADCS-ADL-MCI	1 RCT (Petersen 2005)	MD 0.13 (-1.40, 1.66), I^2 n.a.	512	Low[b]
MCI to AD – 12 mesi	1 RCT (Petersen 2005)	**HR 0.42 (0.24, 0.76), p=0.004**	512	Moderate
MCI to AD – 24 mesi	1 RCT (Petersen 2005)	**HR 0,64 (0,44, 0,95), p=0.03**	512	Moderate
MCI to AD – 36 mesi	1 RCT (Petersen 2005)	HR 0.80 (0.57, 1.13), p=0.21	512	Moderate[b]
MCI to AD 36 mesi ApoE ε4	1 RCT (Petersen 2005)	**HR 0.66 (0.44, 0.98), p=0.04**	512	Low[e]
AE	2 RCT (Salloway 2004, Doody 2009)	**RR 1.18 (1.11, 1.27), I^2 0%**	1,048	High
SAE	2 RCT (Salloway 2004, Doody 2009)	RR 1.12 (0.77, 1.63), I^2 0%	1,048	Moderate[b]
Discontinuation due to AE	2 RCT (Salloway 2004, Doody 2009)	**RR 2.43 (1.73, 3.42), I^2 0%**	1,090	High
Mortality	3 RCT (Salloway 2004, Petersen 2005, Doody 2009)	RR 1.43 (0.55, 3.77), I^2 0%	1,552	Moderate[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%				

Galantamine vs placebo for the treatment of Mild cognitive impairment (MCI)				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
ADAS-Cog	2 RCT (Winblad 2008)	MD -0.03 (-0.12, 0.06), I^2 43%	1,901	High
ADCS-ADL-MCI	2 RCT (Winblad 2008)	MD 0.30 (-0.26, 0.86), I^2 0%	1,896	Low[b]
AE	2 RCT (Winblad 2008)	**RR 1.04 (1.00, 1.07), I^2 0%**	2,048	High
SAE	2 RCT (Winblad 2008)	RR 0.99 (0.82, 1.18), I^2 0%	2,048	Moderate[b]
Discontinuation due to AE	2 RCT (Winblad 2008)	**RR 2.20 (1.78, 2.72), I^2 0%**	2,048	High
Mortality	2 RCT (Winblad 2008)	RR 1.21 (0.83, 1.77), I^2 0%	2,048	Moderate[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%				

Rivastigmine vs placebo for the treatment of Mild cognitive impairment (MCI)				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**

Conversion MCI to AD	1 RCT (Feldman 2007b)	HR 0.85 (0.64, 1.12), p=0,225	1,018	Low[b,c]
AE	1 RCT (Feldman 2007b)	**RR 1.03 (1.00, 1.06), I^2 n.a.**	1,014	Moderate
SAE	1 RCT (Feldman 2007b)	RR 0.92 (0.76, 1.11), I^2 n.a.	1,014	Moderate[b]
Discontinuation due to AE	1 RCT (Feldman 2007b)	**RR 1.84 (1.23, 2.74), I^2 n.a.**	1,014	Moderate
Mortality	1 RCT (Feldman 2007b)	RR 0.71 (0.39, 1.31), I^2 n.a.	1,014	Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%				

Review question 15c (New RQ). How useful (in terms of efficacy and safety) are biological drugs (active and passive immunization) for the treatment of cognitive symptoms in people with Alzheimer's dementia or Mild Cognitive Impairment, and how should they be reviewed?

ACTIVE IMMUNOTHERAPY TARGETING DIFFERENT FORMS OF AMYLOID β

AN1792 vs placebo for the treatment of Alzheimer's dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
AE	2 RCT (Bayer 2005, Gilman 2005)	RR 1.03 (0.92, 1.15), I^2 53%	452	Low[a,b]
SAE	2 RCT (Gilman 2005)	RR 1.73 (0.91, 3.31), I^2 n.a.	372	Low[b,c]
Meningoencephalitis	2 RCT (Bayer 2005, Gilman 2005)	RR 4.91 (0.66, 36.48), I^2 32%	452	Low[b,c]
Mortality	2 RCT (Bayer 2005, Gilman 2005)	RR 2.02 (0.48, 8.49), I^2 0%	452	Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%				

CAD106 vs placebo for the treatment of Alzheimer's dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
AE	2 RCT (Farlow 2015, Vandenberghe 2017)	RR 0.88 (0.41, 1.90), I^2 54%	116	Very Low[a,b,c]
SAE	3 RCT (Farlow 2015, Vandenberghe 2017, Winblad 2012)	RR 1.31 (0.32, 5.43), I^2 58%	237	Very Low[a,b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%				

PASSIVE IMMUNOTHERAPY TARGETING DIFFERENT FORMS OF AMYLOID β

AAB-003 vs placebo for the treatment of Alzheimer's dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
CDR-SB	1 RCT (Delnomdedieu 2016)*	**MD 1.65 (0.54, 2.77), I^2 0%**	88	Low[e]
ARIA-E	1 RCT (Delnomdedieu 2016)	RR 1.43 (0.07, 28.56), I^2 n.a.	88	Low[b,c]
ARIA-H	1 RCT (Delnomdedieu 2016)	RR 4.86 (0.29, 80.56), I^2 n.a.	88	Low[b,c]
AE	1 RCT (Delnomdedieu 2016)	RR 0.83 (0.55, 1.25), I^2 n.a.	88	Low[b]

SAE	1 RCT (Delnomdedieu 2016)	RR 4.86 (0.29, 80.56), I^2 n.a.	88	Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations; *Clinical Outcomes, including the CDR-SB scale, were all exploratory

Aducanumab vs placebo for the treatment of Alzheimer's dementia and Mild Cognitive Impairment				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
CDR-SB – EMERGE High dose	1 RCT (Budd Haeberlein 2022)	**MD -0.39 (-0.78, 0.00), I^2 n.a.**	821	Low[c,e]
CDR-SB – ENGAGE High dose	1 RCT (Budd Haeberlein 2022)	MD 0.03 (-0.34, 0.40), I^2 n.a.	816	Very Low[b,c,e]
CDR-SB	3 RCT (Budd Haeberlein 2022, Sevigny 2016)	MD -0.21 (-0.46, 0.05), I^2 0%	3,449	Low[e]
Amy-PET	4 RCT (Budd Haeberlein 2022, Sevigny 2016, Ferrero 2016)	**SMD -1.73 (-2.16, -1.30), I^2 77%**	865	Very Low[c,e]
Amy-PET – High dose	2 RCT (Budd Haeberlein 2022)	**SMD -2.07 (-2.31, -1.82), I^2 34%**	754	Moderate[e]
AE	4 RCT (Budd Haeberlein 2022, Sevigny 2016, Ferrero 2016)	RR 1.10 (0.92, 1.32), I^2 92%	3,503	Very Low[b,c,d,e]
SAE	4 RCT (Budd Haeberlein 2022, Sevigny 2016, Ferrero 2016)	RR 0.86 (0.62, 1.19), I^2 58%	3,503	Very Low[a,b,c,e]
ARIA-E	4 RCT (Budd Haeberlein 2022, Sevigny 2016, Ferrero 2016)	**RR 9.36 (6.20, 14.14), I^2 10%**	3,471	Low[c,e]
ARIA-E – ApoE4+/+ 10mg/kg	2 RCT (Budd Haeberlein 2022)	**RR 20.89 (9.43, 46.27), I^2 n.a.**	377	Low[c,e]
ARIA-E – ApoE4+/- 10mg/kg	2 RCT (Budd Haeberlein 2022)	**RR 19.29 (10.34, 36.01), I^2 n.a.**	1,108	Low[c,e]
ARIA-E – ApoE4- 10mg/kg	2 RCT (Budd Haeberlein 2022)	**RR 5.19 (2.93, 9.20), I^2 n.a.**	701	Low[c,e]
ARIA-H	4 RCT (Budd Haeberlein 2022, Sevigny 2016, Ferrero 2016)	**RR 2.73 (2.15, 3.46), I^2 0%**	3,503	Moderate[e]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Bapineuzumab vs placebo for the treatment of Alzheimer's dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
CDR-SB	4 RCT (Salloway 2014, Vandenberghe 2016)	MD 0.00 (-0.23, 0.23), I^2 0%	4,121	Moderate[b]
Amy-PET – bapi-IV	4 RCT (Salloway 2014, Vandenberghe 2016)	**SMD -0.36 (-0.62, -0.10), I^2 1%***	253	Low[e]
Amy-PET – bapi-SC	1 RCT (Brody 2016)	SMD -0.18 (-0.58, 0.21), I^2 0%	138	Low[b]
AE – bapi-IV	8 RCT (Salloway 2014, Vandenberghe 2016, Salloway 2009, Black 2010, Arai 2016, Rinne 2010)	RR 0.98 (0.91, 1.06), I^2 65%	4,733	Low[a,b]
AE – bapi-SC	2 RCT (Lu 2018, Brody 2016)	RR 1.39 (0.73, 2.62), I^2 65%	186	Low[a,b]
ARIA-E – bapi-IV	5 RCT (Salloway 2009, Salloway 2014, Vandenberghe 2016)	**RR 20.39 (4.93, 84.34), I^2 67%**	4,664	Very Low[a,c]
ARIA-E – bapi-SC	1 RCT (Brody 2016)	RR 1.67 (0.08, 33.93), I^2 n.a.	146	Very Low[b,c]

ARIA-H – bapi-SC	1 RCT (Brody 2016)	RR 1.00 (0.24, 24.02), I^2 n.a.	146	Very Low[b,c]
SAE	9 RCT (Salloway 2014, Vandenberghe 2016, Salloway 2009, Black 2010, Arai 2016, Rinne 2010, Lu 2018)	**RR 1.16 (1.03, 1.30), I^2 0%**	4,955	Moderate

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; IV: intravenous administration; SC: subcutaneous administration; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Crenezumab vs placebo for the treatment of Alzheimer's dementia and Mild Cognitive Impairment				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
CDR-SB - crenezumab-IV	3 RCT (Ostrowitzki 2022, Cummings 2018)	MD -0.26 (-1.01, 0.48), I^2 50%	450	Low[a,b]
CDR-SB – crenezumab-SC	1 RCT (Cummings 2018)	MD -0.69 (-1.56, 0.18), I^2 n.a.	184	Low[b]
Amy-PET – crenezumab-SC	1 RCT (Cummings 2018)	MD -0.01 (-0.15, 0.13), I^2 n.a.	34	Very Low[b,c]
Amy-PET – crenezumab-IV	3 RCT (Ostrowitzki 2022, Salloway 2018)	SMD -0.07 (-0.28, 0.13), I^2 0%	381	Very Low[b,c]
AE - crenezumab-IV	3 RCT (Ostrowitzki 2022, Cummings 2018)	RR 1.01 (0.97, 1.06), I^2 0%	1,985	Moderate[b]
AE - crenezumab-SC	2 RCT (Cummings 2018, Salloway 2018)	RR 1.01 (0.94, 1.08), I^2 0%	223	Moderate[b]
SAE	5 RCT (Ostrowitzki 2022, Cummings 2018, Salloway 2018, Guthrie 2020)	RR 1.11 (0.89, 1.38), I^2 0%	2,210	Moderate[b]
ARIA-E – crenezumab-IV	3 RCT (Ostrowitzki 2022, Cummings 2018)	RR 1.20 (0.15, 9.70), I^2 0%	1,860	Very Low[b,c]
ARIA-H - crenezumab-IV	3 RCT (Cummings 2018, Salloway 2018, Guthrie 2020)	RR 0.82 (0.42, 1.61), I^2 0%	376	Low[b,c]
ARIA-H - crenezumab-SC	2 RCT (Cummings 2018, Salloway 2018)	RR 1.14 (0.29, 4.54), I^2 30%	223	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; IV: intravenous administration; SC: subcutaneous administration; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Donanemab vs placebo for the treatment of Alzheimer's dementia and Mild Cognitive Impairment				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
iADRS	2 RCT (Mintun 2021, Sims 2023)	**MD 3.06 (1.70, 4.42), I^2 0%**	1,855	Moderate[e]
CDR-SB	2 RCT (Mintun 2021, Sims 2023)	**MD -0.60 (-0.90, -0.29), I^2 30%**	1,527	Moderate[e]
MMSE	2 RCT (Mintun 2021, Sims 2023)	**MD 0.49 (0.10, 0.88), I^2 0%**	1,993	Low[c,e]
ADCS-iADL	2 RCT (Mintun 2021, Sims 2023)	**MD 1.66 (0.81, 2.51), I^2 0%**	1,862	Low[c,e]
Amy-PET (centiloidi)	2 RCT (Mintun 2021, Sims 2023)	**MD -87.29 (-90.67, -83.92), I^2 0%**	1,810	Moderate[e]
AE	3 RCT (Lowe 2021, Mintun 2021, Sims 2023)	RR 1.04 (0.96, 1.13), I^2 55%	1,983	Very Low[a,b,c,e]
SAE	3 RCT (Lowe 2021, Mintun 2021, Sims 2023)	RR 1.08 (0.89, 1.32), I^2 0%	2,032	Low[b,c,e]
ARIA-E	2 RCT (Mintun 2021, Sims 2023)	**RR 13.20 (8.00, 21.78), I^2 2%**	1,984	Low[c,e]
ARIA-E – ApoE4-/-	2 RCT (Mintun 2021, Sims 2023)	**RR 16.51 (4.65, 58.56), I^2 0%**	573	Very Low[c,e]

ARIA-E – ApoE4+/+	2 RCT (Mintun 2021, Sims 2023)	**RR 11.92 (5.32, 26.71), I^2 0%**	342	Very Low[c,e]
ARIA-E – ApoE4+/-	2 RCT (Mintun 2021, Sims 2023)	**RR 12.81 (6.68, 24.54), I^2 0%**	1,060	Very Low[c,e]
ARIA-H	3 RCT (Lowe 2021, Mintun 2021, Sims 2023)	**RR 2.85 (2.11, 3.86), I^2 7%**	2,040	Moderate[e]
ARIA-H – ApoE4-/-	1 RCT (Sims 2023)	**RR 1.68 (1.09, 2.59), I^2 n.a.**	505	Low[c,e]
ARIA-H – ApoE4+/+	1 RCT (Sims 2023)	**RR 2.45 (1.71, 3.51), I^2 n.a.**	289	Low[c,e]
ARIA-H – ApoE4+/-	1 RCT (Sims 2023)	**RR 2.69 (2.03, 3.55), I^2 n.a.**	926	Low[c,e]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Gantenerumab vs placebo for the treatment of Alzheimer's dementia and Mild Cognitive Impairment

Outcomes	No. of Studies	Observed effect (95% CI), I^2	No. of participants	Certainty of evidence (GRADE)
CDR-SB – gante-SC	3 RCT (Ostrowitzki 2017, Bateman 2023)	MD -0.12 (-0.35, 0.12), I^2 0%	2,756	Moderate[b]
Amy-PET – gante-IV	1 RCT (Ostrowitzki 2012)	SMD -0.93 (-2.15, 0.29), I^2 n.a.	16	Very Low[b,c]
Amy-PET – gante-SC	1 RCT (Ostrowitzki 2017, Bateman 2023)	SMD -1.68 (-3.39, 0.03), I^2 97%	271	Very Low[b,c,d]
AE – gante-SC	3 RCT (Ostrowitzki 2017, Bateman 2023)	RR 1.00 (0.93, 1.07), I^2 87%	2,756	Low[b,d]
SAE – gante-SC	3 RCT (Ostrowitzki 2017, Bateman 2023)	**RR 0.84 (0.70, 0.99), I^2 0%**	2,756	Moderate
ARIA-E – gante-IV	1 RCT (Ostrowitzki 2012)	RR 1.67 (0.10, 29.18), I^2 n.a.	18	Very Low[b,c]
ARIA-E – gante-SC	3 RCT (Ostrowitzki 2017, Bateman 2023)	**RR 9.31 (6.37, 13.60), I^2 0%**	2,649	Low[c]
ARIA-E– gante-SC ApoE4+/+	3 RCT (Ostrowitzki 2017, Bateman 2023)	**RR 10.34 (5.06, 21.14), I^2 0%**	486	Low[c]
ARIA-E– gante-SC ApoE4+/-	3 RCT (Ostrowitzki 2017, Bateman 2023)	**RR 12.45 (6.72, 23.09), I^2 0%**	1,369	Low[c]
ARIA-E– gante-SC ApoE4-/-	3 RCT (Ostrowitzki 2017, Bateman 2023)	**RR 4.20 (2.23, 7.90), I^2 0%**	881	Low[c]
ARIA-H – gante-SC	3 RCT (Ostrowitzki 2017, Bateman 2023)	**RR 1.75 (1.43, 2.13), I^2 14%**	2,736	Moderate
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; IV: intravenous administration; SC: subcutaneous administration; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

GSK933776 vs placebo for the treatment of Alzheimer's dementia

Outcomes	No. of Studies	Observed effect (95% CI), I^2	No. of participants	Certainty of evidence (GRADE)
AE	1 RCT (Andreasen 2015)	RR 1.21 (0.84, 1.72), I^2 n.a.	50	Very Low[b,c]
SAE	1 RCT (Andreasen 2015)	RR 2.03 (0.10, 39.77), I^2 n.a.	50	Very Low[b,c]
ARIA-H	1 RCT (Andreasen 2015)	RR 0.14 (0.01, 3.13), I^2 n.a.	50	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Lecanemab vs placebo for the treatment of Alzheimer's dementia and Mild Cognitive Impairment				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
CDR-SB – tutti i dosaggi	1 RCT (Swanson 2021)	MD -0.17 (-0.56, 0.22), I^2 0%	776	Moderate[b]
CDR-SB – 10mg/kg bw	1 RCT (Swanson 2021)	MD -0.40 (-1.04, 0.41), I^2 n.a.	200	Low[b,c]
CDR-SB – 10mg/kg bw	1 RCT (van Dyck 2022)	**MD -0.45 (-0.63, -0.23), I^2 n.a.**	1,734	High
ADAS-Cog_{14}	1 RCT (van Dyck 2022)	**MD -1.44 (-2.27, -0.61), I^2 n.a.**	1,734	Moderate[e]
ADCOMS	1 RCT (van Dyck 2022)	**MD -0.050 (-0.074, -0.027), I^2 n.a.**	1,734	Moderate[e]
ADCS-MCI-ADL	1 RCT (van Dyck 2022)	**MD 2.00 (1.20, 2.80), I^2 n.a.**	1,734	Moderate[e]
Amy-PET (SUVr)	1 RCT (Swanson 2021)	**SMD -1.59 (-2.15, -1.04), I^2 74%**	315	Very Low[b,c]
Amy-PET (centiloidi)	1 RCT (van Dyck 2022)	**MD −59.12 (−62.64, −55.60), I^2 n.a.**	698	High
AE	3 RCT (Logovinsky 2016, Swanson 2021, van Dyck 2022)	**RR 1.05 (1.00, 1.11), I^2 49%**	2,745	Moderate[a]
SAE	2 RCT (Swanson 2021, van Dyck 2022)	RR 1.02 (0.66, 1.56), I^2 77%	2,649	Very Low[b,c,d,e]
ARIA-E	2 RCT (Swanson 2021, van Dyck 2022)	**RR 7.66 (4.66, 12.59), I^2 0%**	2,649	High
ARIA-E – ApoE4-	2 RCT (Swanson 2021, van Dyck 2022)	**RR 13.13 (2.55, 67.72), I^2 0%**	800	Low[c]
ARIA-E – ApoE4+	2 RCT (Swanson 2021, van Dyck 2022)	**RR 6.92 (4.15, 11.54), I^2 0%**	1,820	Low[c,e]
ARIA-E – ApoE4 +/+	1 RCT (van Dyck 2022)	**RR 8.68 (3.56, 21.17), I^2 n.a.**	274	Moderate[c]
ARIA-E – ApoE4 +/-	1 RCT (van Dyck 2022)	**RR 5.77 (2.87, 11.57), I^2 n.a.**	957	Low[c,e]
ARIA-H	3 RCT (Logovinsky 2016, Swanson 2021, van Dyck 2022)	**RR 1.89 (1.50, 2.37), I^2 0%**	2,733	Moderate[e]
ARIA-H – ApoE4-	1 RCT (van Dyck 2022)	**RR 2.83 (1.49, 5.36), I^2 n.a.**	564	Low[c,e]
ARIA-H – ApoE4+	1 RCT (van Dyck 2022)	**RR 1.74 (1.33, 2.29), I^2 n.a.**	1,231	Moderate[e]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Ponezumab vs placebo for the treatment of Alzheimer's dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
AE	3 RCT (Landen 2013, Landen 2017a, Landen 2017b)	**RR 0.92 (0.87, 0.97), I^2 0%**	267	Moderate
SAE	3 RCT (Landen 2013, Landen 2017a, Landen 2017b)	**RR 2.58 (1.25, 5.33), I^2 0%**	267	Moderate
ARIA-E	1 RCT (Landen 2017b)	RR 0.99 (0.04, 23.46), I^2 n.a.	99	Very Low[b,c]
ARIA-H	2 RCT (Landen 2017a, Landen 2017b)	RR 0.58 (0.27, 1.25), I^2 n.a.	230	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; IV: intravenous administration; SC: subcutaneous administration; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Solanezumab vs placebo for the treatment of Alzheimer's dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
CDR-SB	3 RCT (Doody 2014, Honig 2018)	**MD -0.29 (-0.54, -0.04), I^2 8%**	4,181	Low[e]
CDR-SB – EXPEDITION 3	1 RCT (Hong 2018)	**MD -0.34 (-0.63, -0.05), I^2 n.a.**	1,129	Low[e]
Amy-PET	1 RCT (Hong 2018)	SMD -0.07 (-0.17, 0.03), I^2 n.a.	1,596	Low[b]
AE	1 RCT (Hong 2018)	RR 1.01 (0.98, 1.05), I^2 n.a.	2,121	Moderate[b]
SAE	4 RCT (Siemers 2010, Doody 2014, Honig 2018, Uenaka 2012)	RR 0.94 (0.84, 1.06), I^2 0%	4,208	Moderate[b]
ARIA-E	3 RCT (Doody 2014, Honig 2018)	RR 1.56 (0.45, 5.47), I^2 16%	4,181	Low[b,c]
ARIA-H	3 RCT (Doody 2014, Honig 2018)	RR 1.01 (0.72, 1.43), I^2 26%	4,181	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; IV: intravenous administration; SC: subcutaneous administration; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

PASSIVE IMMUNOTHERAPY TARGETED AGAINST DIFFERENT FORMS OF TAU

Tilavonemab vs placebo for the treatment of Alzheimer's dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
CDR-SB – 300mg	1 RCT (Florian 2023)	MD −0.07 (−0.83, 0.69), I^2 n.a.	85	Low[b]
CDR-SB – 1000mg	1 RCT (Florian 2023)	MD −0.06 (−0.81, 0.68), I^2 n.a.	91	Low[b]
CDR-SB – 2000mg	1 RCT (Florian 2023)	MD 0.16 (−0.60, 0.93), I^2 n.a.	81	Low[b]
AE	1 RCT (Florian 2023)	RR 0.98 (0.92, 1.04), I^2 n.a.	453	Moderate[b]
SAE	1 RCT (Florian 2023)	RR 0.77 (0.51, 1.16), I^2 n.a.	453	Moderate[b]
Discontinuation due to AE	1 RCT (Florian 2023)	RR 1.38 (0.47, 4.03), I^2 n.a.	453	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; IV: intravenous administration; SC: subcutaneous administration; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Semorinemab vs placebo for the treatment of Alzheimer's dementia (AD)				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Semorinemab in MCI due to AD/mild AD				
CDR-SB all doses	1 RCT (Teng 2022)	MD 0.19 (-0.19, 0.57), I^2 0%	422	Moderate[b]
Tau-PET 1500mg	1 RCT (Teng 2022)	MD 0.00 (-0.10, 0.10), I^2 n.a.	117	Low[b]
Tau-PET 4000mg	1 RCT (Teng 2022)	MD 0.00 (-0.09, 0.09), I^2 n.a.	143	Low[b]
Tau-PET 8000mg	1 RCT (Teng 2022)	MD 0.02 (-0.10, 0.14), I^2 n.a.	115	Low[b]
AE	1 RCT (Teng 2022)	RR 0.99 (0.85, 1.16), I^2 n.a.	441	Low[b]
SAE	1 RCT (Teng 2022)	RR 1.42 (0.81, 2.50), I^2 n.a.	441	Very Low[b,c]
Semorinemab (4.500mg) in mild-moderate AD				
ADAS-Cog11 (cohort 1, 49 weeks)	1 RCT (Monteiro 2023)	**MD -2.89 (-4.56, -1.21), I^2 n.a.**	198	Low
ADAS-Cog11 (cohort 2, 61 weeks)	1 RCT (Monteiro 2023)	**MD -2.75 (-5.31, -0.20), I^2 n.a.**	68	Low
ADCS-ADL (cohort 1, 49 weeks)	1 RCT (Monteiro 2023)	MD -0.83 (-3.39, 1.72), I^2 n.a.	208	Low[b]
ADCS-ADL (cohort 2, 61 weeks)	1 RCT (Monteiro 2023)	MD -1.72 (-5.50, 2.07), I^2 n.a.	73	Low[b]
CDR-SB (cohort 1, 49 weeks)	1 RCT (Monteiro 2023)	MD 0.26 (-0.29, 0.82), I^2 n.a.	210	Low[b]
CDR-SB (cohort 2, 61 weeks)	1 RCT (Monteiro 2023)	MD 0.17 (-0.87, 1.22), I^2 n.a.	73	Low[b]
MMSE (cohort 1, 49 weeks)	1 RCT (Monteiro 2023)	MD 0.27 (-0.58, 1.11), I^2 n.a.	202	Low[b]
MMSE (cohort 2, 61 weeks)	1 RCT (Monteiro 2023)	MD 1.08 (-0.15, 2.30), I^2 n.a.	68	Low[b]
Tau PET	1 RCT (Monteiro 2023)	MD 0.00 (-0.02, 0.02), I^2 n.a.	188	Low[b]
AE	1 RCT (Monteiro 2023)	RR 1.02 (0.91, 1.15), I^2 n.a.	267	Low[b]
SAE	1 RCT (Monteiro 2023)	RR 0.98 (0.58, 1.65), I^2 n.a.	267	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Gosuranemab vs placebo for the treatment of Mild Cognitive Impairment due to AD or mild AD				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
CDR-SB (low dose)	1 RCT (Shulman 2023)	MD 0.35 (-0.25, 0.95), I^2 n.a.	187	Low[b]
CDR-SB (intermediate dose)	1 RCT (Shulman 2023)	MD 0.39 (-0.22, 1.00), I^2 n.a.	177	Low[b]
CDR-SB (high dose)	1 RCT (Shulman 2023)	MD 0.00 (-0.73, 0.73), I^2 n.a.	286	Low[b]
AE	1 RCT (Shulman 2023)	RR 1.03 (0.97, 1.11), I^2 n.a.	650	Low[b]
SAE	1 RCT (Shulman 2023)	RR 0.94 (0.61, 1.47), I^2 n.a.	650	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Review question 16a (RQ NICE). What effect does modifying risk factors (repositioning drugs acting on possible etiological causes of dementia) have on slowing the progression of dementia?

Antidiabetic drugs (Rosiglitazone) vs placebo for the treatment of Alzheimer's dementia (AD)				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
ADAS-Cog	2 RCT (Gold 2010, Risner 2006)	MD -0.42 (-1.35, 0.51), I^2 0%	764	Low[a,b]
ADAS-Cog – 2mg	2 RCT (Gold 2010, Risner 2006)	MD -0.29 (-1.61, 1.02), I^2 0%	382	Low[a,b]
ADAS-Cog - 8mg	2 RCT (Gold 2010, Risner 2006)	MD -0.55 (-1.86, 0.77), I^2 0%	382	Low[a,b]
CIBIC+	1 RCT (Gold 2010)	MD -0.05 (-0.27, 0.17), I^2 n.a.	391	Low[a,b]
AE	2 RCT (Gold 2010, Risner 2006)	RR 0.97 (0.80, 1.17), I^2 0%	882	Low[a,b]
AE - 2mg	2 RCT (Gold 2010, Risner 2006)	RR 0.89 (0.68, 1.16), I^2 0%	438	Low[a,b]
AE - 8mg	2 RCT (Gold 2010, Risner 2006)	RR 1.05 (0.81, 1.35), I^2 0%	444	Low[a,b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Non-steroidal anti-inflammatory (NSAIDs) drugs vs placebo for the treatment of Alzheimer's dementia (AD)				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
ADAS-Cog	8 RCT (Aisen 2003, Bentham 2008, De Jong 2008, Green 2009, Pasqualetti 2009, Reines 2004, Soininen 2007, Wilcock 2008)	MD -0.37 (-1.94, 1.19), I^2 81%	3,315	Very Low[a,b]
MMSE	6 RCT (Bentham 2008, De Jong 2008, Green 2009, Pasqualetti 2009, Reines 2004, Soininen 2007)	MD -0.22 (-0.47, 0.03), I^2 0%	2,606	Very Low[a,c,d]
ADCS-ADL	4 RCT (Aisen 2003, Green 2009, Reines 2004, Wilcock 2008)	**MD 1.60 (0.31, 2.90), I^2 47%**	2,671	Low[a,e]
NPI	4 RCT (Aisen 2003, De Jong 2008, Green 2009, Pasqualetti 2009)	MD -0.26 (-1.30, 0.77), I^2 39%	2,073	Low[a,d]
CIBIC+	4 RCT (De Jong 2008, Pasqualetti 2009, Reines 2004, Soininen 2007)	MD 0.04 (-0.08, 0.16), I^2 0%	1,196	Low[a,d]
AE	4 RCT (Green 2009, Reines 2004, Soininen 2007, Wilcock 2008)	RR 1.03 (1.00, 1.07), I^2 0%	2,934	Moderate[a]
SAE	6 RCT (Aisen 2003, Bentham 2008, De Jong 2008, Green 2009, Reines 2004, Soininen 2007)	RR 1.13 (0.97, 1.32), I^2 21%	3,475	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations; * Study participants were allowed to use other medications during the study period including antipsychotics, antidepressants, and vitamin E supplements that may have impacted the outcomes of interest, and it was not reported what proportion of participants in each group was taking these medications. In some RCTs, the blindness of assessors was not clear.				

Statins vs placebo for the treatment of Alzheimer's dementia (AD)				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
MMSE - atorvastatina	2 RCT (Feldman 2010, Sparks 2005, Sparks 2006*)	MD 0.84 (-0.35, 2.02), I^2 59%	577	Low[a,b]
ADAS-Cog - atorvastatina	2 RCT (Feldman 2010, Sparks 2005, Sparks 2006*)	MD -1.73 (-4.99, 1.53), I^2 63%	560	Low[a,b]
NPI - atorvastatina	2 RCT (Feldman 2010, Sparks 2005, Sparks 2006*)	MD -2.07 (-5.73, 1.59), I^2 77%	577	Very Low[b,c]
MMSE - simvastatina	2 RCT (Sano 2011, Simons 2002)	MD 0.78 (-1.44, 2.99), I^2 78%	450	Very Low[b,c]
ADAS-Cog - simvastatina	2 RCT (Sano 2011, Simons 2002)	MD 0.30 (-1.05, 1.65), I^2 0%	450	Very Low[b,c]
NPI - simvastatina	1 RCT (Sano 2011)	MD -1.65 (-3.69, 0.39), I^2 n.a.	406	Very Low[b,c]
AE - atorvastatina	2 RCT (Feldman 2010)	**RR 2.86 (2.20, 3.71), I^2 n.a.**	517	Moderate[b]
AE - simvastatin	1 RCT (Sano 2011)	RR 1.03 (0.97, 1.10), I^2 n.a.	406	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations; * secondary study				

Antihypertensive drugs vs placebo for the treatment of Alzheimer's dementia (AD)				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Calcium channel blockers				
ADAS-Cog – nimodipina 90mg	1 RCT (Morich 2012)	MD -0.44 (-1.36, 0.48), I^2 n.a.	713	Low[b]
ADAS-Cog – nimodipina 180mg	1 RCT (Morich 2012)	MD -0.45 (-1.35, 0.45), I^2 n.a.	729	Low[b]
MMSE – nimodipina 90mg	1 RCT (Morich 2012)	**MD 0.29 (0.05, 0.53), I^2 n.a.**	713	Moderate
MMSE – nimodipina 180mg	1 RCT (Morich 2012)	**MD 0.60 (0.10, 1.10), I^2 n.a.**	729	Moderate
MMSE – nimodipina	1 RCT (Pantoni 2005) *	MD 0.60 (-1.64, 2.84), I^2 n.a.	149	Very Low[b,c]
AE – nimodipina 90mg	1 RCT (Morich 2012)	RR 1.00 (0.91, 1.10), I^2 n.a.	811	Low[b]
AE – nimodipina 180mg	1 RCT (Morich 2012)	RR 1.03 (0.94, 1.10), I^2 n.a.	825	Low[b]
ADAS-Cog – nilvadipina	1 RCT (Lawlor 2018)	MD -0.22 (-2.06, 1.62), I^2 n.a.	498	Low[b]
AE - nilvadipina	1 RCT (Lawlor 2018)	RR 1.05 (0.96, 1.14), I^2 n.a.	509	Low[b]
Telmisartan vs amlodipina				
ADAS-Cog	1 RCT (Kume 2012)	MD 1.30 (-1.80, 4.40), I^2 n.a.	20	Very Low[b,c]
MMSE	1 RCT (Kume 2012)	MD -4.20 (-9.42, 1.02), I^2 n.a.	20	Very Low[b,c]
Brain-penetrating ACE-inhibitors vs calcium channel blockers				
MMSE	1 RCT (Ohrui 2004)	**MD 4.30 (4.22, 4.38), I^2 n.a.**	108	Low[e]
Non-brain-penetrating ACE-inhibitors vs calcium channel blockers				
MMSE	1 RCT (Ohrui 2004)**	**MD 0.30 (0.19, 0.38), I^2 n.a.**	108	Low[e]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations;				

Participants IN the included studies were allowed to use other medications during the study period including antipsychotics, antidepressants, and vitamin E supplements that may have impacted the outcomes of interest, and it was not reported what proportion of participants in each group was taking these medications.
* Pantoni 2005: study that included participants with subcortical dementia.
** Orhui 2004: publication does not report whether patients or assessors were blinded to treatment.

Review question 16b (New RQ). What effect does modifying risk factors (repositioning drugs acting on possible etiological causes of dementia) have on slowing the progression of Mild Cognitive Impairment?

Non-steroidal anti-inflammatory (NSAIDs) drugs vs placebo for the treatment of Mild Cogntive Impairment				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Rofecoxib				
ADAS-Cog	1 RCT (Thal 2005)	MD 0.30 (-0.40, 1.10), I^2 n.a.	1,457	Low[b]
MMSE	1 RCT (Thal 2005)	MD 0.20 (-0.70, 0.30), I^2 n.a.	1,457	Low[b]
Conversion to AD	1 RCT (Thal 2005)	**adj. HR 1.46 (1.09, 1.94)**	1,457	Moderate
Discontinuation due to AE	1 RCT (Thal 2005)	RR 1.07 (0.87, 1.31), I^2 n.a.	1,451	Low[b]
Triflusal				
MMSE	1 RCT (Gómez-Isla 2008)	MD 0.19 (-0.47, 0.85), I^2 n.a.	257	Very Low[b,e]
ADAS-Cog	1 RCT (Gómez-Isla 2008)	MD -0.90 (-2.30, 0.50), I^2 n.a.	257	Very Low[b,e]
Discontinuation due to AE	1 RCT (Gómez-Isla 2008)	**RR 2.76 (1.34, 5.67), I^2 n.a.**	257	Moderate[c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; HR: hazard ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations;				

Antihypertensive drugs vs placebo for the treatment of Mild Cogntive Impairment				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Candesartan				
TMT-A	1 RCT (Hajjar 2022)	MD -3.18 (-20.73 – 14.37) I^2n.a.	77	Very Low[b,e]
IADL	1 RCT (Hajjar 2022)	MD 0.45 (-0.35 – 1.25) I^2n.a.	77	Low[b]
hypotensive episodes (BP≤100/40 mmHg)	1 RCT (Hajjar 2022)	**RR 4.11 (1.51 – 11.16) I^2n.a.**	77	Very Low[b,e]
AE	1 RCT (Hajjar 2022)	RR 1.18 (0.48 – 2.94) I^2n.a.	77	Very Low[b,e]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; HR: hazard ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations;				

Antidiabetic drugs (metformina) vs placebo for the treatment of Mild Cogntive Impairment				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
ADAS-Cog	2 RCT (Luchsinger 2016)	MD 0.90 (-0.90, 2.70), I^2 n.a.	80	Very Low[b,c,e]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Review question 17a (RQ NICE). How effective is the co-prescription of acetylcholinesterase inhibitors and memantine for the treatment of Alzheimer's dementia?

Acetylcholinesterase inhibitor plus memantine vs placebo for the treatment of Alzheimer's dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Mild AD (post-hoc analyses per subgroups)				
Global outcomes	1 RCT (Porsteinsson 2008)	SMD -0.09 (-0.45, 0.26), I^2 n.a.	121	Very Low[b,c,e]
Cognitive functions	2 RCT (Dysken 2014, Porsteinsson 2008)	SMD -0.05 (-0.27, 0.17), I^2 0%	315	Very Low[b,c,e]
ADL	2 RCT (Dysken 2014, Porsteinsson 2008)	SMD -0.04 (-0.26, 0.19), I^2 0%	315	Very Low[b,c,e]
Mild/moderate AD				
MMSE	2 RCT (Howard 2012, Dysken 2014)	MD -0.08 (-0.80, 0.65), I^2 0%	709	Moderate[b]
ADAS-Cog	2 RCT (Porsteinsson 2008, Dysken 2014)	MD -1.17 (-2.81, 0.47), I^2 0%	709	Moderate[b]
ADL	2 RCT (Porsteinsson 2008, Dysken 2014)	SMD 0.06 (-0.09, 0.20), I^2 2%	709	Moderate[b]
CIBIC+	1 RCT (Porsteinsson 2008)	MD -0.04 (-0.23, 0.15), I^2 n.a.	427	Low[b]
NPI	2 RCT (Porsteinsson 2008, Dysken 2014)	MD 0.57 (-2.76, 3.91), I^2 0%	579	Moderate[b]
AE	2 RCT (Porsteinsson 2008, Dysken 2014)	RR 0.91 (0.62, 1.33), I^2 0%	740	Moderate[b]
Discontinuation due to AE	1 RCT (Porsteinsson 2008)	RR 0.76 (0.38, 1.53), I^2 n.a.	433	Low[b]
Moderate AD				
NPI	1 RCT (Youn 2021)	MD -1.13 (-5.06, 2.80), I^2 n.a.	148	Low[b,c]
MMSE	1 RCT (Youn 2021)	MD 0.12 (-0.79, 1.03), I^2 n.a.	148	Low[b,c]
Moderate AD (post-hoc analyses per subgroups)				
Global outcomes	2 RCT (Porsteinsson 2008, Tariot 2004)	SMD -0.17 (-0.35, 0.00), I^2 59%	493	Very Low[a,b,c,e]
Cognitive functions	4 RCT (Dysken 2014, Howard 2012, Porsteinsson 2008, Tariot 2004)	**SMD -0.23 (-0.39, -0.08), I^2 0%**	657	Low[e]
ADL	4 RCT (Dysken 2014, Howard 2012, Porsteinsson 2008, Tariot 2004)	SMD -0.11 (-0.26, 0.04), I^2 12%	663	Very Low[b,e]
NPI	1 RCT (Howard 2012)	MD 0.47 (-10.43, 11.37), I^2 n.a.	57	Very Low[b,c,e]
DEMQOL	1 RCT (Howard 2012)	MD -4.45 (-11.34, 2.44), I^2 n.a.	55	Very Low[b,c,e]
Moderate/severe AD				
MMSE	1 RCT (Howard 2012)	MD 0.27 (-1.13, 1.67), I^2 n.a.	112	Low[b]
SIB	2 RCT (Grossberg 2013, Tariot 2004)	MD 1.22 (-1.15, 3.59), I^2 71%	1,063	Low[a,b]
ADL	3 RCT (Grossberg 2013, Howard 2012, Tariot 2004)	**SMD 0.13 (0.01, 0,24), I^2 0%**	1,166	High
CIBIC+	2 RCT (Grossberg 2013, Tariot 2004)	**MD -0.28 (-0.41, -0.14), I^2 0%**	1,056	High
NPI	3 RCT (Grossberg 2013, Howard 2012, Tariot 2004)	**MD -3.19 (-4.83, -1.56), I^2 0%**	1,133	High
DEMQOL	1 RCT (Howard 2012)	MD -2.00 (-6.44, 2.44), I^2 n.a.	113	Low[b]
AE	2 RCT (Grossberg 2013, Howard 2012)	RR 0.99 (0.63, 1.57), I^2 58%	825	Low[a,b]
Discontinuation due to AE	2 RCT (Grossberg 2013, Tariot 2004)	RR 0.99 (0.38, 2.58), I^2 83%	1,079	Very Low[a,b,c]
Severe AD (post-hoc analyses per subgroups)				
Global outcomes	1 RCT (Tariot 2004)	SMD -0.22 (-0.53, 0.09), I^2 n.a.	161	Very Low[b,c,e]
Cognitive functions	2 RCT (Tariot 2004, Howard 2012)	**SMD -0.54 (-0.84, -0.30), I^2 55%**	218	Low[a,e]

ADL	2 RCT (Tariot 2004, Howard 2012)	**SMD -0.33 (-0.60, -0.06), I^2 0%**	218	Low[e]
NPI	1 RCT (Howard 2012)	**MD -10.24 (-20.30, -0.18), I^2 n.a.**	57	Low[e]
DEMQOL	1 RCT (Howard 2012)	MD 0.49 (-6.02, 7,00), I^2 n.a.	57	Very Low[b,c,e]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Co-prescription of acetylcholinesterase inhibitor and memantine vs acetylcholinesterase inhibitor as monotherapy				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Memantine tablets				
MMSE	2 RCT (Araki 2014, Choi 2011)	MD 0.88 (-1.98, 3.75), I^2 82%	183	Very Low[a,b,c]
MMSE – mild/moderate	1 RCT (Choi 2011)	MD -0.40 (-1.29, 0.49), I^2 n.a.	158	Low[b]
MMSE – moderate/severe	1 RCT (Araki 2014)	**MD 2.55 (0.28, 4.82), I^2 n.a.**	25	Very Low[b,c]
Oral pump (solution) of memantine				
MMSE	1 RCT (Kim 2023)	MD 0.20 (-1.48, 1.88), I^2 n.a.	188	Low[b]
CDR-SB	1 RCT (Kim 2023)	MD 0.24 (-1.05, 1.53), I^2 n.a.	188	Low[b]
NPI	1 RCT (Kim 2023)	MD 0.19 (-2.23, 2.68), I^2 n.a.	188	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Co-prescription of acetylcholinesterase inhibitor and memantine vs co-prescription of memantine and placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Mild/moderate AD				
MMSE – don+mem	1 RCT (Shao 2015)	MD 0.37 (-1.04, 1.78), I^2 n.a.	44	Very Low[b,c]
MMSE - gala+mem	1 RCT (Shao 2015)	MD 0.82 (-0.58, 2.22), I^2 n.a.	44	Very Low[b,c]
MMSE - riva+mem	1 RCT (Shao 2015)	MD 0.41 (-1.17, 1.99), I^2 n.a.	44	Very Low[b,c]
ADCS-ADL - don+mem	1 RCT (Shao 2015)	MD -0.64 (-1.88, 0.60), I^2 n.a.	44	Very Low[b,c]
ADCS-ADL - gala+mem	1 RCT (Shao 2015)	MD -1.14 (-2.47, 0.19), I^2 n.a.	44	Very Low[b,c]
ADCS-ADL - riva+mem	1 RCT (Shao 2015)	MD -0.18 (-1.43, 1.07), I^2 n.a.	44	Very Low[b,c]
AE - don+mem	1 RCT (Shao 2015)	RR 1.40 (0.52, 3.74), I^2 n.a.	44	Very Low[b,c]
AE - gala+mem	1 RCT (Shao 2015)	RR 1.60 (0.62, 4.13), I^2 n.a.	44	Very Low[b,c]
AE - riva+mem	1 RCT (Shao 2015)	RR 1.20 (0.43, 3.36), I^2 n.a.	44	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; don: donepezil; riva: rivastigmina; gala: galantamina; mem: memantina; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Switching from acetylcholinesterase inhibitors to memantine				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
MMSE	1 RCT (Howard 2012)	MD -0.47 (-1.77, 0.83), I^2 n.a.	105	Low[b]
ADCS-ADL/BADL	1 RCT (Howard 2012)	MD 0.21 (-2.91, 3.34), I^2 n.a.	105	Low[b]
NPI	1 RCT (Howard 2012)	MD -9.28 (-20.49, 1.93), I^2 n.a.	105	Very Low[b,c]
DEMQOL	1 RCT (Howard 2012)	MD 2.62 (-3.43, 8.66), I^2 n.a.	105	Very Low[b,c]
Insitutionalitation	1 RCT (Howard 2012)	RR 1.40 (0.90, 2.20), I^2 n.a.	149	Low[b]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Review question 17b (RQ NICE). When should treatment with donepezil, galantamine, rivastigmine, and memantine be withdrawn for people with Alzheimer's dementia?

Continuation or withdrawal of acetylcholinesterase inhibitors or memantine				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
MMSE	3 RCT (Herrmann 2016, Howard 2012, Hong 2018)	**MD -1.32 (-2.53, -0.11), I^2 62%**	205	Low[a,c]
MMSE – moderate AD	1 RCT (Herrmann 2016)	**MD -3.72 (-5.92, -1.52), I^2 n.a.**	54	Moderate[c]
MMSE – moderate/severe AD	1 RCT (Herrmann 2016)	MD -1.70 (-3.93, 0.53), I^2 n.a.	40	Very Low[b,c]
MMSE – severe AD	2 RCT (Hong 2018, Herrmann 2016)	MD -0.58 (-1.21, 0.04), I^2 0%	111	Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Review question 18a (RQ NICE). What is the comparative effectiveness of donepezil, galantamine, memantine and rivastigmine for cognitive enhancement in dementia associated with Parkinson's disease?

Acetylcholinesterase inhibitors for the treatment of dementia associated with Parkinson's disease				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
MMSE	4 RCT (Aarsland 2002, Dubois 2012, Emre 2004, Ravina 2005)	**MD 1.36 (0.94, 1.77), I^2 0%**	1,119	High
MMSE - don	3 RCT (Aarsland 2002, Dubois 2012, Ravina 2005)	**MD 1.57 (1.05, 2.09), I^2 0%**	618	High
MMSE - riva	1 RCT (Emre 2004)	**MD 1.00 (0.33, 1.67), I^2 n.a.**	507	High
ADAS-Cog	3 RCT (Aarsland 2002, Dubois 2012, Ravina 2005)	**MD -2.28 (-3.40, -1.15), I^2 0%**	1,035	High
ADAS-Cog - riva	1 RCT (Emre 2004)	**MD -2.80 (-4.26, -1.34), I^2 n.a.**	490	High
MDRS – riva patch vs riva tablets	1 RCT (Emre 2004)	**MD -5.30 (-8.17, -2.43), I^2 n.a.**	546	High
CIBIC+/ADCS-CGIC	3 RCT (Aarsland 2002, Dubois 2012, Emre 2004)	**RR 1.24 (1.05, 1.47), I^2 15%**	1,035	High
CIBIC+/ADCS-CGIC - riva	1 RCT (Emre 2004)	**RR 1.37 (1.05, 1.79), I^2 n.a.**	494	High
ADCS-CGIC - riva	1 RCT (Emre 2004)	**MD -0.50 (-0.77, -0.23), I^2 n.a.**	494	High
CIBIC+ - don	2 RCT (Aarsland 2002, Dubois 2012)	MD -0.43 (-0.93, 0.08), I^2 56%	541	Low[b,c]
UPDRS-III - don	2 RCT (Aarsland 2002, Ravina 2005)	MD -1.50 (-7.87, 4.87), I^2 0%	65	Low[b,c]
ADCS-ADL - riva	1 RCT (Emre 2004)	**MD 2.50 (0.43, 4.57), I^2 n.a.**	498	High
NPI-10 - riva	1 RCT (Emre 2004)	**MD -2.00 (-3.91, -0.09), I^2 n.a.**	500	High
AE - don	3 RCT (Aarsland 2002, Dubois 2012, Ravina 2005)	RR 1.07 (0.96, 1.19), I^2 0%	617	Moderate[b]
AE - riva	1 RCT (Emre 2004)	**RR 1.18 (1.06, 1.31), I^2 n.a.**	541	High
Discontinuation due to AE - Don	2 RCT (Aarsland 2002, Dubois 2012)	RR 1.46 (0.91, 2.35), I^2 0%	576	Moderate[b]
Discontinuation due to AE - Riva	1 RCT (Emre 2004)	**RR 2.19 (1.26, 3.80), I^2 n.a.**	576	High
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; don: donepezil; riva: rivastigmina; gala: galantamina; mem: memantina; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Memantine for the treatment of dementia associated with Parkinson's disease				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
MMSE	1 RCT (Leroi 2009)	MD -1.00 (-6.01, 4.01), I^2 n.a.	24	Very Low[b,c]
ADCS-CGIC	2 RCT (Emre 2010)	MD -0.20 (-0.69, 0.29), I^2 n.a.	116	Moderate[b]
CIBIC+	1 RCT (Leroi 2009)	RR 1.40 (0.64, 3.08), I^2 n.a.	24	Low[b,c]
ADCS-ADL	1 RCT (Emre 2010)	MD 0.80 (-3.22, 4.82), I^2 n.a.	116	Very Low[b,c]
UPDRS-III	2 RCT (Leroi 2009, Emre 2010)	MD 0.88 (-2.35, 4.10), I^2 0%	140	Low[b]
NPI-10	1 RCT (Leroi 2009)	MD -2.00 (-11.64, 7.64), I^2 n.a.	24	Very Low[b,c]
NPI-12	1 RCT (Emre 2010)	MD -1.50 (-6.35, 3.35), I^2 n.a.	116	Very Low[b,c]

AE	2 RCT (Leroi 2009, Emre 2010)	RR 0.97 (0.69, 1.37), I^2 0%	145	Moderate[b]
SAE	2 RCT (Leroi 2009, Emre 2010)	RR 1.09 (0.45, 2.67), I^2 0%	145	Low[b,c]
Discontinuation due to AE	1 RCT (Emre 2010)	RR 1.12 (0.36, 3.48), I^2 n.a.	120	Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; don: donepezil; riva: rivastigmina; gala: galantamina; mem: memantina; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Review question 18b (RQ NICE). What is the comparative effectiveness of donepezil, galantamine, memantine and rivastigmine for cognitive enhancement in dementia with Lewy bodies?

Acetylcholinesterase inhibitors for the treatment of DLB				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
MMSE	3 RCT (Ikeda 2015, Mori 2012, McKeith 2000)	**MD 1.75 (0.75, 2.75), I^2 48%**	394	Moderate[a]
MMSE - don	2 RCT (Ikeda 2015, Mori 2012)	**MD 1.95 (0.70, 3.40), I^2 70%**	272	Moderate[a]
MMSE – riva	1 RCT (McKeith 2000)	MD 1.24 (-0.28, 2.76), I^2 n.a.	120	Low[b,c]
CIBIC+ - don	1 RCT (Mori 2012)	**MD -1.17 (-1.66, -0.68), I^2 n.a.**	121	High
NPI-10	3 RCT (Ikeda 2015, Mori 2012, McKeith 2000)	MD -2.06 (-7.15, 3.02), I^2 0%	372	Low[b,c]
NPI-10 – don	2 RCT (Ikeda 2015, Mori 2012)	MD -1.54 (-9.37, 6.29), I^2 0%	272	Low[b,c]
NPI-10 – riva	1 RCT (McKeith 2000)	MD -3.80 (-9.25, 1.65), I^2 n.a.	100	Low[b,c]
UPDRS-III – don	2 RCT (Ikeda 2015, Mori 2012)	MD -0.65 (-2.24, 0.95), I^2 21%	372	Moderate[b]
AE	3 RCT (Ikeda 2015, Mori 2012, McKeith 2000)	**RR 1.14 (1.02, 1,28), I^2 0%**	401	Moderate
SAE	3 RCT (Ikeda 2015, Mori 2012, McKeith 2000)	RR 0.98 (0.53, 1,82), I^2 0%	401	Moderate[b]
Discontinuation due to AE	3 RCT (Ikeda 2015, Mori 2012, McKeith 2000)	RR 0.89 (0.49, 1.62), I^2 0%	401	Moderate[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; don: donepezil; riva: rivastigmina; mem: memantina; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Memantine for the treatment of DLB				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
ADCS-CGIC	1 RCT (Emre 2010)	MD -0.60 (-1.22, 0.02), I^2 n.a.	74	Low[b]
ADCS-ADL	1 RCT (Emre 2010)	MD 1.60 (-4.90, 8.10), I^2 n.a.	74	Very Low[b,c]
NPI-12	1 RCT (Emre 2010)	MD -6.00 (-12.23, 0.23), I^2 n.a.	74	Very Low[b,c]
UPDRS-III	1 RCT (Emre 2010)	MD -1.40 (-5.52, 2.72), I^2 n.a.	74	Low[b]
AE	1 RCT (Emre 2010)	RR 1.28 (0.79, 2.07), I^2 n.a.	75	Low[b]
SAE	1 RCT (Emre 2010)	RR 2.41 (0.65, 8.93), I^2 n.a.	75	Very Low[b,c]
Discontinuation due to AE	1 RCT (Emre 2010)	RR 0.86 (0.30, 2.47), I^2 n.a.	75	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Review question 19 (RQ NICE). How effective are acetylcholinesterase inhibitors and memantine for types of dementia other than Alzheimer's disease?

Acetylcholinesterase inhibitors for vascular dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Cognitive outcomes				
MMSE	4 RCT (Ballard 2008, Black 2003, Mok 2007, Román 2010)	**MD 0.58 (0.30, 0.86), I^2 0%**	2,301	High
MMSE – don	2 RCT (Black 2003, Román 2010)	**MD 0.57 (0.23, 0.92), I^2 0%**	1,552	High
MMSE – riva	2 RCT (Ballard 2008, Mok 2007)	**MD 0.59 (0.10, 1.09), I^2 0%**	749	High
ADAS-Cog	4 RCT (Ballard 2008, Black 2003, Román 2010, Wilkinson 2003)	**-1.36 (-2.03, -0.70), I^2 52%**	2,734	Moderate[a]
ADAS-Cog – don	3 RCT (Black 2003, Román 2010, Wilkinson 2003)	**MD -1.47 (-2.37, -0.57), I^2 67%**	2,036	Moderate[a]
ADAS-Cog_{11} – gala	2 RCT (Auchus 2007, Small 2003)	**MD -1.59 (-2.39, -0.78), I^2 0%**	926	High
ADAS-Cog – riva	1 RCT (Ballard 2008)	**MD -1.10 (-2.15, -0.05), I^2 n.a.**	698	Moderate[a]
VaDAS-cognitive subscale	1 RCT (Román 2010)	**MD -1.15 (-1.99, -0.31), I^2 n.a.**	818	High
EXIT-25	2 RCT (Auchus 2007, Román 2010)	MD -0.57 (-1.40, 0.25), I^2 66%	1,683	Low[a,b]
Global assessment				
CDR-SB	4 RCT (Black 2003, Mok 2007, Román 2010, Wilkinson 2003)	MD -0.17 (-0.33, -0.00), I^2 58%	2,036	Moderate[a]
VaD assessment scale	1 RCT (Ballard 2008)	MD -1.03 (-2.62, 0.02), I^2 n.a.	682	Low[b]
Neuropsychiatric outcomes				
NPI	2 RCT (Auchus 2007, Mok 2007)	**MD 1.76 (0.28, 3.24), I^2 0%***	757	High
NPI-12 - riva	1 RCT (Ballard 2008)	MD 0.40 (-1.36, 2.16), I^2 n.a.	706	Moderate[b]
Functional abilities				
ADCS-ADL	2 RCT (Auchus 2007, Ballard 2008)	MD -0.13 (-1.16, 0.90), I^2 20%	1,444	Moderate[b]
IADL	3 RCT (Black 2003, Mok 2007, Wilkinson 2003)	MD -0.38 (-1,04, 0.27), I^2 68%	1,126	Very Low[b,c]
Adverse events				
AE	5 RCT (Auchus 2007, Black 2003, Mok 2007, Román 2010, Wilkinson 2003)	**RR 1.05 (1.01, 1.09), I^2 0%**	2,949	High
SAE	5 RCT (Auchus 2007, Ballard 2008, Black 2003, Román 2010, Wilkinson 2003)	RR 1.11 (0.95, 1.30), I^2 0%	3,471	Moderate[b]
Discontinuation due to AE	3 RCT (Auchus 2007, Ballard 2008, Mok 2007)	**RR 2.40 (1.61, 3.59), I^2 39%**	1,533	High
Mortality	6 RCT (Auchus 2007, Ballard 2008, Black 2003, Mok 2007, Román 2010, Wilkinson 2003)	RR 0.99 (0.43, 2.30), I^2 43%	3,726	Low[a,b]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; don: donepezil; riva: rivastigmina; gala: galantamina a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

* A significant worsening of neuropsychiatric symptoms was observed in subjects treated with acetylcholinesterase inhibitors compared to placebo-treated subjects.

Memantine vs placebo for vascular dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Cognitive outcomes				
MMSE	1 RCT (Orgogozo 2002)	**MD 1.23 (0.23, 2.23), I^2 n.a.**	213	Moderate[c]
ADAS-Cog	2 RCT (Orgogozo 2002, Wilcock 2002)	**MD -2.19 (-3.16, -1.21), I^2 11%**	752	High
Adverse events				
AE	1 RCT (Wilcock 2002)	RR 1.03 (0.94, 1.13), I^2 n.a.	579	Moderate[b]
SAE	1 RCT (Orgogozo 2002)	RR 0.97 (0.69, 1.36), I^2 n.a.	188	Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Acetylcholinesterase inhibitors for frontotemporal dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Cognitive outcomes				
MMSE	2 RCT (Vercelletto 2011, Boxer 2013)	MD 0.26 (-1.43, 1.95), I^2 14%	105	Very Low[b,c]
Neuropsychiatric outcomes				
NPI	2 RCT (Vercelletto 2011, Boxer 2013)	MD -3.61 (-8.79, 1.57), I^2 0%	103	Very Low[b,c]
Global assessment				
CGIC	1 RCT (Boxer 2013)	MD -0.50 (-1.35, 0.35), I^2 n.a.	64	Very Low[b,c]
CDR-SB	1 RCT (Boxer 2013)	MD -0.10 (-2.22, 2.02), I^2 n.a.	64	Very Low[b,c]
Motor skilss				
UPDRS	1 RCT (Boxer 2013)	MD -0.30 (-3.46, 2.86), I^2 n.a.	64	Very Low[b,c]
Adverse events				
AE	1 RCT (Vercelletto 2011)	RR 0.90 (0.43, 1.90), I^2 n.a.	49	Very Low[b,c]
SAE	2 RCT (Vercelletto 2011, Boxer 2013)	RR 0.65 (0.29,1.48), I^2 1%	113	Very Low[b,c]
Discontinuation due to AE	1 RCT (Vercelletto 2011)	RR 1.13 (0.25, 5.06), I^2 n.a.	49	Very Low[b,c]
Mortality	1 RCT (Vercelletto 2011)	RR 5.63 (0.28, 111.43), I^2 n.a.	49	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Memantine for frontotemporal dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Cognitive outcomes				
MMSE	2 RCT (Boxer 2013)	MD -0.40 (-3.09, 2.29), I^2 n.a.	17	Very Low[b,c]
Neuropsychiatric outcomes				
NPI	2 RCT (Boxer 2013)	MD 0.00 (-5.36, 5.36), I^2 n.a.	17	Very Low[b,c]
Global assessment				
CGIC	1 RCT (Boxer 2013)	MD 0.00 (-0.36, 0.36), I^2 n.a.	17	Very Low[b,c]
CDR-SB	1 RCT (Boxer 2013)	MD 0.90 (-0.28, 2.08), I^2 n.a.	17	Very Low[b,c]
Motor skills				
UPDRS	1 RCT (Boxer 2013)	MD 3.30 (-3.14, 9.74), I^2 n.a.	17	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Acetylcholinesterase inhibitors for cognitive impairment caused by multiple sclerosis				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Cognitive outcomes				
Multiple Sclerosis Inventarium Cognition Score	1 RCT (Mäurer 2012)	MD -0.86 (-3.17, 1.45), I^2 n.a.	81	Low[b]
Depression				
Montgomery-Asberg Depression Rating Scale	1 RCT (Mäurer 2012)	MD -1.58 (-3.66, 0.50), I^2 n.a.	81	Low[b]
Adverse events				
AE	1 RCT (Mäurer 2012)	RR 1.18 (0.90, 1.55), I^2 n.a.	86	Low[b]
SAE	2 RCT (Krupp 2011, Mäurer 2012)	RR 0.46 (0.12, 1.70)	206	Very Low[b,c]
Relapses	1 RCT (Mäurer 2012)	RR 0.61 (0.18, 2.00), I^2 n.a.	86	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Memantine for cognitive impairment caused by multiple sclerosis				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Disease progression				
Multiple Sclerosis Inventarium Cognition Score	1 RCT (Peyro Saint-Paul 2016)	MD -0.47 (-1.08, 0.12), I^2 n.a.	68	Low[b]
Adverse events				
AE	1 RCT (Peyro Saint-Paul 2016)	**RR 3.56 (1.88, 6.74), I^2 n.a.**	86	Low[c]
Discontinuation due to AE	1 RCT (Peyro Saint-Paul 2016)	RR 3.44 (0.77, 15.34), I^2 n.a.	83	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Rivastigmine for cognitive decline caused by Huntington's disease				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
RCFT delayed recall	1 RCT (Sešok 2014)	MD -2.86 (-10.90, 5.18), I^2 n.a.	18	Low[b]
RCFT immediate recall	1 RCT (Sešok 2014)	MD -3.77 (-11.92, 4.38), I^2 n.a.	18	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations; RCFT: Rey Complex Figure Test				

Review question 20a (RQ NICE). What are the most effective non-pharmacological interventions for supporting cognitive functioning in people living with dementia?

Review question 20b (RQ NICE). What are the most effective non-pharmacological interventions for supporting functional ability in people living with dementia?

Review question 20c (RQ NICE). What are the most effective non-pharmacological interventions to support wellbeing in people living with dementia?

Review question 20d (RQ NICE). What are the most effective methods of supporting people living with dementia to reduce harm and stay independent?

Acupuncture vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Mild to moderate dementia				
MMSE	2 RCT (Liu 2016, Wang 2014)	MD 1.88 (-3.31, 7.07), I^2 88%	223	Very Low[b,c,d]
ADAS-Cog	1 RCT (Jia 2017)	**MD -4.20 (-6.26, -2.14), I^2 n.a.**	87	Moderate
ADL	1 RCT (Jia 2017)	MD 0.57 (-1.58, 2.72), I^2 n.a.	87	Low[b]
Moderate to severe dementia				
MMSE	1 RCT (Peng 2017)	MD 3.53 (-0.74, 7.80), I^2 n.a.	50	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Art therapy vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
MMSE	1 RCT (Li 2017)	MD 3.85 (-0.19, 7.89), I^2 n.a.	40	Very Low[b,c]
MoCA	1 RCT (Johnson 2020)	MD 0.20 (-4.18, 4.58), I^2 n.a.	69	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Physical excercise vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**

Dance				
MMSE	2 RCT (Hwang 2010, Van de Winckel 2004)	MD 2.86 (-0.44, 6.17), I^2 0%	42	Very Low[b,c]
Aerobic exercise				
MMSE – mild dementia	2 RCT (Arcoverde 2014, Yang 2015)	**MD 2.20 (1.04, 3.36), I^2 0%**	70	Moderate
MMSE – moderate dementia	3 RCT (Cancela 2016, Miu 2008, Venturelli 2011)	MD 1.98 (-1.57, 5.53), I^2 91%	292	Very Low[b,c,d]
MMSE – moderate/severe dementia	1 RCT (Pedroso 2017)	MD 0.40 (-4.57, 5.37), I^2 n.a.	36	Very Low[b,c,d]
Functional abilities – moderate dementia	3 RCT (Bossers 2016, Cancela 2016, Venturelli 2011)	SMD 0.70 (-0.03, 1.43), I^2 82%	280	Very Low[b,c,d]
Quality of life	1 RCT (Yang 2015)	MD 2.16 (-0.44, 4.76), I^2 n.a.	50	Low[b]
Non-aerobic exercise				
ACE-R – mild dementia	1 RCT (Papatsimpas 2023)	**MD 11.44 (7.50, 15.38), I^2 n.a.**	114	Low[b,c]
MMSE – mild/moderate dementia	1 RCT (Todri 2019)	**MD 2.26 (0.42, 4.10), I^2 n.a.**	45	Very Low[b,c]
MMSE – moderate dementia	2 RCT (Christofoletti 2008, Telenius 2015)	**MD 1.34 (0.12, 2.80), I^2 47%**	190	Very Low[a,c]
IADL – mild dementia	1 RCT (Papatsimpas 2023)	**MD 1.67 (0.77, 2.57), I^2 n.a.**	114	Very Low[a,c]
Functional abilities – moderate dementia	2 RCT (Littbrand 2009, Telenius 2015)	**SMD 0.29 (0.04, 0.54), I^2 0%**	258	Moderate
Quality of life – mild/moderate dementia	1 RCT (Todri 2019)	MD 3.72 (0.44, 7.00), I^2 n.a.	90	Low[b,c]
Quality of life – moderate dementia	1 RCT (Telenius 2015)	MD -0.90 (-2.99, 1.19), I^2 n.a.	163	Very Low[b,c]
Aerobic/non-aerobic combined exercise				
MMSE – mild dementia	2 RCT (Hoffman 2015, Vreugdenhil 2012)	MD 0.92 (-1.31, 3.15), I^2 38%	230	Moderate[b]
ACE-R – mild dementia	1 RCT (Papatsimpas 2023)	**MD 11.49 (8.01, 14.91), I^2 n.a.**	114	Low[b,c]
MMSE – demenza Moderate	2 RCT (Pitkälä 2013, Shaw 2021)	MD 0.55 (-0.74, 1.85), I^2 0%	194	Low[b]
MoCA – mild dementia	1 RCT (Parvin 2020)	**MD 6.40 (4.07, 8.73), I^2 n.a.**	32	Moderate
Functional abilities – mild dementia	3 RCT (Hoffman 2015, Vreugdenhil 2012, Papatsimpas 2023)	SMD 0.34 (-0.18, 0.85), I^2 79%	344	Very Low[a,b,d]
Functional abilities – mild/moderate dementia	1 RCT (Cezar 2021)	MD -8.70 (-25.18, 7.78), I^2 n.a.	35	Low[b,c]
Functional abilities – moderate dementia	4 RCT (Bossers 2016, Pitkälä 2013, Shaw 2021, Toots 2016)	**SMD 0.30 (0.11, 0.49), I^2 0%**	455	Moderate
Functional abilities – severe dementia	1 RCT (Rolland 2007)	SMD 0.40 (-0.16, 0.96), I^2 n.a.	110	Moderate
Quality of life – mild dementia	2 RCT (Hoffman 2015, Suttanon 2013)	SMD 0.02 (-0.24, 0.29), I^2 0%	219	Low[b]

Quality of life – moderate dementia	2 RCT (Shaw 2021, Steinberg 2009)	SMD -0.14 (-0.75, 0.47), I^2 30%	61	Low[b]
Tai Chi				
MMSE –mild/moderate dementia	1 RCT (Huang 2019)	MD 1.77. (-1.82, 5.36), I^2 n.a.	74	Very Low[b,c]
MMSE – moderate dementia	1 RCT (Cheng 2014)	**MD 3.70 (1.40, 6.00), I^2 n.a.**	74	Very Low[b,c]
MoCA	1 RCT (Huang 2019)	MD 2.93 (-0.26, 6.12), I^2 n.a.	74	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Light therapy with high intensity bright light vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
MMSE	2 RCT (Burns 2009, Graf 2001)	MD 0.68 (-2.46, 3.81), I^2 0%	64	Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Multimodal interventions vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Multidisciplinary program that included physiotherapy, occupational therapy and physical education				
MMSE – moderate dementia	1 RCT (Christofoletti 2008)	**MD 1.30 (0.19, 2.41), I^2 n.a.**	27	Moderate
Intervention including Tai Chi, Cognitive Behavioral Therapy (CBT) and participation in a support group				
MMSE – mild dementia	1 RCT (Burgener 2008)	MD 0.90 (-2.27, 4.07), I^2 n.a.	43	Very Low[b,c]
Intervention including motor stimulation, training of activities of daily living and cognitive stimulation				
ADL	1 RCT (Luttenberger 2012)	MD 0.80 (-5.35, 6.95), I^2 n.a.	119	Very Low[b,c]
Cognitive stimulation intervention in combination with Tai Chi				
MMSE – mild/moderate dementia	1 RCT (Young 2020)	MD 3.16 (2.35, 3.97), I^2 n.a.	80	Low[b,c]
Quality of life – mild/moderate dementia	1 RCT (Young 2020)	MD -0.15 (-0.59, 0.28), I^2 n.a.	80	Low[b]
Cognitive training and coping strategies administered both in groups and individually				
MMSE	1 RCT (Koltai 2001)	MD -0.96 (-3.21, 1.29), I^2 n.a.	22	Low[b]
Physical exercise combined with music listening and personalized support based on the preferences and habits of individual participants, provided by specifically trained multidisciplinary staff				
BADL	1 RCT (Gebhard 2022)	MD -1.18 (-2.98, 0.62), I^2 n.a.	50	Very Low[b,c]
QUALIDEM	1 RCT (Gebhard 2022)	MD -4.19 (-15.11, 6.73), I^2 n.a.	50	Low[b]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Nutritional interventions vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Folic acid				
MMSE	1 RCT (Shinto 2014)	MD -0.40 (-1.06, 0.26), I^2 n.a.	26	Low[b]
ADL	2 RCT (Chen 2016, Connelly 2008)	SMD 0.28 (-0.38, 0.95), I^2 70%	162	Very Low[a,b,c]
Ketogenic diet				
MMSE	1 RCT (Phillips 2021)	**MD 3.13 (1.14, 5.12), I^2 n.a.**	52	Low[c]
Quality of life	1 RCT (Phillips 2021)	**MD 3.37 (0.43, 6.31), I^2 n.a.**	52	Very Low[c]
Different doses of ginseng extract (1,5 g, 3 g, 4,5 g, 9 g)				
MMSE	3 RCT (Heo 2008, Heo 2012, Lee 2008)	MD 0.31 (-0.52, 1.15), I^2 90%	226	Very Low[b,c,d]
Ginkgo biloba				
ADL	6 RCT (Herrschaft 2012, Ihl 2012, Kanowski 2003, Napryenko 2007, Nikolova 2013, van Dongen 2000)	**SMD 0.41 (0.11, 0.71), I^2 90%**	1.922	Very Low[d]
Quality of life	2 RCT (Herrschaft 2012, Ihl 2012)	**SMD 0.24 (0.11, 0.38), I^2 0%**	806	Moderate
Omega-3				
MMSE	3 RCT (Freund-Levi 2006, Quinn 2010, Shinto 2014)	MD 0.17 (-0.38, 0.72), I^2 0%	604	Low[b]
ADL	2 RCT (Quinn 2010, Shinto 2014)	SMD -0.05 (-0.48, 0.39), I^2 38%	426	Low[b]
Selenium				
MMSE	1 RCT (Tamtaji 2019)	**MD 0.70 (0.07, 1.33), I^2 n.a.**	52	Low
Sodium oligomannate				
ADAS-Cog	3 RCT (Wang 2020, Xiao 2021, Zhang 2022)	MD -2.77 (-6.80, 1.26), I^2 97%	1.108	Very Low[b,c,d]
ADL	3 RCT (Wang 2020, Xiao 2021, Zhang 2022)	SMD 0.13 (-0.04, 0.30), I^2 12%	1.108	Very Low[b]
Uperzina A				
MMSE	7 RCT (Dong 2002, Liu 1995, Rafil 2011, Xu 1997, Yang 2003, Zhang 2002, Zhou 2004)	**MD 2.80 (1.61, 3.99), I^2 76%**	648	Very Low[d]
ADL	7 RCT (Dong 2002, Liu 1995, Rafil 2011, Xu 1997, Yang 2003, Zhang 2002, Zhou 2004)	**SMD 0.54 (0.23, 0.85), I^2 65%**	648	Low[a]
Other supplements (based on EPA, DHA, phospholipids, choline, uridine monophosphate, vitamin E, vitamin C, selenium, vitamin B12, vitamin B6, folic acid)				
MMSE	1 RCT (Scheltens 2010)	MD -0.30 (-1.46, 0.86), I^2 n.a.	210	Low[b]
ADAS-Cog	1 RCT (Shah 2013)	MD 0.52 (-2.01, 3.05), I^2 n.a.	515	Very Low[b,c]
NTB (*z-scores*)	1 RCT (Scheltens 2012)	MD 0.09 (-0.03, 0.21), I^2 n.a.	206	Very Low[b,c]
ADCS-ADL	2 RCT (Scheltens 2010, Shah 2013)	MD -0.25 (-2.91, 2.42), I^2 0%	739	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Psychological interventions vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
***Journeying through dementia* aimed at promoting the autonomy and independence of people in the early stages of the disease**				
IADL	1 RCT (Mountain 2022)	MD 0.10 (-0.30, 0.40) I^2 n.a.	371	Moderate[b]
SMAS*	1 RCT (Mountain 2022)	MD 1.50 (-2.30, 5.30), I^2 n.a.	347	Moderate[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations; * Self-Management Ability Scale				

Cognititve interventions vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Cognitive rehabilitation (individual)				
MMSE	1 RCT (Brueggen 2017)	MD 0.87 (-0.96, 2.70), I^2 n.a.	16	Low[b]
ADL	4 RCT (Amieva 2016, Clare 2010, Clare 2019, Kim 2015)	SMD 0.52 (0.04, 1.00), I^2 86%	728	Low[b,d]
Functional abilities	2 RCT (Brueggen 2017, Clarkson 2021)	SMD -0.15 (-0.89, 0.59), I^2 59%	484	Very Low[a,b,c]
Quality of life	5 RCT (Amieva 2016, Brueggen 2017, Clare 2010, Clare 2019, Kim 2015)	SMD 0.22 (-0.08, 0.53), I^2 62%	789	Very Low[a,b]
Cognitive stimulation (group)				
MMSE – mild dementia	10 RCT (Baldelli 1993, Baldelli 2002, Bottino 2005, Breuil 1994, Buschert 2011, Chapman 2004, Cove 2014, Juárez-Cedillo 2020, Requena 2004, Requena 2006)	**MD 2.61 (1.45, 3.77), I^2 42%**	408	Moderate[a]
MMSE – mild/moderate dementia	2 RCT (López 2020, Young 2018)	**MD 2.24 (0.01, 4.46), I^2 40%**	121	Very Low[a,c]
MMSE – moderate dementia	9 RCT (Alves 2014, Capotosto 2017, Coen 2011, Kim 2016, Mapelli 2013, Orrell 2014, Spector 2001, Spector 2003, Yamanaka 2013)	**MD 1.31 (0.59, 2.04), I^2 21%**	639	Moderate
ADAS-Cog – mild/moderate dementia	2 RCT (Alvares-Pereira 2020, López 2020)	**MD -2.76 (-4.70, -0.83), I^2 0%**	125	Moderate
ADAS-Cog – mild dementia	1 RCT (Juárez-Cedillo 2020)	MD -4.21 (-10.26, 1.84), I^2 n.a.	50	Low[b,c]
ADAS-Cog	1 RCT (Bhowmik 2023)	MD -5.89 (-11.01, -0.77), I^2 n.a.	57	Very Low[a,c]
MoCA	1 RCT (Bhowmik 2023)	MD 3.59 (0.72, 6.46), I^2 n.a.	57	Very Low[a,c]
Functional abilities – mild dementia	4 RCT (Baldelli 1993, Baldelli 2002, Bottino 2005, Ferrario 1991)	SMD 0.19 (-0.20, 0.57), I^2 0%	142	Low[b]
Functional abilities – moderate dementia	2 RCT (Capotosto 2017, Orrell 2014)	SMD 0.07 (-0.17, 0.31), I^2 0%	275	Low[b]
Quality of life – moderate dementia	7 RCT (Alves 2014, Capotosto 2017, Coen 2011, Kim 2016, Orrell 2014, Spector 2003, Yamanaka 2013)	**SMD 0.25 (0.09, 0.41), I^2 0%**	595	Moderate

Quality of life – mild dementia	3 RCT (Buschert 2011, Chapman 2004, Cove 2014)	SMD 0.09 (-0.29, 0.46), I^2 0%	111	Low[b]
Quality of life – mild/moderate dementia	1 RCT (Alvares-Pereira 2020)	MD 0.47 (-1.11, 2.05), I^2 n.a.	105	Low[b]
Cognitive stimulation (individual)				
MMSE – mild/moderate dementia	2 RCT (Justo-Henriques 2023, Oliveira 2021)	**MD 4.96 (2.61, 7.30), I^2 0%**	63	Moderate
MoCA	1 RCT (Justo-Henriques 2023)	**MD 7.01 (3.91, 10.11), I^2 n.a.**	46	Moderate
MMSE – mild dementia	4 RCT (Camargo 2015, Onder 2005, Orgeta 2015, Tsantali 2017)	MD 0.38 (-0.66, 1.41), I^2 66%	457	Very Low[a,b,c,]
Functional abilities – mild dementia	2 RCT (Onder 2005, Orgeta 2015)	SMD 0.15 (-0.04, 0.35), I^2 0%	406	Moderate[b]
Quality of life – mild dementia	1 RCT (Orgeta 2015)	MD -0.02 (-1.04, 1.00), I^2 n.a.	272	Moderateb[b]
Quality of life – mild/moderate dementia	1 RCT (Justo-Henriques 2023)	MD 4.14 (-0.07, 8.35), I^2 n.a.	46	Low[b,c]
Cognitive training (group)				
MMSE– mild dementia	2 RCT (Bergamaschi 2013, Trebbastoni 2018)	**MD 5.18 (3.04, 7.31), I^2 69%**	172	Very Low[a,c]
MMSE – moderate dementia	1 RCT (Tanaka 2021)	MD 0.00 (-5.41, 5.41), I^2 n.a.	25	Very Low[b,c]
Quality of life – moderate dementia	1 RCT (Tanaka 2021)	MD 3.40 (-1.32, 8.12), I^2 n.a.	25	Very Low[b,c]
ADL – mild dementia	3 RCT (Amieva 2016, Bergamaschi 2013, Cahn-Weiner 2003)	SMD 0.13 (-0.34, 0.60), I^2 57%	299	Very Low[a,b,c]
Cognitive training (individual)				
MMSE – mild dementia	9 RCT (Cavallo 2019, Davis 2001, de Luca 2016, Galante 2007, Heiss 1994, Kang 2019, Shyu 2022, Tsantali 2017, Yang 2017)	MD 2.43 (0.86, 4.00), I^2 75%	311	Very Low[b,c,d]
MMSE – moderate dementia	2 RCT (de Vreese 1999, Lee 2013a)	MD -0.80 (-3.75, 2.16), I^2 0%	31	Very Low[b,c]
ADAS-Cog	1 RCT (Kallio 2018)	MD -0.90 (-2.36, 0.56), I^2 n.a.	147	Low[b]
ADL – mild dementia	2 RCT (Galante 2007, Loewenstein 2004)	SMD 0.02 (-0.22, 0.25), I^2 0%	277	Very Low[b]
ADL – moderate dementia	2 RCT (de Vreese 1999, Lee 2013a)	SMD 0.42 (-0.29, 1.14), I^2 0%	31	Low[b]
Quality of life – mild/moderate dementia	1 RCT (Kallio 2018)	MD 0.00 (-0.03, 0.03), I^2 n.a.	147	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Music therapy vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Receptive music therapy (including listening to personalized music)				
MMSE – mild/moderate dementia	2 RCT (Guétin 2009, Särkämö 2016)	MD 1.66 (-0.42, 3.74), I^2 0%	70	Very Low[b,c]
Quality of life – mild/moderate dementia	1 RCT (Särkämö 2016)	MD 3.60 (1.18, 6.02), I^2 n.a.	51	Low[b,c]
Quality of life – moderate/severe dementia	1 RCT (Raglio 2015)	MD 2.30 (-1.64, 6.24), I^2 n.a.	80	Low[b,c]
Active music therapy (including playing instruments and singing)				
MMSE – mild/moderate dementia	2 RCT (Särkämö 2016, Wang 2018)	MD 0.45 (-0.50, 1.39), I^2 0%	94	Very Low[b,c]
MMSE – moderate/severe dementia	2 RCT (Chu 2014, Zhang 2020b)	**MD 2.19 (0.48, 3.89), I^2 0%**	173	Low[c]
MMSE – demenza Moderate	3 RCT (Ceccato 2012, Hong 2011, Lyu 2018)	MD 1.29 (-1.62, 4.21), I^2 88%	272	Very Low[b,c,d]
MoCA – mild dementia	1 RCT (Wang 2018)	MD 0.70 (-0.67, 2.07), I^2 n.a.	60	Low[b,c]
Quality of life – mild/moderate dementia e	1 RCT (Särkämö 2016)	MD 0.80 (-1.83, 3.43), I^2 n.a.	46	Low[b,c]
Quality of life – moderate/severe dementia	1 RCT (Raglio 2015)	MD 2.20 (-1.32, 5.72), I^2 n.a.	80	Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Psychotherapy vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
MMSE – mild/mdoerate dementia	2 RCT (Burns 2005, Marshall 2015)	MD -0.82 (-2.47, 0.84), I^2 0%	92	Moderate[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Robot therapy vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Utilizzo di una bambola elettronica interattiva che risponde a diversi stimoli				
MoCA – moderate dementia	1 RCT (Chen 2020)	MD -0.39 (-1.73, 0.94), I^2 0%	103	Moderate[b]
ADL	1 RCT (Chen 2020)	MD -1.90 (-17.02, 13.22), I^2 n.a.	103	Low[b,c]
Quality of life	1 RCT (Chen 2020)	MD 1.30 (-1.94, 4.54), I^2 n.a.	103	Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Transcranial Stimulation vs trattamento sham				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Repetitive Transcranial Magnetic Stimulation				
MMSE – mild/moderate dementia	9 RCT (Ahmed 2012, Cotelli 2011, Jia 2021, Khedr 2020, Koch 2022, Lee 2016, Rabey 2013, Yao 2022, Zhao 2017)	**MD 1.76 (0.72, 2.79), I^2 59%**	295	Very Low[a,c]
MMSE – severe dementia	1 RCT (Ahmed 2012)	MD 0.80 (-1.13, 2.73), I^2 n.a.	9	Low[b,c]
ADAS-Cog – mild/moderate dementia	3 RCT (Koch 2022, Yao 2022, Zhao 2017)	MD -2.41 (-5.73, 0.91), I^2 0%	107	Very Low[b,c,d]
MoCA – mild/moderate dementia	3 RCT (Koch 2022, Yao 2022, Zhao 2017)	MD 1.59 (-1.04, 4.22), I^2 0%	90	Low[b,c]
ADL – mild/moderate dementia	3 RCT (Koch 2022, Khedr 2020, Cotelli 2011)	SMD 0.19 (-0.19, 0.57), I^2 0%	107	Low[b,c]
Repetitive Transcranial Magnetic Stimulation - intermittent theta burst protocol				
MMSE	1 RCT (Wu 2022)	MD 2.41 (-1.59, 6.41), I^2 n.a.	47	Very Low[b,c]
MoCA	1 RCT (Wu 2022)	MD 2.88 (-1.70, 7.46), I^2 n.a.	47	Very Low[b,c]
ADL	1 RCT (Wu 2022)	MD -1.02 (-6.93, 4.89), I^2 n.a.	47	Very Low[b,c]
Transcranial Direct-Current Stimulation				
MMSE	2 RCT (Cotelli 2014, Im 2019)	MD 1.72, (-2.32, 5.76), I^2 0%	28	Very Low[b,c]
IADL	1 RCT (Cotelli 2014)	MD 0.00. (-2.80, 2.80), I^2 n.a.	9	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Pet therapy vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
MMSE	2 RCT (Quintavalla 2021, Vegue Parra 2021)	MD 2.07 (-2.22, 6.37), I^2 51%	374	Very Low[a,b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Doll therapy vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
MMSE – mild/moderate dementia	1 RCT (Yilmaz 2021)	MD -0.40 (-1.87, 2.67), I^2 n.a.	29	Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Reminescence therapy vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Reminescence therapy (group)				
MMSE – mild dementia	1 RCT (Wu 2016)	MD 0.50 (-0.10, 1.10), I^2 n.a.	103	Low[b]
MMSE – moderate dementia	5 RCT (Lök 2019, Ito 2007, Tadaka 2007, Tanaka 2017, Wang 2007)	**MD 2.33 (1.69, 2.97), I^2 0%**	278	Moderate
MMSE – mild/moderate dementia	1 RCT (Deponte 2007)	MD 3.30 (-1.03, 7.63), I^2 n.a.	18	Low[b,c]
Functional abilities – mild/moderate dementia	2 RCT (Charlesworth 2016, Woods 2012, Woods 2016)	SMD -0.04 (-0.28, 0.20), I^2 56%	684	Low[b]
Functional abilities – moderate/severe dementia	1 RCT (Deponte 2007)	MD -2.40. (-6.93, 2.13), I^2 n.a.	18	Very Low[b,c]
Quality of life – demenza lieve	1 RCT (Amieva 2016)	MD 0.11. (-1.13, 1.35), I^2 n.a.	227	Moderate[b]
Quality of life – mild/moderate dementia	2 RCT (Charlesworth 2016, Woods 2012, Woods 2016)	SMD 0.07 (-0.09, 0.23), I^2 0%	639	Moderate[b]
Reminescence therapy (individual)				
MMSE – moderate dementia	2 RCT (Tanaka 2017, Van Bogaert 2013)	**MD 1.68 (0.43, 2.94), I^2 18%**	69	Low
MMSE – mild dementia	2 RCT (Lopes 2016, Van Bogaert 2013)	MD 1.18 (-1.99, 4.36), I^2 72%	81	Very Low[a,b,c]
Quality of life – mild/moderate dementia	1 RCT (Subramaniam 2014)	**MD 7.00 (2.13, 11.87), I^2 n.a.**	23	Moderate
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Occupational therapy vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Occupational theapy				
MMSE	2 RCT (Kim 2020, Wenborn 2021)	MD 0.68 (-0.37, 1.73), I^2 4%	503	Low[b]
ADL	3 RCT (Gitlin 2010, Voigt-Radloff 2011, Wenborn 2021)	SMD 0.09 (-0.14, 0.31), I^2 53%	781	Low[b]
Quality of life	6 RCT (Gitlin 2008, Gitlin 2010, Graff 2007, Kim 2020, Voigt-Radloff 2011, Wenborn 2021)	**SMD 0.39 (0.04, 0.73), I^2 83%**	994	Low[c]
Tailored Activity Program				
ADL e IADL*	1 RCT (Gitlin 2018)	**MD -0.80 (-1.41, -0.20), I^2 n.a.**	160	Low
ADL*	1 RCT (Gitlin 2018)	**MD -0.61 (-1.08, -0.14), I^2 n.a.**	160	Low
IADL*	1 RCT (Gitlin 2018)	**MD -0.25 (-0.54, -0.04), I^2 n.a.**	160	Low
ADL e IADL	1 RCT (Gitlin 2018)	**MD 4.09 (1.06, 7.13), I^2 n.a.**	160	Very Low

ADL	1 RCT (Gitlin 2018)	**MD 2.37 (0.32, 4.42), I^2 n.a.**	160	Very Low
IADL	1 RCT (Gitlin 2018)	**MD 1.57 (0.05, 3.08), I^2 n.a.**	160	Very Low
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations; * needing assistance				

Review question 20e (New RQ). What are the most effective non-pharmacological interventions for supporting cognitive functioning, functional ability and wellbeing in people with Mild Cognitive Impairment?

Acupuncture vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
MoCA	3 RCT (Choi 2021, Sun 2021, Tan 2017)	**MD 2.73. (0.60, 4.87), I^2 85%**	147	Very Low[c,d]
MMSE	2 RCT (Sun 2021, Tan 2017)	**MD 2.72 (2.06, 3.39), I^2 0%**	108	Low
ADAS-Cog	2 RCT (Choi 2021, Tan 2017)	**MD -1.57 (-2.42, -0.72), I^2 0%**	71	Low
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Aromatherapy vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
MMSE	1 RCT (Kohanpour 2017)	**MD 1.60 (0.35, 2.85), I^2 n.a.**	20	Very Low[c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Art therapy vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
MMSE	1 RCT (Lin 2022)	**MD 1.72 (0.58, 2.87), I^2 n.a.**	90	Low[c]
MoCA	1 RCT (Lin 2022)	**MD 1.88 (0.42, 3.34), I^2 n.a.**	90	Low[c]
RAVL - recognition	1 RCT (Lin 2022)	**MD 2.94 (1.41, 4.48), I^2 n.a.**	90	Moderate
RAVL – immediate recall	1 RCT (Lin 2022)	**MD 4.23 (1.67, 6.80), I^2 n.a.**	90	Moderate
RAVL – delayed recall	1 RCT (Mahendran 2018)	**MD 1.58 (0.24, 2.92,) I^2 n.a.**	44	Moderate
RAVL – memory (z-scores)	1 RCT (Mahendran 2018)	**MD 0.31 (0.03, 0.59), I^2 n.a.**	44	Moderate
RAVL – recognition (z-scores)	1 RCT (Mahendran 2018)	MD 0.32 (-0.25, 0.89), I^2 n.a.	44	Low[b]
RAVL – delayed recall (z-scores)	1 RCT (Mahendran 2018)	MD 0.14 (-0.12, 0.40), I^2 n.a.	44	Low[b]
Depressive symptoms – GDS	2 RCT (Lin 2022, Mahendran 2018)	MD -1.70 (-4.11, 0.72), I^2 64%	134	Low[a,b]
Anxiety	2 RCT (Lin 2022, Mahendran 2018)	SMD -0.37 (-0.96, 0.21), I^2 62%	134	Low[a,b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Physical excercise vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Dance				
MoCA	4 RCT (Chang 2021, Dominguez 2018, Qi 2019, Zhu 2018)	**MD 0.99 (0.27, 1.71), I^2 26%**	371	Moderate
ADAS-Cog	1 RCT (Dominguez 2018)	**MD -2.30 (-4.56, -0.04), I^2n.a.**	171	Low
MMSE	3 RCT (Doi 2017, Lazarou 2017, Qi 2019)	MD 0.48 (-1.09, 2.05), I^2 86%	295	Very Low[b,c,d]
WMS-R LM*	2 RCT (Qi 2019, Zhu 2018)	**MD 3.84 (1.42, 6.25), I^2 31%**	92	Low[c]
TMT-A	3 RCT (Doi 2017, Qi 2019, Zhu 2018)	MD -5,83 (-15.34, 3.68), I^2 51%	225	Very Low[a,b,c]
TMT-B	3 RCT (Doi 2017, Qi 2019, Zhu 2018)	MD -8.29 (-23.75, 7.17), I^2 35%	225	Low[b,c]
Depressive symptoms – GDS	3 RCT (Chang 2021, Dominguez 2018, Zhu 2018)	**MD -0.81 (-1.32, -0.29), I^2 0%**	340	Moderate
IADL	1 RCT (Dominguez 2018)	MD -0.50 (-1.62, 0.62), I^2n.a.	171	Low[b]
Aerobic exercise				
MMSE	3 RCT (Avenali 2021, Bademli 2019, Kohanpour 2017)	MD 2.36 (0.03, 4.69), I^2 86%	114	Very Low[b,c,d]
MoCA	2 RCT (Avenali 2021, Tao 2019)	MD 0.10 (-1.04, 1.24), I^2 11%	71	Low[b]
Digit Span Forward	1 RCT (Combourieu Donnezan 2018)	MD 0.41 (-0.49, 1.31), I^2 n.a.	32	Low[b]
Digit Span Backward	1 RCT (Combourieu Donnezan 2018)	MD 0.57 (-0.35, 1.49), I^2 n.a.	32	Low[b]
IADL	1 RCT (Law 2022)	MD 0.83 (-1.90, 3.56), I^2 n.a.	73	Low[b,c]
Non-aerobic exercise				
MMSE	1 RCT (Wei 2014)	**MD 1.53 (0.61, 2.45), I^2 n.a.**	60	Moderate
ADAS-Cog	1 RCT (Lü 2016)	**MD -4.32 (-6.95, -1.69), I^2 n.a.**	45	Moderate
MoCA	2 RCT (Hong 2018, Tao 2019)	MD 0.97 (-0.17, 2.11), I^2 0%	62	Low[b]
Digit Span Forward	2 RCT (Hong 2018, Lü 2016)	MD -0.02 (-0.61, 0.58), I^2 0%	67	Low[b]
Digit Span Backward	2 RCT (Hong 2018, Lü 2016)	MD 0.64 (-0.52, 1.81), I^2 65%	67	Very Low[a,b]
ADL	1 RCT (Wei 2014)	**MD -1.27 (-2.25, -0.29), I^2 n.a.**	73	Moderate
Aerobic/non-aerobic combined exercise				
MMSE	2 RCT (de Oliveira Silva 2019, Suzuki 2013)	MD 0.41 (-0.58, 1.40), I^2 0%	111	Low[b]
ADAS-Cog	1 RCT (Suzuki 2013)	MD -0.60 (-1.43, 0.23), I^2 n.a.	92	Low[b]
IADL	1 RCT (Fonte 2019)	MD 21.60 (3.07, 40.13), I^2 n.a.	57	Low[b,c]
Executive functions	1 RCT (Fonte 2019)	MD 0.00 (-2.19, 2.19), I^2 n.a.	57	Low[b]
Tai Chi				
MoCA	1 RCT (Liu 2022)	MD 1.00 (-1.78, 3.78), I^2 n.a.	34	Low[b,c]
TMT-B-A	1 RCT (Sungkarat 2018)	**MD -0.40 (-0.57, -0.23), I^2 n.a.**	66	Low
Digit Span	1 RCT (Sungkarat 2018)	MD 0.04 (-0.04, 0.12), I^2 n.a.	66	Low[b]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations; * Wechsler Memory Scale-revised logical memory

Games and videogames vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Games and board games				
MoCA	2 RCT (Xue 2021, Zhang 2020b)	MD 0.97 (-0.73, 2.67), I^2 73%	141	Low[a,b,c]
Depressive symtoms – GDS	1 RCT (Xue 2021)	**MD -1.36 (-1.91, -0.81), I^2 n.a.**	72	Moderate
Videogames				
MoCA	3 RCT (Liu 2022, Park 2020, Schwenk 2016)	MD 1.10 (-1.37, 3.58), I^2 64%	88	Very Low[a,b,c]
MMSE	1 RCT (Thapa 2020)	MD 0.80 (-0.83, 2.43), I^2 n.a.	68	Low[b,c]
TMT-A	2 RCT (Park 2020, Schwenk 2016)	**MD -7.05 (-10.35, -3.76), I^2 0%**	55	Moderate
TMT-B	2 RCT (Park 2020, Schwenk 2016)	MD -6.06 (-14.57, 2.46), I^2 0%	55	Low[b,c]
Digit Span Forward	1 RCT (Park 2020)	MD 0.20 (-0.35, 0.75), I^2 n.a.	35	Low[b]
Digit Span Backward	1 RCT (Park 2020)	**MD 1.10 (0.39, 1.81), I^2 n.a.**	35	Moderate
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Cognitive interventions vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Multimodal cognitive interventions delivered at home				
m-ADAS-Cog	1 RCT (Jeong 2016)	**MD -1.70 (-3.17, -0.23), I^2 n.a.**	153	Moderate
CDR-SB	1 RCT (Jeong 2016)	**MD -0.24 (-0.43, -0.05), I^2 n.a.**	153	Moderate
MMSE	1 RCT (Jeong 2016)	MD 0.40 (-0.20, 1.00), I^2 n.a.	153	Low[b]
Depressive symptoms - GDS	1 RCT (Jeong 2016)	MD -0.40 (-1.22, 0.42), I^2 n.a.	153	Low[b]
BADL	1 RCT (Jeong 2016)	MD 0.10 (-0.19, 0.39), I^2 n.a.	153	Low[b]
Multimodal cognitive interventions delivered as group sessions in local facilities				
MMSE	2 RCT (Jeong 2016, Rojas 2013)	MD 0.69 (-1.00, 2.38), I^2 72%	193	Very Low[a,b,c]
mADAS-Cog	1 RCT (Jeong 2016)	MD -1.50 (-3.02, 0.02), I^2 n.a.	147	Low[b]
CDR-SB	1 RCT (Jeong 2016)	MD -0.09 (-0.29, 0.11), I^2 n.a.	147	Low[b]
CDR	1 RCT (Rojas 2013)	MD -0.06 (-0.16, 0.04), I^2 n.a.	46	Low[b]
CVLT	1 RCT (Kurtz 2009)	MD 1.40 (-2.73, 5.53), I^2 n.a.	30	Low[b]
BADL	2 RCT (Jeong 2016, Kurz 2009)	MD -0.03 (-0.35, 0.29), I^2 0%	177	Low[b]
Depressive symptoms - GDS	2 RCT (Jeong 2016, Kurz 2009)	SMD -0.38 (-1.12, 0.37), I^2 80%	177	Very Low[b,c,d]
Memory trianing – visual imagery				
Depressive symptoms - GDS	1 RCT (Lajeunesse 2022)	MD -0.85 (-6.26, 4.56), I^2 n.a.	24	Low[b,c]
CAPM - frequency	1 RCT (Lajeunesse 2022)	MD -2.90 (-18.64, 12.84), I^2 n.a.	24	Low[b]
CAPM - impact	1 RCT (Lajeunesse 2022)	MD -10.85 (-33.66, 11.96), I^2 n.a.	24	Low[b]

WL immediate	1 RCT (Konsztowicz 2013)	MD -0.42 (-2.33, 1.49), I^2 n.a.	12	Low[b]
WL delayed	1 RCT (Konsztowicz 2013)	MD -0.25 (-2.79, 2.29), I^2 n.a.	12	Low[b]
MMQ	1 RCT (Konsztowicz 2013)	MD 4.10 (-9.43, 17.63), I^2 n.a.	12	Low[b]
Memory trianing – based on memory aids and supports				
MMSE	1 RCT (Greenaway 2013)	MD -0.40 (-2.17, 1.37), I^2 n.a.	40	Low[b,c]
Depressive symptoms – CES-D	1 RCT (Greenaway 2013)	MD 0.30 (-6.45, 7.05), I^2 n.a.	40	Low[b,c]
Memory trianing – compensatory intervention				
WL immediate	1 RCT (Konsztowicz 2013)	**MD -0.94 (-1.85, -0.03), I^2 n.a.**	11	Moderate
WL delayed	1 RCT (Konsztowicz 2013)	MD 1.67 (-0.56, 3.90), I^2 n.a.	11	Low[b]
MMQ	1 RCT (Konsztowicz 2013)	MD -1.00 (-16.90, 14.90), I^2 n.a.	11	Low[b]
Cognitive rehabilitation				
MMSE – computer based	1 RCT (Bernini 2021)	MD -0.18 (-2.31, 1.95), I^2 n.a.	36	Very Low[b,c]
MMSE – pen and paper	1 RCT (Bernini 2021)	MD -0.29 (-2.35, 1.77), I^2 n.a.	30	Very Low[b,c]
MoCA – computer based	1 RCT (Bernini 2021)	MD 2.42 (-0.23, 5.07), I^2 n.a.	36	Very Low[b,c]
MoCA – pen and paper	1 RCT (Bernini 2021)	MD 0.63 (-2.56, 3.82), I^2 n.a.	30	Very Low[b,c]
Executive functions – computer based	1 RCT (Bernini 2021)	MD 0,25 (-0.49, 0.99), I^2 n.a.	36	Low[b]
Executive functions – pen and paper	1 RCT (Bernini 2021)	MD 0.40 (-0.31, 1.11), I^2 n.a.	30	Low[b]
FAB – pen and paper	1 RCT (Fonte 2019)	**MD 2.90 (0.90, 4.90), I^2 n.a.**	60	Moderate
RBMT – pen and paper	1 RCT (Fonte 2019)	**MD 25.40 (6.09, 44.71), I^2 n.a.**	60	Moderate
IADL – pen and paper	1 RCT (Fonte 2019)	**MD 30.00 (12.55, 47.45), I^2 n.a.**	60	Moderate
Cognitive training				
MMSE standardized	1 RCT (Li 2019)	**MD 0.73 (0.42, 1.04), I^2 n.a.**	141	Moderate
MMSE	3 RCT (Giuli 2016, Han 2017, Sun 2021)	MD 1.31 (-0.13, 2.76), I^2 77%	258	Very Low[b,c]
MoCA	2 RCT (Sukontapol 2018, Sun 2021)	MD 3.36 (-0.11, 6.83), I^2 93%	136	Very Low[b,c]
NCSE	1 RCT (Law 2019)	MD 0.10 (-8.65, 8.85), I^2 n.a.	29	Low[b]
RAVL	1 RCT (Li 2019)	**MD 0.40 (0.06, 0.74), I^2 n.a.**	141	Moderate
WLMT	1 RCT (Giuli 2016)	**MD 17.48 (16.22, 18.74), I^2 n.a.**	97	Moderate
Verbal Span Backward	1 RCT (Han 2017)	**MD 0.63 (0.17, 1.09), I^2 n.a.**	85	Moderate
Reasoning Matrix	1 RCT (Comborieu Donnezan 2018)	**MD 5.73 (0.45, 11.01), I^2 n.a.**	30	Moderate
CVVLT	1 RCT (Low 2019)	MD -1.56 (-6.07, 2.95), I^2 n.a.	29	Low[b]
Verbal Span Forward	1 RCT (Giuli 2016)	MD 0.35 (-0.10, 0.80), I^2 n.a.	97	Low[b]
Digit Span Forward	1 RCT (Comborieu Donnezan 2018)	MD 0.85 (-0.07, 1.77), I^2 n.a.	30	Low[b]
Digit Span Backward	1 RCT (Comborieu Donnezan 2018)	MD 0.64 (-0.21, 1.49), I^2 n.a.	30	Low[b]
Depressive symptoms – GDS	3 RCT (Giuli 2016, Han 2017, Sukontapol 2018)	MD -0.59 (-1.30, 0.12), I^2 0%	242	Low[b]
IADL	2 RCT (Giuli 2016, Law 2019)	MD 0.33 (-0.21, 0.87), I^2 0%	126	Low[b]
Rate of conversion from MCI to AD	1 RCT (Li 2019)	RR 0.57 (0.30, 1.08), I^2 n.a.	160	Low[b]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Multimodal interventions vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
MMSE	5 RCT (Jeong 2021, Li 2021a, Park 2019a, Shimada 2018, Suzuki 2012)	MD 1.00 (-0.01, 2.01), I^2 66%	517	Very Low[a,b,c]
ADAS-Cog	2 RCT (Jeong 2021, Park 2019a)	MD -2.04 (-4.14, 0.06), I^2 0%	63	Very Low[b,c]
MoCA	2 RCT (Li 2021a, Yang 2022)	**MD 3.96 (1.29, 6.62), I^2 95%**	196	Very Low[c,d]
WMS-R LM*	2 RCT (Shimada 2018, Suzuki 2012)	MD 0.52 (-1.00, 2.04), I^2 66%	358	Low[a,b,c]
Depressive symptoms – GDS	2 RCT (Park 2019a, Yang 2022)	MD -1.24 (-3.06, 0.58), I^2 91%	161	Very Low[c,d]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations; * Wechsler Memory Scale-revised logical memory				

Interventions included the combination of dietary interventions, physical and cognitive training, monitoring of metabolic and vascular risk indicators (Yang 2022); aerobic exercise, promotion of physical activity, cognitive, behavioural and multi-task exercises (Jeong 2021, Park 2019a); aerobic, strength, balance and coordination training, and sensory stimulation (Li 2021a); aerobic and muscle strength training, postural balance, and dual-task exercises (Shimada 2018, Suzuki 2012).

Nutritional interventions vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Polyunsaturated fatty acids				
Digit Span	4 RCT (Bai 2021*, Lee 2013b, Li 2021b, Mengelberg 2022)	**MD 0.98 (0.30, 1.66), I^2 34%**	270	Moderate
WAIS	2 RCT (Bai 2021*, Li 2021b)	MD 0.81 (-0.70, 2.32), I^2 0%	175	Low[b]
MMSE	1 RCT (Lee 2013b)	MD 0.10 (-1.83, 2.03), I^2 n.a.	35	Low[b]
RAVL immediate	1 RCT (Lee 2013b)	MD 3.00 (-3.26, 9.26), I^2 n.a.	35	Low[b,c]
RAVL delayed	1 RCT (Lee 2013b)	MD 2.50 (-0.23, 5.23), I^2 n.a.	35	Low[b]
Depressive symptoms	2 RCT (Lee 2013b, Mengelberg 2022)	SMD 0.00 (-0.40, 0.41), I^2 0%	95	Low[b]
RBANS	1 RCT (Mengelberg 2022)	MD 1.30 (-2.06, 4.66), I^2 n.a.	60	Low[b]
Ginkgo biloba				
Rate of conversion from MCI to AD	1 RCT (DeKosky 2008)	RR 1.14 (0.92, 1.41), I^2 n.a.	482	Low[b]
Ginseng				
RCFT immediate	1 RCT (Park 2019)	**MD 2.56 (0.23, 4.89), I^2 n.a.**	83	Low
RCFT delayed	1 RCT (Park 2019)	**MD 2.42 (0.21, 4.63), I^2 n.a.**	83	Low
SVLT immediate	1 RCT (Park 2019)	MD 0.14 (-2.08, 2.36), I^2 n.a.	83	Low[b]
SVLT delayed	1 RCT (Park 2019)	MD -0.04 (-2.19, 2.11), I^2 n.a.	83	Low[b]
MMSE	1 RCT (Park 2019)	MD 0.06 (-0.60, 0.72), I^2 n.a.	83	Low[b]
IADL	1 RCT (Park 2019)	MD -0.16 (-0.69, 0.37), I^2 n.a.	83	Low[b]
Resveratrol				
RAVL learning	1 RCT (Köbe 2007)	MD 0.40 (-8.16, 8.96), I^2 n.a.	40	Low[b]

RAVL memory	1 RCT (Köbe 2007)	MD -1.30 (-4.28, 1.68), I^2 n.a.	40	Low[b]
RAVL retention	1 RCT (Köbe 2007)	MD -0.90 (-2.78, 0.98), I^2 n.a.	40	Low[b]
RAVL recognition	1 RCT (Köbe 2007)	MD 0.20 (-4.47, 4.87), I^2 n.a.	40	Low[b]
Vitamin B				
WAIS	3 RCT (Bai 2021, Li 2021b, Ma 2017)	MD 2.52 (-2.45, 7.50), I^2 93%	355	Very Low[b,c,d]
Digit Span	3 RCT (Bai 2021, Li 2021b, Ma 2017)	MD 1.92 (-1.04, 4.89), I^2 98%	355	Very Low[b,c,d]
CDR-SB	1 RCT (Kwok 2020)	MD 0.14 (-0.13, 0.41), I^2 n.a.	241	Low[b]
Depressive symptoms - HDRS	1 RCT (Kwok 2020)	MD -0.32 (-1.08, 0.44), I^2 n.a.	241	Low[b]
Vitamin E				
MMSE	1 RCT (Petersen 2005)	MD 0.55 (-0.11, 1.21), I^2 n.a.	516	Low[b]
ADAS-Cog	1 RCT (Petersen 2005)	MD 0.85 (-0.32, 2.02), I^2 n.a.	516	Low[b]
CDR	1 RCT (Petersen 2005)	MD 0.03 (-0.38, 0.44), I^2 n.a.	516	Low[b]
ADCS-ADL-MCI	1 RCT (Petersen 2005)	MD 0.76 (-0.77, 2.29), I^2 n.a.	516	Low[b]
Other supplements – omega 3 and omega 6 fatty acids				
MMSE	1 RCT (Stravinou 2020)	MD 2.50 (-0.61, 5.61), I^2 n.a.	36	Very Low[b,c]
ACE-R	1 RCT (Stravinou 2020)	MD 8.20 (-2.33, 18.73), I^2 n.a.	36	Very Low[b,c]
Other supplements – astaxanthin and sesamin				
ADAS-Cog	1 RCT (Ito 2019)	MD -0.99 (-4.01, 2.0), I^2 n.a.	14	Very Low[b,c]
Memory	1 RCT (Ito 2019)	MD -8.80 (-27.95, 10.35), I^2 n.a.	14	Very Low[b,c]
Executive funtions	1 RCT (Ito 2019)	MD -7.10 (-19.74, 5.54), I^2 n.a.	14	Very Low[b,c]
Other supplements – EPA, DHA, phospholipids, choline, uridine monophosphate, vitamin E, vitamin C, selenium, vitamin B12, vitamin B6, folic acid				
CDR-SB	1 RCT (Soininen 2017)	**MD -0.56 (-0.95, -0.17), I^2 n.a.**	275	Low
NTB composite (z-scores)	1 RCT (Soininen 2017)	MD 0,08 (-0.04, 0.20), I^2 n.a.	275	Low[b]
NTB total (z-scores)	1 RCT (Soininen 2017)	MD 0.01 (-0.08, 0.10), I^2 n.a.	275	Low[b]
Other supplements – medium chain ketogenic triglycerides				
Episodic memory	1 RCT (Fortier 2019)	MD 0.28 (-0.47, 1.03), I^2 n.a.	39	Low[b]
Executive functions	1 RCT (Fortier 2019)	MD 0.01 (-0.74, 0.76), I^2 n.a.	39	Low[b]
Attention	1 RCT (Fortier 2019)	MD 0.20 (-0.42, 0.82), I^2 n.a.	39	Low[b]
Linguage	1 RCT (Fortier 2019)	MD 0.04 (-1.08, 1.16), I^2 n.a.	39	Low[b]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
* Study retracted due to issues with ethical approval and clinical trial registry.

Psychosocial intervention vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
MoCA	1 RCT (Young 2017)	MD 2.56 (1.07, 4.05), I^2n.a.	38	Low

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Music therapy vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Active music therapy – percussion instruments				
MMSE	1 RCT (Doi 2017)	**MD 0.82 (0.07, 1.57), I^2 n.a.**	134	Low
TMT-A	1 RCT (Doi 2017)	MD -1.38 (-3.13, 0.37), I^2 n.a.	134	Low[b]
TMT-B	1 RCT (Doi 2017)	MD -1.00 (-4.96, 2.96), I^2 n.a.	134	Low[b]
Receptive music therapy – music listening aimed at recalling memories and experiences				
Depressive symptoms – GDS	1 RCT (Mhendran 2018)	**MD -0.68 (-1.03, -0.33), I^2 n.a.**	46	Moderate
Ansia	1 RCT (Mhendran 2018)	**MD -0.70 (-1.1, -0.3), I^2 n.a.**	46	Moderate
RAVL memory domains (z-scores)	1 RCT (Mhendran 2018)	MD 0.12 (-0.16, 0.40), I^2 n.a.	46	Low[b]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Transcranial Stimulation vs usual care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Repetitive Transcranial Magnetic Stimulation				
MMSE	1 RCT (Roque Roque 2021)	**MD 1.40 (0.20, 2.60), I^2n.a.**	24	Low
MoCA	1 RCT (Roque Roque 2021)	MD 1.10 (-0.56, 2.76), I^2 n.a.	24	Low[b,c]
Depressive symptoms – GDS	1 RCT (Roque Roque 2021)	MD 0.30 (-2.11, 2.71), I^2 n.a.	24	Low[b,c]
RBMT	1 RCT (Drumond Marra 2015)	MD 1.47 (-0.01, 2.95), I^2 n.a.	34	Low[b]
Repetitive Transcranial Magnetic Stimulation - intermittent theta burst stimulation protocol				
RBANS	1 RCT (He 2021) *	**MD 12.00 (1.37, 22.63), I^2 n.a.**	40	Low
MoCA	1 RCT (He 2021) *	MD 2.70 (-0.12, 5.52), I^2 n.a.	40	Low[b]
Transcranial Direct-Current Stimulation				
MMSE	2 RCT (Gomes 2019, Lawrence 2018)	MD 0.07 (-1.27, 1.40), I^2 0%	72	Moderate
MoCA	1 RCT (Gu 2022)	MD -0.05 (-2.25, 2.15), I^2n.a.	40	Moderate
Depressive symptoms – HDRS	1 RCT (Gomes 2019)	MD 0.74 (-0.04, 1.52), I^2n.a.	58	Low[b]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
* included also peopla with Parkinson's Disease.

Review question 21a (RQ NICE). What are the most effective pharmacological interventions for managing illness emergent non-cognitive symptoms, such as psychosis, depression, behavioural changes in people living with dementia?

ANTIDEPRESSANTS

Antidepressants vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
CSDD	5 RCT (An 2017, Banerjee 2011, Jeong 2022, Lyketsos 2003, Weintraub 2010)	MD -1.17 (-2.37, 0.03), I^2 52%	561	Low[a]
GDS-15	2 RCT (An 2017, Jeong 2022)	**MD -0.60 (-1.00, -0.19), I^2 0%**	160	Moderate
NPI	7 RCT (Banerjee 2011, Banerjee 2021, Finkel 2004, Lyketsos 2003, Maier 2020, Porsteinsson 2014, Zhou 2019)	MD 0.04 (-2.88, 2.96), I^2 51%	1,041	Very Low[a,b]
ADL	5 RCT (An 2017, Banerjee 2011, Jeong 2022, Lyketsos 2003, Maier 2020)	MD -0.08 (-0,29, 0,13), I^2 29%	538	Low[b]
MMSE	9 RCT (An 2017, Banerjee 2011, Banerjee 2021, Finkel 2004, Jeong 2022, Lyketsos 2003, Maier 2020, Porsteinsson 2014, Zhou 2019)	MD 0.21 (-0.25, 0.67), I^2 45%	1,092	Low[a,b]
ADAS-Cog	3 RCT (An 2017, Finkel 2004, Maier 2020)	MD -0.24 (-1.50, 1.01), I^2 0%	408	Low[b]
CMAI	5 RCT (Auchus 1997, Banerjee 2021, Finkel 2004, Porsteinsson 2014, Teri 2000)	MD -0.63 (-2.55, 1.28), I^2 0%	675	Very Low[b,c]
DEM-QoL	2 RCT (Banerjee 2011, Banerjee 2021)	MD -0.58 (-3.55, 2.40), I^2 0%	274	Very Low[b,c]
BEHAVE-AD	2 RCT (Auchus 1997, Finkel 2004)	MD -0.59 (-1.80, 0.62), I^2 0%	250	Low[b,c]
AE	6 RCT (An 2017, Banerjee 2011, Banerjee 2021, Lyketsos 2003, Maier 2020, Weintraub 2010)	**RR 1.32 (1.11, 1.58), I^2 44%**	1,000	Low[a]
SAE	5 RCT (An 2017, Banerjee 2011, Banerjee 2021, Maier 2020, Weintraub 2010)	RR 1.03 (0.62, 1.73), I^2 49%	962	Very Low[a,b]
Discontinuation due to AD	5 RCT (Auchus 1997, Finkel 2004, Nyth 1990, Olafssom 1992, Jeong 2022)	RR 1.08 (0.72, 1.62), I^2 0%	499	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Citalopram vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
NPI	2 RCT (Porsteinsson 2014, Zhou 2019)	**MD -4.67 (-8.97, -0.38), I^2 0%**	264	Moderate[c]
MMSE	2 RCT (Porsteinsson 2014, Zhou 2019)	MD 0.03 (-1.37, 1.44), I^2 55%	264	Low[a]
CMAI	1 RCT (Porsteinsson 2014)	MD -1.38 (-3.93, 1.17), I^2 n.a.	186	Low[b]
NBRS	2 RCT (Pollock 2002, Porsteinsson 2014)	MD -0.85 (-2.06, 0.37), I^2 52%	238	Very Low[a,b]
Discontinuation due to AE	1 RCT (Nyth 1998)	RR 1.25 (0.36, 4.38), I^2 n.a.	98	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
Nyth 1990: people with AD, VD, AD senile dementia, dementia severity (GBS); geriatric setting; doses from 20 mg die to 30 mg die.
Pollock 2002: people with AD and NBS ≥ 3 score; geriatric unit setting; 10 mg die for three days and then 20 mg die.
Porsteinsson 2014: 30 mg die. Initial tritated dose at 10 mg die to 30 mg/die.
Zhou 2019: 30 mg die. Initial tritated dose at 10 mg die to 30 mg/die. In case of non-tolerability, it was allowed to go down to 20 or 10 mg die.

Escitalopram vs placebo

Outcomes	No. of Studies	Observed effect (95% CI), I^2	No. of participants	Certainty of evidence (GRADE)
MMSE	1 RCT (An 2017)	MD 0.97 (-2.20, 4.14), I^2 n.a.	60	Very Low[b,c]
ADAS-Cog	1 RCT (An 2017)	MD 0.99 (-5.28, 7.26), I^2 n.a.	60	Very Low[b,c]
Sleep quality – PSQI	1 RCT (An 2017)	MD 0.38 (-2.54, 3.30), I^2 n.a.	60	Very Low[b,c]
NPI	1 RCT (An 2017)	MD -0,01 (-2,58, 2.56), I^2 n.a.	60	Very Low[b,c]
ADL	1 RCT (An 2017)	MD 0.55 (-6.87, 7.97), I^2 n.a.	60	Very Low[b,c]
CSDD	1 RCT (An 2017)	MD -1.25 (-5.50, 3.00), I^2 n.a.	60	Very Low[b,c]
Depressive symptoms – GDS	1 RCT (An 2017)	MD -0.90 (-3.28, 1.48), I^2 n.a.	60	Very Low[b,c]
AE	1 RCT (An 2017)	RR 1.42 (0.90, 2.24), I^2 n.a.	60	Low[b]
SAE	1 RCT (An 2017)	RR 1.05 (0.22, 4.90), I^2 n.a.	60	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
An 2017: people with AD and at least three depressive symptoms (Olin criteria for depression in AD); memory clinics setting; Started at 5 mg die and increased to 15 mg die. Every two weeks the dosage was increased in absebce of adverse events.

Fluoxetine vs placebo

Outcomes	No. of Studies	Observed effect (95% CI), I^2	No. of participants	Certainty of evidence (GRADE)
BEHAVE-AD	1 RCT (Auchus 1997)	MD 0.80 (-3.73, 5.33), I^2 n.a.	10	Very Low[b,c]
CMAI	1 RCT (Auchus 1997)	MD 2.8 (-5.83, 11.43), I^2 n.a.	10	Very Low[b,c]
Discontinuation due to AE	1 RCT (Auchus 1997)	RR 0.33 (0.02, 6.65), I^2 n.a.	10	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
Auchus 1997: people with AD (NINCDS-ADRDA) and CMAI ≥25 score; community setting; Fixed dose at 20 mg die preceded by a 6-week washout phase in which other drugs with psychotropic activity were carefully discontinued.

Fluvoxamine vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Discontinuation due to AE	1 RCT (Olafsson 1992)	RR 0.55 (0.19, 1.56), I^2 n.a.	46	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations **Olfasson 1992:** people with AD or multi-infarct dementia; psychogeriatric deprtement setting; after a washout phase, initial dose of 50 mg die to 150 mg die, if sedation was necessary, oxazepam use was allowed.				

Mirtazapine vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
CSDD	1 RCT (Banerjee 2011)	MD -0.66 (-2.12, 0.80), I^2 n.a.	158	Low[b]
NPI	2 RCT (Banerjee 2011, Banerjee 2021)	MD -1.00 (-5.05, 3.06), I^2 0%	317	Very Low[b,c]
ADL	1 RCT (Banerjee 2011)	MD 1.19 (-1.37, 3.75), I^2 n.a.	158	Low[b]
MMSE	2 RCT (Banerjee 2011, Banerjee 2021)	MD 1.19 (-5.41, 7.79), I^2 83%	208	Very Low[b,c,d]
DEM-QoL	2 RCT (Banerjee 2011, Banerjee 2021)	MD 0.11 (-3.16, 3.38), I^2 0%	206	Low[b]
CMAI	1 RCT (Banerjee 2021)	MD -0.70 (-9.05, 7.65), I^2 n.a.	166	Very Low[b,c]
AE	2 RCT (Banerjee 2011, Banerjee 2021)	RR 1.23 (0.81, 1.88), I^2 74%	423	Very Low[a,b]
SAE	2 RCT (Banerjee 2011, Banerjee 2021)	RR 0.67 (0.32, 1.42), I^2 53%	423	Very Low[a,b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations **Banerjee 2011**: people with AD (NINCDS-ADRDA) and coexisting depression (at least 4 weeks); setting old-age psychiatry services; dose target 45 mg die **Banerjee 2021**: people with AD and coexisting CMAI ≥ 45; setting AD outpatients; dose target 45 mg die. Every two weeks the dosage was increased if no adverse events were present.				

Sertraline vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
CSDD	3 RCT (Banerjee 2011, Lyketsos 2003, Weintraub 2010)	MD -1.70 (-5.02, 1.62), I^2 76%	325	Very Low[b,d]
NPI	3 RCT (Banerjee 2011, Finkel 2004, Lyketsos 2003)	MD 1.51 (-1.43, 4.45), I^2 0%	434	Very Low[b,c]
ADL	2 RCT (Banerjee 2011, Lyketsos 2003)	MD 0.30 (-3.81, 4.41), I^2 41%	194	Very Low[b,c]
MMSE	3 RCT (Banerjee 2011, Finkel 2004, Lyketsos 2003)	MD 0.13 (-0.80, 1.07), I^2 23%	434	Low[b]
ADAS-Cog	1 RCT (Finkel 2004)	MD -0.30 (-1.69, 1.09), I^2 n.a.	240	Low[b]
CMAI	1 RCT (Finkel 2004)	MD -0.90 (-4.51, 2.71), I^2 n.a.	240	Very Low[b,c]

HDRS	1 RCT (Finkel 2004)	MD 0.00 (-1.11, 1.11), I^2 n.a.	240	Low[b]
DEM-QoL	1 RCT (Banerjee 2011)	MD -1.76 (-5.75, 2.23), I^2 n.a.	150	Very Low[b,c]
BEHAVE-AD	1 RCT (Finkel 2004)	MD -0.70 (-1.95, 0.55), I^2 n.a.	240	Low[b]
AE	3 RCT (Banerjee 2011, Lyketsos 2003, Weintraub 2010)	**RR 1.59 (1.23, 2.04), I^2 0%**	385	Moderate
SAE	2 RCT (Banerjee 2011, Weintraub 2010)	RR 1.34 (0.51, 3.54), I^2 71%	347	Very Low[a,b,c]
Discontinuation due to AE	1 RCT (Finkel 2004)	RR 1.83 (0.81, 4.16), I^2 n.a.	245	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Banerjee 2011: people with AD (NINCDS-ADRDA) and cohexisting depression (at least 4 weeks); setting old-age psychiatry services; Initial dose at 50 mg die, at 2 weeks at 100 mg die, if needed up to 150 mg die.

Finkel 2004: people with AD and NPI total score >5; setting AD outpatients; titrated doses starting from 25 mg die up to 200 mg die.

Lyketsos 2003: people with AD (MMSE ≥10), diagnosis of major depression disorder; setting AD outpatients; titrated doses starting at 25 mg die, after one week to 50 mg die, up to a maximum tolerated dose or 150 mg die.

Weintraub 2010: people with AD (MMSE ≥10), diagnosis of major depression disorder; setting memory clinics; Initial 50 mg die, after one-week target dose of 100 mg die. Then up to the clinician to increase or decrease the dosage according to the patient's tolerability.

Trazodone vs placebo

Outcomes	No. of Studies	Observed effect (95% CI), I^2	No. of participants	Certainty of evidence (GRADE)
CMAI	1 RCT (Teri 2000)	MD 5.18 (-2.86, 13.22), I^2 n.a.	73	Low[b]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Teri 2000: people with AD (NINCDS-ADRDA) and presence of two or more beahvioural disorders for at least two weeks; Alzheimer disease Cooperative Study settings; starting from 50 mg die titrated up to 300 mg die depending on response and tolerability.

Vortioxetine vs placebo

Outcomes	No. of Studies	Observed effect (95% CI), I^2	No. of participants	Certainty of evidence (GRADE)
CSDD	1 RCT (Jeong 2022)	**MD -1.62 (-2.27, -0.97), I^2 n.a.**	100	Moderate
GDS-15	1 RCT (Jeong 2022)	**MD -0.59 (-1.00, -0.18), I^2 n.a.**	100	Moderate
ADL	1 RCT (Jeong 2022)	MD -0.17 (-0.39, 0.05), I^2 n.a.	100	Low[b]
MMSE	1 RCT (Jeong 2022)	**MD 0.59 (0.18, 1.00), I^2 n.a.**	100	Moderate
Discontinuation due to AE	1 RCT (Jeong 2022)	RR 1.04 (0.59, 1.84), I^2 n.a.	100	Low[b]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Jeong 2022: people with AD and at least three depression symptoms (Olin criteria for depression in AD); hospital psychiatric unit setting; 5 mg die. If the effect was insufficient, from weeks 4 to 12 participants could get to take up to 20 mg die.

Bupropion vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
NPI	1 RCT (Maier 2020)	**MD 5.51 (1.69, 9.33), I^2 n.a.***	108	Moderate
ADL	1 RCT (Maier 2020)	MD -2.92 (-6.10, 0.26), I^2 n.a.	108	Low[b]
MMSE	1 RCT (Maier 2020)	MD -0.45 (-2.00, 1.10), I^2 n.a.	108	Very Low[b,c]
ADAS-Cog	1 RCT (Maier 2020)	MD -0.27 (-3.55, 3.01), I^2 n.a.	108	Very Low[a,b]
MADRS	1 RCT (Maier 2020)	**MD 2.10 (0.40, 3.80), I^2 n.a.**	108	Moderate
AE	1 RCT (Maier 2020)	RR 1.18 (0.90, 1.55), I^2 n.a.	108	Low[b]
SAE	1 RCT (Maier 2020)	RR 2.50 (0.51, 12.33), I^2 n.a.	108	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Maier 2020: people with AD and apathy symptoms (Marin and Starkstein apathy in AD criteria) and ≥ 4 score in each NPI item; setting psychiatric and neurological outpatients; 150 mg die initially. In case of good tolerability, the dose was increased to a maximum of 300 mg die. In case of adverse events it was reset to 150 mg die

***** Significant worsening of neuropsychiatric symptoms in the bupropion-treated group

ANTIPSYCHOTICS

Antipsychotics vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
CMAI	12 RCT (Auchus 1997, Ballard 2005, Ballard 2018, Brodaty 2003, Deberdt 2005, De Deyn 1999, Grossberg 2020, Katz 1999, Lee 2023, Streim 2008, Teri 2000, Zhong 2007)	**MD -1.87 (-2.83, -0.92), I^2 41%**	3,432	Moderate
NPI	13 RCT (Ballard 2018, Deberdt 2005, De Deyn 2004, De Deyn 2005, Kurlan 2007, Lee 2023, Mintzer 2007, Paleacu 2008, Schneider 2006, Street 2000, Streim 2008, Tariot 2006, Zhong 2007)	**MD -3.44 (-4.82, -2.06), I^2 0%**	3,479	Moderate
BPRS	7 RCT (Deberdt 2005, De Deyn 2004, De Deyn 2005, Schneider 2006, Street 2000, Streim 2008, Tariot 2006)	**MD -1.70 (-2.73, -0.67), I^2 0%**	1,957	Moderate
AE	2 RCT (Ballard 2018, Grossberg 2020, Lee 2023)	RR 1.10 (0.95, 1.28), I^2 64%	1,224	Low[b,c]
AE - extrapyramidal	14 RCT (Brodaty 2003, Deberdt 2005, De Deyn 1999, De Deyn 2005, Grossberg 2020, Katz 1999, Lee 2023, Mintzer 2006, Mintzer 2007, Streim 2008, Paleacu 2008, Schneider 2006, Tariot 2006, Zhong 2007)	**RR 1.47 (1.17, 1.85), I^2 24%**	5,505	Moderate
AE - drowsiness	13 RCT (Brodaty 2003, Deberdt 2005, De Deyn 1999, De Deyn 2005, Grossberg 2020, Katz 1999, Lee 2023, Mintzer 2006, Mintzer 2007, Street 2000, Streim 2008, Tariot 2006, Zhong 2007)	**RR 2.58 (1.96, 3.38), I^2 31%**	4,543	Low[a]
AE - cerebrovascular	9 RCT (Brodaty 2003, Deberdt 2005, De Deyn 2005, Mintzer 2006, Mintzer 2007, Schneider 2006, Streim 2008, Tariot 2006, Zhong 2007)	**RR 2.65 (1.34, 5.25), I^2 0%**	3,568	Low[c]

AE - mortality	17 RCT (Ballard 2005, Ballard 2018, Brodaty 2003, Deberdt 2005, De Deyn 1999, De Deyn 2004, De Deyn 2005, Grossberg 2020, Katz 1999, Lee 2023, Mintzer 2006, Mintzer 2007, Schneider 2006, Street 2000, Streim 2008, Tariot 2006, Zhong 2007)	**RR 1.47 (1.03, 2.11), I^2 0%**	6,252	Moderate[c]
SAE	2 RCT (Ballard 2018, Lee 2023)	**RR 1.43 (0.69, 2.99), I^2 0%**	523	Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Haloperidolvs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
CMAI	2 RCT (Auchus 1997, Teri 2000)	MD -1.15 (-7.85, 5.54), I^2 0%	80	Very Low[b,c]
BEHAVE-AD	1 RCT (Auchus 1997)	MD -3.60 (-9.73, 2.53), I^2 n.a.	10	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations **Auchus 1997:** people with AD (NINCDS-ADRDA) and CMAI ≥25; setting community dwelling outpatients; Dose starting at 0.5 mg die up to a maximum of 3 mg die preceded by a washout phase of 6 weeks in which other drugs with psychotropic activity were carefully discontinued. **Teri 2000:** people with AD (NINCDS-ADRDA) and two or more behavioural symtpoms for at least two weeks; Alzheimer disease Cooperative Study settings; Starting from 0.5 mg die titrated up to 3 mg die depending on response and tolerability.				

Aripiprazole vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
CMAI	1 RCT (Streim 2008)	**MD -4.09 (-7.52, -0.66), I^2 n.a.**	247	Moderate
NPI	3 RCT (De Deyn 2005, Mintzer 2007, Streim 2008)	**MD -3.82 (-6.36, -1.27), I^2 0%**	926	Moderate
NPI 2 mg die	1 RCT (Mintzer 2007)	MD -1.10 (-5.70, 3.50), I^2 n.a.	233	Low[b]
NPI 5 mg die	1 RCT (Mintzer 2007)	MD -2.90 (-7.31, 1.51), I^2 n.a.	237	Low[b]
NPI 10 mg die	1 RCT (Mintzer 2007)	**MD -4.60 (-8.79, -0.41), I^2 n.a.**	238	Bass[c]
BPRS	2 RCT (De Deyn 2005, Streim 2008)	**MD -2.41 (-4.24, -0.58), I^2 0%**	435	Moderate
AE- extrapyramidal	3 RCT (De Deyn 2005, Mintzer 2007, Streim 2008)	RR 1.28 (0.71, 2.29), I^2 0%	951	Low[b]
AE - drowsiness	3 RCT (De Deyn 2005, Mintzer 2007, Streim 2008)	**RR 2.95 (1.46, 5.96), I^2 0%**	951	Moderate
AE-cerebrovascular	3 RCT (De Deyn 2005, Mintzer 2007, Streim 2008)	RR 1.25 (0.23, 6.76), I^2 0%	951	Very Low[b,c]
Mortality	3 RCT (De Deyn 2005, Mintzer 2007, Streim 2008)	RR 1.62 (0.65, 4.06), I^2 0%	951	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

De Deyn 2005: people with AD non-istutionalized and with hallucinations and delusions (at least intermittent, NPI ≥ 6); flexible dose starting at 2 mg die titrated up to 15 mg die after a 7-day washout period in which treatments with other psychotropic drugs (carbamazepine, valproate, lithium, sleeping pharmavi (no zolpidem), psychotropic drugs (except antidepressants), and benzodiazepines (except lorazepam 4 mg die) were discontinued. AChEI discontinued in the washout phase but allowed in the randomized phase as well as antidepressants.
Mintzer 2007: people with AD and persistent or intermittent hallucinations or delusions; hospital setting; Fixed dose 2 mg die, 5 mg die or 10 mg die.
Streim 2008: institutionalized people with AD and persistent or intermittent hallucinations or delusions; setting nursing homes; Flexible dose starting from 2 mg die titrated up to 15 mg die.

Brexpiprazole vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
CMAI	1 RCT (Grossberg 2020)	MD -2.03 (-4.23, 0.18), I^2 18%	669	Low[b]
CMAI flexible doses	1 RCT (Grossberg 2020)	MD -2.40 (-5.59, 0.79), I^2 n.a.	266	Low[b]
CMAI fixed dose 1mg	1 RCT (Grossberg 2020)	MD 0.20 (-2.92, 3.32), I^2 n.a.	265	Low[b]
CMAI fixed dose 2 mg	1 RCT (Grossberg 2020)	**MD -3.80 (-6.92, -0.68), I^2 n.a.**	269	Moderate
NPI-AG	1 RCT (Grossberg 2020)	**MD -0.53 (-0.98, -0.09), I^2 21%**	669	Moderate
NPI-AG flexible doses	1 RCT (Grossberg 2020)	**MD -0.88 (-1.52, -0.24), I^2 n.a.**	266	Moderate
NPI-AG fixed dose 1mg	1 RCT (Grossberg 2020)	MD -0.10 (-0.72, 0.52), I^2 n.a.	265	Low[b]
NPI-AG fixed dose 2mg	1 RCT (Grossberg 2020)	MD -0.55 (-1.16, 0.06), I^2 n.a.	269	Low[b]
AE	1 RCT (Grossberg 2020)	RR 1.09 (0.87, 1.38) I^2 60%	701	Very Low[a,b]
AE flexible doses	1 RCT (Grossberg 2020)	RR 0.97 (0.79, 1.19), I^2 n.a.	269	Low[b]
AE fixed dose	1 RCT (Grossberg 2020)	**RR 1.23 (1.00, 1.52), I^2 n.a.**	432	Moderate
AE - extrapyramidal	1 RCT (Grossberg 2020)	RR 2.64 (0.29, 23.80) I^2 0%	701	Very Low[b,c]
AE - extrapyramidal flexible doses	1 RCT (Grossberg 2020)	RR 3.11 (0.13, 75.74), I^2 n.a.	269	Very Low[b,c]
AE - extrapyramidal fixed dose	1 RCT (Grossberg 2020)	RR 2.28 (0.11, 47.21), I^2 n.a.	432	Very Low[b,c]
AE - drowsiness flexible doses	1 RCT (Grossberg 2020)	RR 1.66 (0.56, 4.95), I^2 n.a.	269	Very Low[b,c]
Mortality	1 RCT (Grossberg 2020)	RR 2.70 (0.42, 17.46) I^2 0%	703	Very Low[b,c]
Mortality flexible doses	1 RCT (Grossberg 2020)	RR 1.03 (0.06, 16.64), I^2 n.a.	270	Very Low[b,c]
Mortality fixed dose	1 RCT (Grossberg 2020)	RR 5.13 (0.28, 93.50), I^2 n.a.	433	Very Low[b,c]
CMAI	1 RCT (Lee 2023)	**MD -5.30 (-8.79, -1.81), I^2 n.a.**	342	Moderate
NPI	1 RCT (Lee 2023)	**MD -4.60 (-7.54, -1.66), I^2 n.a.**	342	Moderate
AE	1 RCT (Lee 2023)	RR 1.31 (0.96, 1.79) I^2 0%	342	Low[b]
SAE	1 RCT (Lee 2023)	RR 1.03 (0.25, 4.18), I^2 n.a.	342	Very Low[b,c]
AE - extrapyramidal	1 RCT (Lee 2023)	RR 2.58 (0.12, 53.24), I^2 n.a.	342	Very Low[b,c]
AE - drowsiness	1 RCT (Lee 2023)	RR 4.11 (0.52, 32.44), I^2 n.a.	342	Very Low[b,c]
Mortality	1 RCT (Lee 2023)	RR 2.55 (0.06, 37.66) I^2 n.a.%	342	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
Grossberg 2020: people with AD, diagnosis also confirmed by MRI or CT; care facility or community setting but the participant did not have to live alone; fixed dose: 2 or 1 mg die; flexible dose 0.5-2 mg die. Benzodiazepine use allowed.

Olanzapine vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
NPI	4 RCT (Deberdt 2005, De Deyn 2004, Schneider 2006, Street 2000)	MD -2.13 (-4.90, 0.64), I^2 0%	1.212	Low[b]
NPI 1 mg die	1 RCT (De Deyn 2004)	MD -1.10 (-5.59, 3.39), I^2 n.a.	236	Low[b]
NPI 2,5 mg die	1 RCT (De Deyn 2004)	MD -2.00 (-6.32, 2.32), I^2 n.a.	236	Low[b]
NPI 5 mg die	2 RCT (De Deyn 2004, Street 2000)	MD -3.63 (-7.81, 0.54), I^2 6%	352	Low[b]
NPI 7,5 mg die	1 RCT (De Deyn 2004)	MD -4.00 (-8.43, 0.43), I^2 n.a.	236	Low[b]
NPI 10 mg die	1 RCT (Street 2000)	MD -3.60 (-13.67, 6.47), I^2 n.a.	94	Very Low[b,c]
NPI 15 mg die	1 RCT (Street 2000)	MD 0.70 (-10.06, 11.46), ^{2} n.a.	96	Very Low[b,c]
BPRS overall	4 RCT (Deberdt 2005, De Deyn 2004, Schneider 2006, Street 2000)	MD -1.20 (-2.66, 0.25), I^2 0%	1.098	Low[b]
BPRS 1 mg die	1 RCT (De Deyn 2004)	MD 0.60 (-2.09, 3.29), ^{2} n.a.	236	Low[b]
BPRS 2,5 mg die	1 RCT (De Deyn 2004)	MD -1.80 (-4.40, 0.80), ^{2} n.a.	254	Low[b]
BPRS 5 mg die	2 RCT (De Deyn 2004, Street 2000)	MD -1.02 (-3.36, 1.33), I^2 78%	311	Very Low[b,d]
BPRS 7,5 mg die	1 RCT (De Deyn 2004)	MD -2.60 (-5.32, 0.12), ^{2} n.a.	242	Low[b]
BPRS 10 mg die	1 RCT (Street 2000)	MD -4.20 (-9.17, 0.77), ^{2} n.a.	70	Very Low[b,c]
BPRS 15 mg die	1 RCT (Street 2000)	MD -2.60 (-7.70, 2.50), ^{2} n.a.	72	Very Low[b,c]
CMAI	1 RCT (Deberdt 2005)	MD -0.40 (-1.33, 0.53), I^2 n.a.	283	Low[b]
AE-extrapyramidal	2 RCT (Deberdt 2005, Schneider 2006)	RR 5.06 (0.13, 191.77), I^2 65%	537	Very Low[a,b,c]
AE- drowsiness	2 RCT (Deberdt 2005, Street 2000)	**RR 3.14 (1.72, 5.71), I^2 0%**	504	Low[c]
AE-cerebrovascular	2 RCT (Deberdt 2005, Schneider 2006)	RR 5.90 (0.73, 47.60), I^2 0%	537	Very Low[b,c]
Mortality	4 RCT (Deberdt 2005, De Deyn 2004, Schneider 2006, Street 2000)	RR 2.45 (0.82, 7.27), I^2 0%	1.402	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Street 2000: people with AD and ≥ 3 score at NPI-NH items such as agitation, hallucinations, aggression, delusions; nursing homes setting; fixed dose at 5 mg die, 10 mg die, 15 mg die

De Deyn 2004: people with AD and psychotic symptoms such as hallucinations and delusions; nursing homes or continuing-care hospitals setting; Fixed dose at 1 mg die, 2.5 mg die, 5 mg die, 7.5 mg die after titration for the doses of 5 mg die and 7.5 mg die.

Deberdt 2005: poeple with AD, VaD or mixed dementia (DSM-IV) and NPI score ≥ 6 on hallucinations and delusions items; nursing homes o outpatients setting (mostly outpatients living in their own homes); flexible dose from 2.5 mg die to 10 mg die.

Schneider 2006: people with AD who lived in their own home or in an assisted living facility and had psychotic symptoms such as aggression, hallucinations, delusions; outpatients o care facilities setting; mean stated dose 5.5 mg die, the study physicians established initial doses and adjusted them according to their clinical judgment and patient responses.

Perphenazine vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
NBRS	1 RCT (Pollock 2002)	MD -4.90 (-15.05, 5.25), I^2 n.a.	54	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
Pollock 2002: people with AD and NBS score ≥ 3; geriatric unit setting; dose starting at 0.05mg/kg for three days and rising to 0.1mg/kg.

Pimavanserin vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
CMAI	1 RCT (Ballard 2018)	MD 0.30 (-2.04, 2.64), I^2 n.a.	181	Low[b]
ADCS-ADL	1 RCT (Ballard 2018)	MD -0.22 (-2.23, 1.79), I^2 n.a.	181	Low[b]
NPI	1 RCT (Ballard 2018)	MD -5.12 (-10.73, 0.29), I^2 n.a.	181	Very Low[b,c]
NPI-NH PS*	1 RCT (Ballard 2018)	**MD -1.83 (-3.60, -0.06), I^2 n.a.**	178	Moderate
AE	1 RCT (Ballard 2018)	RR 1.05 (0.98, 1.11), I^2 n.a.	181	Low[b]
SAE	1 RCT (Ballard 2018)	RR 1.52 (0.72, 3.20), I^2 n.a.	181	Very Low[b,c]
Mortality	1 RCT (Ballard 2018)	RR 1.01 (0.26, 3.92), I^2 n.a.	181	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
Ballard 2018: people with AD insititutionalized from at least 4 weeks but not bedridden, with psychotic symptoms such as hallucinations (visual and auditory) and delusions; network of 133 nursing homes setting; fixed dose of two tablets of 17mg each per die.
*Neuropsychiatric Inventory-Nursing Homes version Psycosis Subscale

Quetiapine vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
CMAI overall	2 RCT (Ballard 2005, Zhong 2007)	MD -0.33 (-4.86, 4.21), I^2 0%	382	Very Low[b,c]
CMAI 100 mg die	1 RCT (Zhong 2007)	MD -0.40 (-6.37, 5.57), I^2 n.a.	212	Very Low[b,c]
CMAI 200 mg die	1 RCT (Zhong 2007)	MD -2.20 (-8.30, 3.90), I^2 n.a.	206	Very Low[b,c]
NPI	5 RCT (Kurlan 2007, Paleacu 2008, Schneider 2006, Tariot 2006, Zhong 2007)	**MD -3.45 (-6.78, -0.11), I^2 0%**	659	Moderate
NPI 100 mg die	1 RCT (Zhong 2007)	MD -0.70 (-6.95, 5.55), I^2 n.a.	212	Very Low[b,c]
NPI 200 mg die	1 RCT (Zhong 2007)	MD -1.50 (-7.88, 4.88), I^2 n.a.	206	Very Low[b,c]
BPRS	2 RCT (Schneider 2006, Tariot 2006)	**MD -2.70 (-5.24, -0.16), I^2 0%**	257	Moderate
AE-extrapyramidal	4 RCT (Paleacu 2008, Schneider 2006, Tariot 2006, Zhong 2007)	RR 0.87 (0.40, 1.87), I^2 26%	796	Low[b]
AE- drowsiness	2 RCT (Tariot 2006, Zhong 2007)	**RR 5.38 (2.34, 12.37), I^2 0%**	423	Low[c]
AE-cerebrovascular	3 RCT (Schneider 2006, Tariot 2006, Zhong 2007)	RR 0.64 (0.15, 2.76), I^2 0%	664	Very Low[b,c]
Mortality	4 RCT (Ballard 2005, Schneider 2006, Tariot 2006, Zhong 2007)	RR 1.80 (0.80, 4.06), I^2 0%	877	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
Ballard 2005: people with dementia and CMAI ≥ 39 and an agitation level as a clinically relevant problem based on physician's judgment; care facilities setting; flexible dose of 50 mg die to 100 mg die (by clinical practice considered as the effective dose for behavioral disorders).

Kurlan 2007: people with dementia (AD, PDD, DLB) with complication of parkinsonism (extrapyramidal symptoms) and presence of psychosis and agitation; setting in the participant's private residences or assisted living facilities; dose of 25 mg die titrated up to 150 mg die if tolerated. Physicians were urged to go to at least 100 mg die.
Paleacu 2008: people with AD (DSM-IV) and a score of at least 6 on all items of the NPI; setting non-specified; starting dose 50 mg die up to 150 mg die with increase of 50 mg die each week, washout period of 2 weeks if already being treated with other antipsychotic.
Schneider 2006: people with AD living in their own homes or in an assisted living facility; outpatients or care facilities setting; mean stated dose 56.5 mg die, the Study physicians established initial doses and adjusted them according to their clinical judgment and patients' responses. Compared with RCTs in nursing homes, quetiapine use was about ¼ lower, motivated by possible excessive sedation. It still remained up to clinical judgment to adjust the dose based on the individual person; no washout and run-in period was performed in this study for reasons related to participants' acute symptoms.
Tariot 2006: people with AD nad presence of psychosis defined as: BPRS ≥ 24, CGI-S ≥ 4 at screeing and baseline; a score of 3 on two or more of the following items of the BPRS: 4, conceptual disorganization; 11, distrust; 12, hallucinatory behavior; 15, unusual thought content; and frequency scores of 3 on at least one of the two psychosis items (delusions or hallucinations) of the NPI-NH; nursing homes setting; 25 mg die up to 100 mg die based on tolerability.
Zhong 2007: people with AD, PANSS-EC >14 total score and a score >4 on one of the 5 tiems of PANSS-EC (hostility, tension, non-cooperation, arousal, poor impulse control) both at the time of screening and at the time of randomization; nursing homes and assisted care facilities setting; fixed doses 100 mg die and 200 mg die with titration starting at 25 mg die and increasing to 100 mg die at day 4 and 200 mg die at day 8.

Risperidone vs placebo nel trattamento della demenza

Outcomes	No. of Studies	Observed effect (95% CI), I^2	No. of participants	Certainty of evidence (GRADE)
CMAI	4 RCT (Brodaty 2003, Deberdt 2005, De Deyn 1999, Katz 1999)	**MD -2.38 (-4.15, -0.62), I^2 72%**	1.339	Low[a]
NPI	2 RCT (Deberdt 2005, Scheider 2006)	MD -1.97 (-11.73, 7.80), I^2 77%	359	Very Low[b,c,d]
BPRS	2 RCT (Deberdt 2005, Scheider 2006)	MD -1.51 (-6.51, 3.50), I^2 66%	347	Very Low[a,b]
AE-extrapyramidal	6 RCT (Brodaty 2003, Deberdt 2005, De Deyn 1999, Katz 1999, Mintzer 2006, Scheider 2006)	**RR 1.71 (1.29, 2.26), I^2 26%**	2.178	Moderate
AE- drowsiness	5 RCT (Brodaty 2003, Deberdt 2005, De Deyn 1999, Katz 1999, Mintzer 2006)	**RR 2.17 (1.50, 3.15), I^2 48%**	1.954	Low[a]
AE-cerebrovascular	4 RCT (Brodaty 2003, Deberdt 2005, Mintzer 2006, Scheider 2006)	**RR 4.03 (1.55, 10.46), I^2 0%**	1.185	Low[c]
Mortality	6 RCT (Brodaty 2003, Deberdt 2005, De Deyn 1999, Katz 1999, Mintzer 2006, Scheider 2006)	RR 1.45 (0.83, 2.54), I^2 0%	2.178	Low[b]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Brodaty 2003: people with dementia (AD, VaD, mista) and behavioural disorders (CMAI ≥ 4 on at least one item of aggresion, CMAI ≥ 3 on at least one item of aggresion, o CMAI ≥ 2 in three items of aggression); nursing homes e care facilities settings;
De Deyn 1999: people with (DSM-IV), FAST ≥ 4, BEHAVE-AD global rating ≥ 1; non-specified setting; Dose 0.25 mg die titrated up to 1 mg die on day 4.
Deberdt 2005 (Unexpected trial failure, an unexpected improvement was observed in the placebo group, making the differences between groups non-significant): people with AD, VaD or mixed demntia (DSM-IV) and an NPI score of at least 6 on the hallucinations and delusions items; nursing homes or oupatients setting (mostly outpatients living in their own homes); flexible dose from 0.5 mg die to 2 mg die.
Katz 1999: popolazione persone con AD e disturbi psicotici; setting non disponibile; dose 0.5 mg die, 1 mg die, or 2 mg die.
Mintzer 2006: people with AD and psychosis; outpatients, nursing homes or assisted care facilities setting; dose of 0.5 mg die titrated up to 1 mg die, if no response dose up to 1.5 mg die.
Schneider 2006: people with AD living at their own homes or in assisted living facility; outpatients or care facility setting; mean stated dose 1 mg die, study clinicians established initial doses and adjusted them according to their clinical judgment and patients' responses. No washout and run-in period was performed in this study for reasons related to participants' acute symptoms.

ANTIPSYCHOTIC SUSPENSION VERSUS CONTINUATION

Antipsychotic suspension vs continuation				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
BPSD severity	3 RCT (Ballard 2004, Ballard 2008, Ruths 2008)	SMD 0.19 (-0,20, 0,58), I^2 51%	214	Low[a,b]
BPSD worsening	7 RCT (Ballard 2004, Bridges-Parlet 1997, Devenand 2011, Devenand 2012, Ruths 2004, Ruths 2008, van Reekum 2002)	**RR 1.78 (1.31, 2.41), I^2 0%**	366	Moderate
Mortality	5 RCT (Ballard 2004, Ballard 2008, Bridges-Parlet 1997, Devenand 2012, van Reekum 2002)	RR 0.83 (0.49, 1.39), I^2 0%	407	Low[b]
Discontinuation of pimavanserin vs continuation				
SAPS - hallucinations and delusions	1 RCT (Tariot 2021)	MD -0.10 (-2.78, 2.58), I^2 n.a.	80	Low[b]
Relapse of psychotic episodes	1 RCT (Tariot 2021)	**RR 2.24 (1.21, 4.14), I^2 n.a.**	194	Low[c]
AE	1 RCT (Tariot 2021)	RR 0.89 (0.64, 1.25), I^2 n.a.	217	Low[c]
Migraine	1 RCT (Tariot 2021)	RR 0.47 (0.17, 1.33), I^2 n.a.	217	Low[b]
Prolongation QT interval	1 RCT (Tariot 2021)	RR 0.13 (0.01, 2.56), I^2 n.a.	217	Low[b]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations.

Ballard 2004: people with AD in care facilities without severe behavioural disorders who had been taking neuroleptics for at least 3 months: care facilities setting; discontinuation of antipsychotic treatment.

Ballard 2008: people with possible or probable AD (NINCDS-ADRDA), residing in nursing homes, MMSE of at least 6 or SIB of at least 30; setting nursing homes; already taking 10 mg chlorpromazine, typical antipsychotics, or at least 0.5 mg risperidone per day.

Bridges-Parlet 1997: people with dementia and history of BPSD and residing in nursing homes; setting nursing homes; continuation of neuroleptic already taken by participants.

Devenand 2011: people with AD, score of at least 4 on the BPRS on one of the items hallucination or unusual behaviour or a score of at least 6 in the sum of the items; titrated dose of haloperidol in the open-label phase up to 5 mg die, then randomised phase of 24 weeks to discontinuation or continuation of treatment.

Devenand 2012: people with AD and psychotic or agitation disorder; setting memory clinics, geriatric units; risperidone 0.25 mg die up to 3 mg die in open-label phase of 16 weeks, then randomised phase of 32 (16wk + 16wk) weeks to withdrawal or continuation of treatment. Group 1 risperidone 32wk, Group 2 risperidone 16wk + placebo 16wk, Group 3 placebo 32wk

Ruths 2004: people with dementia in nursing homes taking antipsychotic medication; nursing homes setting; randomisation to discontinuation or continuation of antipsychotic treatment

Ruths 2008: people with dementia treated for more than 3 months with haloperidol, risperidone, or olanzapine for BPSD; nursing homes setting; stable doses of olanzapine, risperidone, olanzapine

Tariot 2021: people with dementia (AD, PDD, DLB, FTD, VaD) and psychotic symptoms; setting clinical sites not specified; 12-week open-label phase, followed by a 26-week randomised phase + 4 weeks safety monitoring; pimavanserin 20mg when pimavanserin 34mg not tolerated

van Reekum 2002: people with dementia on antipsychotics for at least 6 months; setting nursing homes and geriatric units in academic-hospital centres; 2-week pretrial, 2-week dose-reduction period, 6-month randomised study.

CHANGE IN ANTIPSYCHOTIC VERSUS CONTINUATION

Change in antipsychotic vs continuation				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
CMAI	1 RCT (Ballard 2015)	MD 3.24 (-3.81, 10.29), I^2 n.a.	164	Very Low[b,c]
NPI	1 RCT (Ballard 2015)	MD 3.39 (-3.23, 10.01), I^2 n.a.	163	Very Low[b,c]
MMSE	1 RCT (Ballard 2015)	MD 2.38 (-0.92, 5.68), I^2 n.a.	113	Very Low[b,c]
EAS	1 RCT (Ballard 2015)	RR 0.74 (0.44, 1.24), I^2 n.a.	164	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations **Ballard 2015:** people with AD and previous use of antipsychotics; setting care facilities; dose of at least 0.5 mg per day of haloperidol, 0.5 mg per day of risperidone, 5 mg per day of olanzapine or 25 mg per day of quetiapine for a minimum of 3 months prior to entering the study.				

CANNABINOIDS

Cannabinoids vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
delta-9-tetrahydrocannabinol (THC)				
CMAI	1 RCT (Hermush 2022)	MD -10.90 (-26.59, 4.79), I^2 n.a.	52	Very Low[b,c]
NPI	1 RCT (Hermush 2022)	MD -8.50 (-23.29, 6.29), I^2 n.a.	52	Very Low[b,c]
MMSE	1 RCT (Hermush 2022)	MD -0.30 (-5.35, 4.75), I^2 n.a.	52	Very Low[b,c]
Memory impairment	1 RCT (van den Elsen 2015)	RR 3.24 (0.80, 13.08), I^2 n.a.	57	Very Low[b,c]
EA	1 RCT (Hermush 2022)	RR 1.02 (0.86, 1.22), I^2 n.a.	57	Low[b]
EA - hallucinations	1 RCT (van den Elsen 2015)	RR 4.32 (0.58, 32.16), I^2 n.a.	57	Very Low[b,c]
Cannabis oil extract				
CMAI	1 RCT (van den Elsen 2015)	MD 5.60 (-7.95, 19.15), I^2 n.a.	47	Very Low[b,c]
NPI	1 RCT (van den Elsen 2015)	MD 2.10 (-8.79, 12.99), I^2 n.a.	47	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations **van den Elsen 2015**: people with dementia (AD, VaD, mixed dementia) and clinically relevant behavioural disorders with an NPI score of at least 10; outpatients setting from geriatric wards, psychiatry, and nursing homes; THC lozenges 1.5mg three times daily for a duration of 3 weeks. **Hermush 2022:** people with dementia (DSM-V) and clinically relevant behavioural disorders with a score of at least 3 on the NPI agitation subscale; hospital setting; cannabis oil extract as drops under the tongue, 1 drop up to a maximum of 21 drops depending on tolerability (1 drop: 11.8mg CBD + 0.5mg THC).				

CHOLINE ALPHOSCERATE

Choline alphoscerate vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
NPI-apathy	1 RCT (Rea 2015)	**MD -3.90 (-6.40, -1.40), I^2 n.a.**	113	Moderate
NPI	1 RCT (Rea 2015)	**MD -12.10 (-20.49, -3.71), I^2 n.a.**	113	Low[c]
FAB	1 RCT (Rea 2015)	MD 1.20 (-0.39, 2.79), I^2 n.a.	113	Low[b]
MMSE	1 RCT (Rea 2015)	**MD 2.90 (0.73, 5.07), I^2 n.a.**	113	Low[c]
ADAS-Cog	1 RCT (Rea 2015)	**MD -5.80 (-11.58, -0.02), I^2 n.a.**	113	Low[c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations **Rea 2015 (ASCOMALVA trial):** people with AD (MMSE 14-24) with apathy scores measured with the frequency x severity subtest of the NPI; unspecified setting; 24-month treatment with 10 mg per day donepezil and 1200 mg per day choline alphoscerate.				

DEXTROMETHORPHAN/QUINIDINE

Dextromethorphan/quinidine vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
NPI-Agitation	1 RCT (Cummings 2015)	**MD -1.70 (-2.82, -0.58), I^2 n.a.**	159	Moderate
NPI	1 RCT (Cummings 2015)	**MD -5.90 (-11.58, -0.22), I^2 n.a.**	159	Moderate
CSDD	1 RCT (Cummings 2015)	**MD -1.60 (-2.86, -0.34), I^2 n.a.**	152	Moderate
MMSE	1 RCT (Cummings 2015)	MD 0.70 (-0.36, 1.76), I^2 n.a.	151	Low[b]
EA	1 RCT (Cummings 2015)	**RR 1.41 (1.12, 1.79), I^2 n.a.**	279	Moderate
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations **Cummings 2015:** people with AD (MMSE 8-28) and clinically significant agitation; outpatients setting and persons in nursing homes or care facilities; 20mg dextrometorphane + 10mg quinidine initially once daily (week 1), then increased to twice daily (weeks 2-3), then increased to 30/10 twice daily (weeks 4-5) for a total duration of 10 weeks.				

DRUGS FOR SLEEP DISORDERS

Orexin antagonists (Lemborexant) vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Total Nightime Sleep Time	1 RCT (Moline 2021)	MD -12.07 (-50.65, 26.52), I^2 0%	62	Very Low[b,c]
Total Daytime Sleep Time	1 RCT (Moline 2021)	MD 25.07 (-37.07, 87.21), I^2 0%	62	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations **Moline 2021:** people with AD (MMSE 10-26) with clinically proven sleep disorders (DSM-V and ICD-10); persons with available caregivers; lemborexant in four arms under study: 2.5 mg die, 5 mg die, 10 mg die, 15 mg die.				

Zopiclone vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Total Nightime Sleep Time	1 RCT (Louzada 2022)	MD 79.10 (-10.59, 168.79), I^2 n.a.	28	Very Low[b,c]
Total Daytime Sleep Time	1 RCT (Louzada 2022)	MD -35.50 (-152.93, 81.93), I^2 n.a.	28	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations **Louzada 2022:** people with AD (DSM-V, NINCDS-ADRDA), sleep disorders (DSM-V, NPI), MMSE 0-24, CSDD < 6; persons with available caregivers; zopiclone at a fixed dose of 7.5 mg die				

Zolpidem vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Total Nightime Sleep Time	1 RCT (Louzada 2022)	MD 17.00 (-58.29, 92.29), I^2 n.a.	31	Very Low[b,c]
Total Daytime Sleep Time	1 RCT (Louzada 2022)	MD 39.30 (-76.39, 154.99), I^2 n.a.	31	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations **Louzada 2022:** people with AD (DSM-V, NINCDS-ADRDA), sleep disorders (DSM-V, NPI), MMSE 0-24, CSDD < 6; persons with available caregivers; zolpidem at a fixed dose of 10 mg die				

Trazodone vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Total Nightime Sleep Time	1 RCT (Camargos 2014)	MD 42.50 (-31.62, 116.62), I^2 n.a.	30	Very Low[b,c]
Total Daytime Sleep Time	1 RCT (Camargos 2014)	MD 5.10 (-53.19, 63.39), I^2 n.a.	30	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
Camargos 2014: people with AD (MMSE ≤ 24) with clinically relevant sleep disturbances (NPI and criteria recommended by Yesavage et al.); outpatients setting from geriatric wards; 50 mg per day (sleep dose).

Melatonin vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Melatonin 5mg o 10mg immediate-release				
Total Nightime Sleep Time	2 RCT (Dowling 2008, Singer 2003)	MD -1.34 (-37.13, 34.45), I^2 0%	106	Low[b,c]
TDST/TNST*	2 RCT (Dowling 2008, Singer 2003)	MD -0.12 (-0.28, 0.05), I^2 n.a.	106	Low[b]
Melatonin 2,5mg medium/fast-release				
Total Nightime Sleep Time	1 RCT (Riemersma-van der Lek 2008)	MD 48.00 (-14.46, 110.46), I^2 n.a.	91	Very Low[b,c]
Melatonin 2mg o 2,5mg extended-release				
Total Nightime Sleep Time	2 RCT (Singer 2003, Wade 2014)	MD 26.18 (-9.17, 61.52), I^2 0%	89	Very Low[b,c]
TDST/TNST*	1 RCT (Singer 2003)	MD -0.25 (-0.78, 0.28), I^2 n.a.	78	Low[b]
Melatonin 5mg (non-specified release)				
Pittsburgh Sleep Quality Index	1 RCT (Morales-Delgado 2018)	MD 0.17 (-1.45, 1.79), I^2 n.a.	31	Low[b]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations; * ratio of total daytime sleep and total night-time sleep				

Memantine vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Epworth Sleepiness Scale	1 RCT (Larsson 2010)	MD 0.40 (-3.52, 4.32), I^2 n.a.	60	Very Low[b,c]
Stavanger Sleep Questionnaire	1 RCT (Larsson 2010)	MD 0.48 (0.06, 0.90), I^2 n.a.	55	Moderate
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations **Larsson 2010:** people with DLB or PDD (MMSE ≥ 12); outpatients from neurology and psychiatry departments; initial dose 5mg in the morning, increased to 20 mg die for 4 weeks (10mg in the morning and 10mg in the evening)				

Paracetamol/buprenorphine vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Total Nightime Sleep Time	1 RCT (Blytt 2018)	MD 40.20 (-15.08, 95.48), I^2 n.a.	106	Very Low[b,c]
Total Daytime Sleep Time	1 RCT (Blytt 2018)	**MD -48.30 (-93.39, -3.21), I^2 n.a.**	106	Low[c]
CSDD	1 RCT (Erdal 2018)	**MD 2.64 (0.55, 4.73), I^2 n.a.**	162	Moderate

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
Blytt 2018: people with AD residing in nursing homes with MMSE < 20 and CSDD ≥ 8; in participants already on treatment with no analgesics or paracetamol 1 g die, were randomised to paracetamol 3 g die or matching placebo; in participants already being treated with non-opioid analgesics/paracetamol >1 g die and/or NSAIDs (excluding cardioaspirin) or were not taking any analgesic but had swallowing difficulties, they were randomised either to transdermal buprenorphine 5-10 micrograms/h or transdermal placebo
Erdal 2018: people with AD residing in nursing homes with MMSE < 20 and CSDD ≥ 8; in participants already on treatment with no analgesics or paracetamol 1 g die, were randomised to paracetamol 3 g die or matching placebo; in participants already being treated with non-opioid analgesics/paracetamol >1 g die and/or NSAIDs (excluding cardioaspirin) or were not taking any analgesics but had swallowing difficulties, they were randomised either to transdermal buprenorphine 5-10 micrograms/h or transdermal placebo

GINKGO BILOBA

Ginkgo biloba vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
NPI	4 RCT (Herrschaft 2012, Ihl 2011, Napryeyenko 2007, Nikolova 2013)	**MD -3.86 (-7.62, -0.10), I^2 97%**	1.596	Very Low[d]
ADL	4 RCT (Herrschaft 2012, Ihl 2011, Napryeyenko 2007, Nikolova 2013)	**SMD -0.54 (-0.91, -0.18), I^2 93%**	1.598	Very Low[d]
QoL	2 RCT (Herrschaft 2012, Ihl 2011)	**MD 2.00 (0.88, 3.12), I^2 0%**	806	Moderate

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
Herrschaft 2012: people with AD or VaD (mild to moderate dementia) and neuropsychiatric symptoms at the NPI with an NPI score of at least 4 on items such as agitation, apathy, anxiety, irritability; psychiatric units or neurological clinics; EGb761 in 240 mg dose formulation
Ihl 2011: population with AD or VaD, 12-item NPI score of at least 5, with at least one item score (other than delirium or hallucination) of 3 or more; setting not specified; EGb761 in 240 mg die formulation
Napreyeyenko 2007: people with AD or VaD, 12-item NPI score of at least 5, with at least one item score (other than delirium or hallucination) of 3 or higher; psychiatric or neurological hospital setting; EGb761 in 120mg formulation twice daily.

ACETYLCHOLINESTERASE INHIBITORS

Acetylcholinesterase inhibitors vs placebo nel trattamento della demenza				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Donepezil for cognitive symptoms				
NPI	1 RCT (Howard 2007)	MD -0.22 (-4.69, 5.13), I^2 n.a.	201	Very Low[a,b,c]
CMAI	1 RCT (Howard 2007)	MD 1.35 (-3.84, 6.54), I^2 n.a.	221	Very Low[b,c]
MMSE standardized	1 RCT (Howard 2007)	**MD 1.50 (0.15, 2.85), I^2 n.a.**	113	Low[c]
Discontinuing versus continuing donepezil for cognitive symptoms				
NPI	1 RCT (Holmes 2004)	**MD -6,20 (-11.37, -1.03), I^2 n.a.**	96	Moderate
NPI-Depression	1 RCT (Holmes 2004)	**MD -2.80 (-5.36, -0.24), I^2 n.a.**	96	Moderate
MMSE	1 RCT (Holmes 2004)	**MD 1.70 (0.17, 3.23), I^2 n.a.**	96	Moderate

Rivastigmine for nON-cognitive symptoms				
NPI	1 RCT (Mahlberg 2007)	MD -11.90 (-26.87, 3.07), I^2 n.a.	20	Very Low[b,c]
NPI-ag	1 RCT (Mahlberg 2007)	MD -2.70 (-6.62, 1.22), I^2 n.a.	20	Very Low[b,c]
CMAI	1 RCT (Ballard 2005)	MD -1.80 (-11.71, 8.11), I^2 n.a.	54	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Holmes 2004 (donepezil): people with AD and behavioural disorders with NPI ≥ 11; unspecified setting; open-label phase with dose up to 10 mg per day at 12 weeks, then randomisation to continuation of treatment or discontinuation for a further 12 weeks

Howard 2007 (donepezil): people with AD with pronounced agitation disturbances resulting in distress for caregiver and patient for at least two days per week for at least two weeks (CMAI ≥ 39); hospital setting; donepezil for 12 weeks (week 1 to 4 donepezil 5 mg die, week 5-12 donepezil 10 mg die)

Mahlberg 2007 (rivastigmine): people with AD and behavioural disorders; geriatric psychiatry unit setting; dose 3 mg die

Ballard 2005 (rivastigmine): people with AD and evident agitation by CMAI ≥ 39, agitation for at least 6 weeks and a score ≥ 4 on irritability and aberrant motor behaviour; care facilities setting; dose starting at 3-6 mg die and increasing to 9 mg die at weeks 12-26

MEMANTINE

Memantine vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
ADAS-Cog	3 RCT (Bakchine 2008, Peskind 2006, Porsteinsson 2008)	MD -0.17 (-1.60, 1.26), I^2 0%	425	Low[b]
ADCS-ADL	3 RCT (Bakchine 2008, Peskind 2006, Porsteinsson 2008)	MD 0.70 (-1.54, 2.93), I^2 10%	427	Low[b]
NPI	4 RCT (Bakchine 2008, Fox 2012, Peskind 2006, Porsteinsson 2008)	MD -1.75 (-5.49, 1.99), I^2 53%	565	Very Low [a,b,c]
CMAI	1 RCT (Fox 2012)	MD -3.80 (-12.09, 4.49), I^2 n.a.	149	Very Low[b,c]
MMSE standardized	1 RCT (Fox 2012)	MD 1.40 (-1.41, 4.21), I^2 n.a.	149	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Bakchine 2008 (Erratum of Bakchine 2007): people with AD (NINCDS-ADRDA) without previous treatment with drugs with psychotropic activity; setting not stated; treatment with 3 weeks titration and 21 weeks memantine (20 mg die).

Fox 2012: people with AD, two weeks of clinically relevant symptoms of agitation (CMAI ? 45); nursing or residential care homes setting; memantine (20 mg die) with 4 weeks titration from 5 mg die.

Peskind 2004: people with AD with MMSE from 10 to 22 and a MADRS score < 22 at screening; outpatients setting with caregiver availability; memantine (20 mg die) with 4-week titration starting at 5 mg die.

Porsteinsson 2008: AD populations with MMSE from 10 to 22 and a MADRS score < 22 at screening; community-dwelling patients; memantine (20 mg die) at a fixed dose for 24 weeks.

METHYLPHENIDATE

Methylphenidate vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
NPI	3 RCT (Herrmann 2008, Padala 2018, Rosenberg 2013)	MD -0.78 (-2.50, 0.94), I^2 65%	265	Very Low[b,d]

AES	3 RCT (Herrmann 2008, Padala 2018, Rosenberg 2013)	**MD -5.11 (-9.93, -0.29), I^2 80%**	144	Very Low[c,d]
CSDD	1 RCT (Padala 2018)	**MD -2.50 (-4.13, -0.87), I^2 n.a.**	59	Moderate
ADCS-CGIC	1 RCT (Mintzer 2021)	RR 1.25 (0.87, 1.79), I^2 n.a.	180	Low[b]
ADCS-CGIC improvment	1 RCT (Padala 2018)	**MD -1.20 (-1.88, -0.52), I^2 n.a.**	59	Moderate
MMSE	2 RCT (Herrmann 2008, Padala 2018)	MD 1.71 (-0.32, 3.74), I^2 63	84	Very Low[a,b,c]
IADL	1 RCT (Padala 2018)	**MD 2.30 (0.88, 3.72), I^2 n.a.**	59	Moderate
AE	1 RCT (Padala 2018)	RR 1.40 (0.71, 2.75), I^2 n.a.	59	Low[b,c]
SAE	3 RCT (Herrmann 2008, Padala 2018, Rosenberg 2013)	RR 1.87 (0.96, 3.63), I^2 0%	298	Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Mintzer 2021: people with AD (MMSE 10-28) with frequent or very frequent clinically significant apathy for at least 4 weeks at the NPI; First phase at 10 mg die. For the remaining study time, dose at 20 mg die with possibility of dose reduction in case of adverse events; duration 6 months

Padala 2018: population people with AD and clinically evident apathy according to AES-C with score >40; hospital setting; First phase at 10 mg die. For the remaining study time, dose at 20 mg die with possibility of dose reduction in case of adverse events; duration of treatment 12 weeks

Rosenberg 2013: population with AD, clinically evident apathy for at least 4 weeks at NPI; first phase at 10 mg die. For the remaining study time, dose at 20 mg die with possibility of dose reduction in case of adverse events, duration of treatment 6 weeks

Herrmann 2008: population people with AD and clinically relevant symptoms of apathy measured with a score of at least 1 on the NPI-Apathy subscale; hospital setting; first phase at 10 mg die. For the remaining study time, dose at 20 mg die with possibility of dose reduction in the event of adverse events, duration 2 weeks

MODAFINIL

Modafinil vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
FrSBe	1 RCT (Frackey 2012)	MD 0.27 (-11.74, 12.28), I^2 n.a.	22	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Frakey 2012: peple with AD and clinically relevant symptoms of apathy observed at FrsBe; hospital setting; modafinil at a dose of 100 mg per day the first week, increased to 200 mg per day in the second week, 8-week treatment.

PRAZOSIN

Prazosin vs placebo				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
BPRS	1 RCT (Wang 2009)	MD -18.00 (-41.93, 5.93), I^2 n.a.	13	Very Low[b,c]
NPI	1 RCT (Wang 2009)	**MD -12.00 (-19.15, -4.85), I^2 n.a.**	13	Low[c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
Wang 2009: AD population with the presence of aggressive behaviour and agitation at least twice a week for 2 weeks, and a score of at least 4 in at least one of the following BPRS scale items: anxiety, tension, hostility, arousal, non-cooperation; single nursing home facility setting; prazosin 1 mg per day increased to 6 mg per day according to a flexible RCT design for a duration of 8 weeks

MOOD STABILIZERS

Carbamazepine vs placebo

Outcomes	No. of Studies	Observed effect (95% CI), I^2	No. of participants	Certainty of evidence (GRADE)
BPRS	2 RCT (Olin 2001, Tariot 1998)	**MD -5.48 (-8.49, -2.47), I^2 68%**	72	Low[a]
PSMS	1 RCT (Wang 2009)	MD 0.10 (-1.28, 1.48), I^2 n.a.	13	Low[b]
MMSE	1 RCT (Olin 2009)	MD 0.40 (-2.01, 2.81), I^2 n.a.	21	Very Low[b,c]
AE	2 RCT (Olin 2001, Tariot 1998)	RR 1.19 (0.40, 3.58), I^2 76%	72	Very Low[b,c,d]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
Olin 2001: people with AD and significant agitation for at least one month and a BPRS score ≥ 2 for at least two items: tension, hostility, non-cooperation and arousal; caregiver setting; initial dose of 100mg/day increased after three days to 100mg/tridie
Tariot 1998: people with AD in care facilities with agitation disorders and a score of at least 3 on the following items of the BPRS: tension, hostility, non-cooperation, arousal; care facilities setting; carbamazepine initial dose of 100mg/day increased by 50mg every 2-4 days if no adverse events occurred

Valproate vs placebo

Outcomes	No. of Studies	Observed effect (95% CI), I^2	No. of participants	Certainty of evidence (GRADE)
CMAI	3 RCT (Herrmann 2007, Porsteinsson 2001, Tariot 2005)	MD 1.81 (-7.64, 11.27), I^2 72%	230	Very Low[a,b,c]
NPI	2 RCT (Herrmann 2007, Profenno 2005)	MD 4.05 (-0.19, 8.29), I^2 58%	47	Very Low[a,b,c]
BPRS	2 RCT (Porsteinsson 2001, Tariot 2005)	MD 0.23 (-2.14, 2.59), I^2 0%	224	Very Low[b,c]
MMSE	4 RCT (Herrmann 2007, Porsteinsson 2001, Profenno 2005, Tariot 2005)	**MD -1.02 (-1.89, -0.16), I^2 0%**	248	Moderate
PSMS*	2 RCT (Porsteinsson 2001, Tariot 2005)	MD 0.76 (-0.03, 1.55), I^2 0%	203	Low[b]
AE	3 RCT (Herrmann 2007, Porsteinsson 2001, Tariot 2005)	RR 1.33 (0.85, 2.09), I^2 71%	149	Very Low [a,b]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
Herrmann 2007: people with probable AD (NINCDS-ADRDA) for at least one year and residing in care facilities and with NPI score ≥ 8; care facilities setting; dose started at 125mg/day, with titration to 500mg/day, in the first 2 weeks. Then, the dose could be increased to a maximum of 1,500mg/day or decreased according to efficacy and tolerability.
Porsteinsson 2001: people with AD, vascular dementia or mixed dementia and a BPRS score ≥ 3 on items such as anxiety, hostility, uncooperativeness or arousal; setting care facilities; initial dose at 375 mg per day increased by 125 mg every 3 days or reduced according to the subject's response, until an optimal dose was reached, final dose range was 375 mg per day-1375 mg per day
Profenno 2005: people with AD without symptoms of agitation or psychosis; university-hospital setting; target dose 1000 mg die and 1500 mg die starting at 250 mg die in increments of 250mg per week until target dose is reached

Tariot 2005: people with AD and behavioural disorders from BPRS ≥ 14 and scores of at least 2 on items such as aggression, hostility, arousal; nursing homes setting; dose 250 mg die with increments of 125 mg die every three days up to target dose of 750 mg die
* Physical Self-Maintenance Scale, scale on activities of daily living

Review question 21b (RQ NICE). What are the most effective non-pharmacological interventions for managing illness emergent non-cognitive symptoms, such as psychosis, depression, behavioural changes in people living with dementia?

ACUPUNCTURE

Acupuncture for people with dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
CMAI	1 RCT (Kwan 2017)	MD 1.21 (-4.96, 9.38), I^2 n.a.	78	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations **Kwan 2017:** people with dementia and agitation in residential care homes; two weekes-intervention and follow-up at 6 weeks.				

AROMATHERAPY

Aromatherapy for people with dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Aromatherapy – lavander				
CMAI	2 RCT (Lin 2007, Yang 2015)	**MD -6.32 (-9.21, -3.44), I^2 0%**	200	Moderate
NPI	2 RCT (Fujii 2008, Lin 2007)	**MD -7.24 (-12.60, -1.89), I^2 0%**	98	Very Low[b,c]
Aromatherapy – lemon balm				
CMAI	1 RCT (Ballard 2002)	**MD -8.10 (-14.78, -1.42), I^2 n.a.**	72	Low[b,c]
NPI	1 RCT (Burns 2011)	MD 2.80 (-5.84, 11.44), I^2 n.a.	63	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations **Ballard 2002:** people with dementia and agitation; care home setting; lemon balm oil twice a day for 4 weeks. **Burns 2011:** people with moderate dementia and agitation for at least 4 weeks; clinical centers e nursing homes; lemon balm oil for 12 weeks. **Fujii 2008:** people with moderate/severe dementia and at least one BPSD; long-term care facility; lavender three times a day for 4 weeks. **Lin 2007:** people with dementia and significant agitation; care homes setting; lavender for 3 weeks, wash-out for 2 weeks and crossover. **Yang 2015:** people with dementia and agitation; long-term care facilities; lavender for 5 times per week for 4 weeks.				

RECREATIONAL ACTIVITIES

Recreational activities for people with dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Recreational and creative activities to relieve pain				
PAINAD	1 RCT (Tse 2018)	**MD -1.70 (-2.52,-0.88), I^2 n.a.**	53	Moderate
Sintomi depressivi – GDS	1 RCT (Tse 2018)	MD -1.60 (-4.25, 1.05), I^2 n.a.	53	Very Low[b,c]
Recreational and individual/group artistic activities				
CMAI	1 RCT (Yuen 2019)	MD 8.52 (0.72, 16.32), I^2 n.a.	46	Low[b,c]
ABMI*	2 RCT (Cohen-Mansfield 2007, Cohen-Mansfield 2012)	MD -3.94 (-10.24, 2.35), I^2 89%	292	Very Low[b,c,d]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

*Agitated Behaviors Mapping Instrument

Tse 2018: people with dementia suffering from chronic pain (self-reported or PAINAD ≥ 1; nursing home in Hong Kong; 1h "play activity program" intervention one time per week for 8 weeks. Each session had a different theme: interventions were aimed at entertaining participants, creative interventions (e.g. art, puzzle), interventions to help people remove the thought of pain from their lives.

Cohen-Mansfield 2007: people with dementia and agitation institutionalized from at least 3 weeks; 12 nursing homes; intervention (TREA protocol tree) involving the identification of an individualised plan aimed at identifying the aetiology of agitated behaviour and activating a protocol based on the individual's unique characteristics.

Cohen-Mansfield 2012: people with dementia and agitation institutionalized from at least 3 weeks; setting nursing homes; TREA protocol; when the person's problem was depression and loneliness, interventions included animal-assisted therapy, one-to-one interaction with the assistant, simulated interaction (family videos), lifelike baby dolls, group activities; when the problem was boredom, standard interventions were artistic or creative activities, outdoor play activities, exercise activities, stimulation such as massage, music or videos; when problems of malaise were evident, tmodification of the pharmacological approach or vision or hearing problems were assessed.

Yuen 2019: people with dementia and Global Deterioration Scale (GDS) > 4 and significant agitation measured with CMAI; setting long-term care facilities; Montessori method.

PSYCHOSOCIAL INTERVENTIONS

Psychosocial intervention for people with dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
CMAI	1 RCT (Fossey 2006)	MD -0.40 (-1.81, 1.01), I^2 n.a.	334	Low[b]
CSDD	1 RCT (Bruvik 2013)	MD -0.20 (-2.27, 1.87), I^2 n.a.	225	Low[b]
QoL-AD	1 RCT (Yang 2021)	**MD 2.20 (1.19, 3.21), I^2 n.a.**	215	Moderate
Depressive symptoms– GDS	1 RCT (Yang 2021)	**MD -1.66 (-2.77, -0.55), I^2 n.a.**	215	Moderate
MMSE	1 RCT (Yang 2021)	MD 0.06 (-1.54, 1.66), I^2 n.a.	215	Low[b]
RAID*	1 RCT (Yang 2021)	MD 0.00 (-0.92, 0.92), I^2 n.a.	215	Low[b]
NPI	1 RCT (Yang 2021)	MD -2.02 (-5.59, 1.55), I^2 n.a.	215	Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
* Rating Anxiety in Dementia
Fossey 2006: people with dementia; nursing homes; multidimentional activities intervention.
Bruvik 2013: people with dementia and caregiver stress; community-dwelling setting; counselling, education and group meetings for 12 months.
Yang 2021: people with AD and at least one negative experience on psychosocal intervention; outpatients; stressor assessment intervention, identification of therapeutic goals for 12 months.

COMPUTER

Computer use for people with dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
MoCA	1 RCT (Sautter 2021)	**MD 5.57 (0.28, 10.86), I^2 n.a.**	62	Low
Depressive symptoms – GDS mild dementia	1 RCT (Sautter 2021)	**MD -5.00 (-8.08,-1.92), I^2 n.a.**	62	Low
Depressive symptoms – GDS moderate dementia	1 RCT (Sautter 2021)	MD 0.42 (-6.07, 6.91), I^2 n.a.	62	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations **Sautter 2021:** people with mild, moderate/severe dementia; nursing homes; iN2L user-friendly computer intervention for 1h a day for 5 days a week for 12 weeks (guided phase) followed by a phase where the person could use it independently (supported phase) for 12 weeks.				

PHYSICAL EXERCISE

Physical exercise for people with dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Intervention based on increasing levels of physical exercise aimed at improving activities of daily living				
Depressive symptoms – GDS	1 RCT (Boström 2016)	MD -0.06 (-0.87, 0.75), I^2 n.a.	148	Low[b]
MADRaS	1 RCT (Boström 2016)	MD 0.16 (-1.54, 1.86), I^2 n.a.	148	Low[b]
Intervention based on exercises specifically aimed at strengthening both upper and lower limbs in hospitalized people with dementia				
CMAI	1 RCT (Fleiner 2017)	MD -3.90 (-11.25, 3.45), I^2 n.a.	70	Very Low[b,c]
NPI	1 RCT (Fleiner 2017)	MD -5.90 (-13.01, 1.21), I^2 n.a.	70	Low[b]
Intervention based on exercises specifically targeted to muscle strengthening, balance, and motor coordination				
NPI	1 RCT (MHighis 2019)	MD -4.60 (-14.02, 4.82), I^2 n.a.	98	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations **Boström 2016:** people with dementia and dependent in IADL; residential care facilities setting; 40 sessions over 4 months, exercises simulating daily activities with gradual intensity.				

Fleiner 2017: people with dementia hospitalized for at least 1 week before enrollment; hospital setting; ankle or upper and lower limb strengthening exercises for 2 weeks.
MHighis 2019: people with dementia; nursing homes; strengthening, coordination, balance and aerobic intervention for 24 weeks.

LIGHT THERAPY

Light therapy for people with dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
CAM	1 RCT (Zou 2022)	**MD -1.68 (-3.20, -0.16), I^2 n.a.**	61	Moderate
CMAI	2 RCT (Burns 2009, Riemersma-van der Lek 2008)	MD -3.08 (-10.32, 4.17), I^2 0%	142	Very Low[b,c]
NPI	2 RCT (Dowling 2005, Zou 2022)	MD -1.89 (-7.79, 4.00), I^2 0%	131	Very Low[b,c]
BEHAVE-AD	1 RCT (Lyketsos 1999)	MD 0.70 (-3.25, 4.65), I^2 n.a.	30	Low[b]
CSDD	1 RCT (Riemersma-van der Lek 2008)	MD -0.10 (-3.91, 3.71), I^2 n.a.	94	Low[b]
MMSE	1 RCT (Riemersma-van der Lek 2008)	MD 1.50 (-1.77, 4.77), I^2 n.a.	94	Very Low[b,c]
CRBRS*	1 RCT (Burns 2009)	MD 1.00 (-3.11, 5.11), I^2 n.a.	48	Low[b]
MOUSEPAD**	1 RCT (Burns 2009)	MD 0.20 (-6.32, 6.72), I^2 n.a.	48	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
* Modified Crichton Royal Behavioural Rating Scale
** Manchester and Oxford Universities Scale for the Psychopathological Assessment of Dementia
Dowling 2005: people with AD; long-term care facilities; treatment for 11 weeks, first phase morning bright light.
Zou 2022: people with AD and sleep disorders; morning light therapy for 4 weeks.
Burns 2009: people with dementia, sleep disorders and ai least 1 agitation problem; nursing home setting; bright light therapy for 8 weeks.
Lyketsos 1999: people with dementia and BPSD assessed by BEHAVE-AD; long-term care facilities setting; morning bright light for 4 weeks.
van der Lek 2008: people with dementia and sleep disorders; nursing homes setting; bright LT intervention from 9 a.m. to 6 p.m.

THERAPEUTIC GARDEN

Therapeutic garden for people with dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
NPI	1 RCT (Pedrinolla 2019)	**MD -32.60 (-39.64, -25.56), I^2 n.a.**	163	Moderate
Reduction in the mean dose (in mg) of quetiapine	1 RCT (Pedrinolla 2019)	**MD -160 (-179.29, -140.71), I^2 n.a.**	163	Moderate

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
Pedrinolla 2019: people with AD and NPI > 55; nursing home setting; 2h session, 5 time per week for 6 months.

SLEEP INTERVENTIONS

Sleep interventions for people with dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Intervention based on personalized activities specifically tailored based on disease severity				
Total Nightime Sleep Time	1 RCT (Richards 2005)	MD 39.76 (-43.02, 122.54), I^2 n.a.	50	Low[b,c]
Total Daytime Sleep Time	1 RCT (Richards 2005)	**MD -43.59 (-82.84 -4.34), I^2 n.a.**	50	Very Low[c]
Multicomponent interventions including improving sleep hygiene, exposure to light, and physical activity				
Total Nightime Sleep Time	2 RCT (Alessi 2005, McCurry 2011)	MD 18.04 (-14.05, 50.13), I^2 0%	184	Low[b,c]
Total Daytime Sleep Time	1 RCT (McCurry 2011)	MD 14.90 (-62.17, 91.97), I^2 n.a.	66	Very Low[b,c]
Interventions based on exposure to bright light and controlled light				
Total Nightime Sleep Time	4 RCT (Dowling 2005, Hjetland 2021, McCurry 2011, Riemersma-van der Lek 2008)	MD 9.58 (-23.38, 42.54), I^2 0%	300	Low[b,c]
Total Daytime Sleep Time	2 RCT (Hjetland 2021, McCurry 2011)	MD 0.81 (-43.49, 45.11), I^2 0%	136	Low[b,c]
Intervention based on a daily 30-minute walk				
Total Nightime Sleep Time	1 RCT (McCurry 2011)	MD 16.10 (-57.48, 89.68), I^2 n.a.	65	Very Low[b,c]
Total Daytime Sleep Time	1 RCT (McCurry 2011)	MD 13.10 (-64.25, 90.45), I^2 0%	65	Very Low[b,c]
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

PSYCHOLOGICAL INTERVENTIONS

Psychological interventions for people with dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Cognitive Behavioral Therapy for the treatment of psychological and behavioral disorders				
MMSE	2 RCT (Spector 2015, Teri 1997)	MD -0.02 (-1.65, 1.60), I^2 0%	112	Very Low[b,c]
Depressive symptoms – CSDD	2 RCT (Spector 2015, Teri 1997)	**MD -4.30 (-6.09, -2.52), I^2 0%**	112	Moderate
Depressive symptoms – GDS	1 RCT (Stanley 2013)	MD 1.70 (-3.49, 6.89), I^2 n.a.	32	Very Low[b,c]
Ansia – RAID	2 RCT (Spector 2015, Stanley 2013)	**MD -4.64 (-8.87, -0.40), I^2 0%**	82	Low[c]
QoL-AD	2 RCT (Spector 2015, Stanley 2013)	MD -0.69 (-3.78, 2.39), I^2 0%	82	Low[b]
NPI	1 RCT (Spector 2015)	MD -10.06 (-20.63, 0.51), I^2 n.a.	50	Very Low[b,c]
Anxiety – HADS*	1 RCT (Spector 2015)	MD -0.05 (-5.60, 5.50), I^2 n.a.	50	Very Low[b,c]
Psychodynamic and interpersonal therapy				
MADRaS	1 RCT (Tappen 2009)	**MD -8.46 (-16.66, -0.26), I^2 n.a.**	30	Low

Depressive symptoms – CSDD	1 RCT (Burns 2005)	MD -0.90 (-3.18, 1.38), I^2 n.a.	40	Low[b]
MMSE	1 RCT (Burns 2005)	MD -0.90 (-4.20, 2.40), I^2 n.a.	40	Very Low[b,c]
BADL	1 RCT (Burns 2005)	MD 1.80 (-3.10, 6.70), I^2 n.a.	40	Very Low[b,c]
Individual/group sessions of counselling and structured support				
Depressive symptoms – GDS	1 RCT (Young 2014)	**MD -8.67 (-10.05, -7.29), I^2 n.a.**	36	Moderate
Depressive symptoms – CSDD	1 RCT (Waldorff 2012)	**MD -1.58 (-2.79, -0.37), I^2 n.a.**	330	Moderate
NPI	1 RCT (Waldorff 2012)	MD 0.42 (-0.55, 1.39), I^2 n.a.	330	Low[b]
MMSE	1 RCT (Waldorff 2012)	MD 0.25 (-0.74, 1.24), I^2 n.a.	330	Low[b]
QoL-AD	1 RCT (Waldorff 2012)	MD 0.22 (-1.15, 1.59), I^2 n.a.	330	Low[b]
ADL	1 RCT (Waldorff 2012)	MD -1.76 (-4.86, 1.34), I^2 n.a.	330	Low[b]
Mindfulness intervention				
Depressive symptoms – CSDD	1 RCT (Churcher Clarke 2017)	MD 1.58 (-2.53, 5.69), I^2 n.a.	31	Very Low[b,c]
Ansia – RAID	1 RCT (Churcher Clarke 2017)	MD 0.07 (-4.82, 4.96), I^2 n.a.	31	Very Low[b,c]
MMSE	1 RCT (Churcher Clarke 2017)	MD 1.65 (-2.97, 6.27), I^2 n.a.	31	Very Low[b,c]
QoL-AD	1 RCT (Churcher Clarke 2017)	MD 4.14 (-0.03, 8.31), I^2 n.a.	31	Very Low[b,c]
Reminiscence based on recalling personal memories, history, and traditions				
ARS*	1 RCT (Inel Manav 2019)	**MD 11.82 (7.97, 15.67), I^2 n.a.**	32	Low
Depressive symptoms – GDS	1 RCT (Ching-Teng 2020)	**MD -7.10 (-12.64, -1.56), I^2 n.a.**	24	Low
Depressive symptoms – CSDD	1 RCT (Bademli 2018)	**MD -2.13 (-4.09, -0.17), I^2 n.a.**	60	Low

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

* Anxiety Rating Scale

Spector 2015: people with dementia and anxiety; outpatients setting; CBT intervention for 6 months

Stanley 2012: people with AD referred to geriatrics, psychiatry, and neurology departments with anxiety disorders demonstrated by NPI-Anxiety subscale; Intervention: Peaceful Mind programme comprised up to 12 weekly sessions carried out at home for up to 3 months and then short telephone interventions (up to 8 weekly) from 3-6 months. The sessions included self-monitoring of anxiety symptoms, deep breathing and other skills.

Teri 1997: people with AD with criteria for major or minor depressive disorder; community-based setting; 9 sessions of 1h, once a week (pleasant events) and problem solving, counselling and caregiver support activities.

Burns 2005: people with mild AD; outpatients living in the community; 6 conversational model sessions for a duration of 3 months.

Tappen 2009: people with AD; long term care facility setting; therapeutic conversation intervention for 16 weeks, 3 times a week.

Waldorff 2012: people with mild AD; outpatient setting; counselling, support and psychosocial intervention semi-coupled for 12 months.

Young 2014: people with dementia; non-specified setting; support group intervention of 10 sessions, once a week.

Churcher-Clarke 2017: people with dementia; care homes setting; adapted mindfulness programme twice a week for 5 weeks.

MUSIC THERAPY

Music therapy for people with dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Active music therapy				
CMAI	2 RCT (Ceccato 2012, Sung 2012)	MD 1.05 (-3.59, 5.68), I^2 0%	89	Very Low[b,c]
MADRaS	1 RCT (Baker 2022)	**MD -4.65 (-7.68, -1.62), I^2 0%**	239	Moderate
MMSE	3 RCT (Ceccato 2012, Giovagnoli 2018, Lyu 2018)	MD -0.24 (-1.34, 0.86), I^2 0%	287	Low[b]
NPI	4 RCT (Baker 2022, Choi 2009, Giovagnoli 2018, Lyu 2018)	**MD -3.92 (-5.35, -2.48), I^2 0%**	496	Moderate
NPI-Ag	1 RCT (Choi 2009)	**MD -0.80 (-1.41, -0.19),** I^2 0%	20	Moderate
RAID	1 RCT (Sung 2012)	MD 0.63 (-5.12, 6.38), I^2 n.a.	55	Very Low[b,c]
GDS	3 RCT (Ceccato 2012, Choi 2009, Liu 2021)	MD -0.21 (-0.62, 0.20), I^2 60%	120	Low[a,b]
HAMA	1 RCT (Liu 2021)	**MD -2.88 (-3.87, -1.89), I^2 n.a.**	50	Moderate
ADL	2 RCT (Ceccato 2012, Giovagnoli 2018)	**MD -0.57 (-1.02, -0.12), I^2 0%**	79	Low[e]
IADL	1 RCT (Giovagnoli 2018)	MD 0.53 (-1.56, 2.62), I^2 n.a.	45	Low[b]
QoL-AD	1 RCT (Baker 2022)	**MD -3.51 (-6.05, -0.98), I^2 0%**	239	Moderate
Receptive music therapy				
NPI	1 RCT (D'Aniello 2021)	**MD -10.00 (-16.42, -3.58), I^2 n.a.**	60	Low[c]
RAID	1 RCT (Sung 2010)	MD -1.83 (-5.21, 1.55), I^2 n.a.	52	Low[b]
CMAI	1 RCT (McCreedy 2022)	MD 1.33 (-7.93, 10.59), I^2 n.a.	976	Low[b]
n. medio persone su antipsicotici	1 RCT (McCreedy 2022)	MD -3.40 (-7.14, 0.34), I^2 n.a.	976	Very Low[b,]
n. medio persone su antidepressivi	1 RCT (McCreedy 2022)	MD -1.30 (-5.46, 2.86), I^2 n.a.	976	Very Low[b,c]
n. medio persone su ansiolitici	1 RCT (McCreedy 2022)	MD -3.50 (-7.94, 0.94), I^2 n.a.	976	Very Low[b,]
Combined active/receptive music therapy (group sessions based on singing and playing musical instruments)				
AES	1 RCT (Tang 2018)	MD -3.85 (-9.45, 1.75), I^2 n.a.	77	Very Low[b,c]
CSDD	1 RCT (Chu 2014)	MD -1.89 (-7.07, 3.29), I^2 n.a.	104	Very Low[b,c]
CMAI	2 RCT (Lin 2011, Ridder 2013)	**MD -6.23 (-11.97, -0.49), I^2 0%**	142	Moderate
MMSE	2 RCT (Chu 2014, Tang 2018)	MD 1.37 (-0.73, 3.46), I^2 n.a.	181	Very Low[b,c]
MADRaS	1 RCT (Baker 2022)	**MD -5.30 (-8.79, -1.81), I^2 n.a.**	159	Moderate
NPI	1 RCT (Baker 2022)	**MD -3.10 (-5.74, -0.46), I^2 n.a.**	159	Moderate
QoL-AD	1 RCT (Baker 2022)	**MD -3.70 (-6.78, -0.62), I^2 n.a.**	159	Moderate
CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Baker 2022: people with dementia, care home residents with mild to Moderate depression MADRaS > 8; care home setting; group music therapy (GMT) intervention consisting of small classes of 8-10 subjects with the aim of assessing psychosocial needs, familiar songs, music-stimulated reminiscence, making music with percussion instruments, spontaneous music; recreational choir intervention (RCS) consisting of groups of 15-20 persons. The RCS sessions were structured around singing, using familiar and favourite repertoire with texts displayed on a screen. The RCS aimed at fostering connection, emotional well-being and enjoyment of music making in a group. Assessments at 3, 6, 12 months after baseline.
Giovagnoli 2018: outpatients population with AD and cognitive-behavioural disorders; Active music therapy intervention was in combination with memantine vs memantine alone, AChEIs were also allowed. The intervention comprised two sessions per week (each 40 minutes), the sessions involved improvised music therapy and the choice of musical instruments to be played with free technique. No musical competence required. The treatment lasted 24 weeks.
Liu 2021: people with mild/moderate AD, male veterans homes residents with anxiety level (HAMA score) in stable therapy for at least 3 months with psychotropic medication; group music therapy intervention once a week in the morning (60 min) for 12 weeks. Use of percussion instruments and familiar music.
Lyu 2018: people with AD; hospital setting (community-based); singing their favourite songs for 3 months.
Choi 2009: people with dementia; day centre setting; intervention singing, playing drawing and writing songs for 50 min 3 times a week for 5 weeks.
Ceccato 2012: people with dementia; outpatients setting; protocol with a series of music sessions 2 times a week for 12 weeks.
Sung 2012: people with dementia and at least one BPSD; residential care setting; intervention twice a week for 6 weeks also using percussion instruments.
D'Aniello 2021: people with moderate-severe dementia; nursing homes setting; listening to chosen music with the patient for 16 sessions for 8 weeks.
Sung 2010: people with moderate-severe dementia; long-term care facilities setting; listening to own favourite music for 12 sessions for 6 weeks.
Lin 2011: people with dementia; nursing homes setting; singing, rhythmic and listening music intervention for 12 sessions for 6 weeks.
Ridder 2013: people with moderate-severe dementia and symptoms of agitation; setting nursing homes; intervention playing instruments, singing and listening to music twice a week for 6 weeks.
Tang 2018: people with mild-moderate dementia with apathy; setting nursing homes; listening to music and sounds, singing nostalgic songs, use of musical instruments for 12 weeks.
Chu 2014: people with dementia; setting nursing homes; intervention playing of instruments, singing and listening to music for 6 weeks twice a week.

CARE COORDINATION

Care coordination for people with dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Interdisciplinary model for the treatment of neuropsychiatric symptoms (TIME, Targeted Interdisciplinary Model for Evaluation and Treatment of Neuropsychiatric Symptoms)				
CMAI	1 RCT (Lichtwarck 2018)	MD -6.00 (-13.69, 1.69), I^2 n.a.	229	Low[b]
CSDD	1 RCT (Lichtwarck 2018)	MD -2.00 (-4.94, 0.94), I^2 n.a.	222	Low[b]
NPI	1 RCT (Lichtwarck 2018)	MD -5.50 (-13.72, 2.72), I^2 n.a.	229	Low[b,]
NPI-Ag	1 RCT (Lichtwarck 2018)	**MD -1.60 (-2.93, -0.27), I^2 n.a.**	229	Moderate
Implementation of Guidelines produced by AGS* and AAGP*				
CMAI	1 RCT (Rapp 2013)	**MD -9.22 (-15.03, -3.41), I^2 n.a.**	229	Low[c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
Lichtwark 2018: people with dementia and agitation; nursing homes setting; educational intervention on staff for the management of non-cognitive symptoms for a duration of 12 weeks.
Rapp 2013: nursing homes setting; follow-up at 10 months.
* American Geriatrics Society
** dall'American Association of Geriatric Psychiatry

ROBOT THERAPY

Robot therapy for people with dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Interactive robot with the appearance of a baby seal				
CMAI	1 RCT (Koh 2018)	**MD -6.07 (-9.57, -2.57), I^2 n.a.**	33	Moderate
MMSE	1 RCT (Koh 2018)	MD 0.74 (-0.15, 1.63), I^2 n.a.	33	Low[b]
CMAI-SF	3 RCT (Liang 2017, Moyle 2017, Pu 2020)	MD -1.40 (-4.36, 1.56), I^2 0%	342	Low[b]
CSDD	3 RCT (Liang 2017, Petersen 2017, Pu 2020)	**MD -1.85 (-3.08, -0.62), I^2 7%**	128	Moderate
NPI-Q	1 RCT (Liang 2017)	MD 0.26 (-5.41, 5.93), I^2 n.a.	24	Very Low[b,c]
RAID	2 RCT (Petersen 2017, Pu 2020)	**MD -1.92 (-3.13, -0.72), I^2 0%**	104	Low[c]
Interaction with a humanoid companion robot dressed in knitted cloth				
NPI	1 RCT (Chen 2020)	MD -0.60 (-3.04, 1.84), I^2 n.a.	103	Low[b]
Depressive symptoms – GDS	1 RCT (Chen 2020)	MD -0.10 (-1.31, 1.11), I^2 n.a.	103	Low[b]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
Koh 2018: people with dementia; nursing homes setting; 12 sessions for 6 weeks
Liang 2017: people with dementia; day care centre setting; 2/3 sessions per week for 6 weeks
Moyle 2017: people with dementia; nursing homes setting; 3 sessions per week for 10 weeks
Pu 2020: people with dementia and chronic pain; nursing homes setting; 6 sessions per week for 6 weeks
Petersen 2017: people with mild to moderate dementia; setting nursing homes; 3 sessions per week for 3 months
Chen 2020: people with dementia; setting nursing homes; weeks 1-8 baseline, weeks 9-16 intervention, weeks 17-24 removal of intervention, weeks 25-32 reintroduction of intervention

TRANSCRANIAL STIMULATION

Transcranial stimulation for people with dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
AES	1 RCT (Padala 2020)	**MD -10.20 (-15.18, -5.22), I^2 n.a.**	19	Low[c]
ADL	2 RCT (Padala 2020, Zhou 2022)	MD -0.19 (-1.21, 0.83), I^2 0%	84	Low[b]
IADL	1 RCT (Padala 2020)	MD 3.40 (-0.42, 7.22), I^2 n.a.	19	Very Low[b,c]
MMSE	1 RCT (Padala 2020)	MD 0.90 (-1.53, 3.33), I^2 n.a.	19	Very Low[b,c]
PSQI	1 RCT (Zhou 2022)	**MD -2.31 (-3.56, -1.06), I^2 n.a.**	65	Moderate
ADAS-Cog	1 RCT (Zhou 2022)	MD 1.59 (-0.92, 4.10), I^2 n.a.	65	Low[b]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
Padala 2020: people with AD and apathy; outpatient setting; intervention for 12 weeks
Zhou 2022: people with AD and sleep disorders; outpatient setting; intervention for 4 weeks

TAILORED ACTIVITY PROGRAM

Tailored Activity Program for people with dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
NPI-Ag	2 RCT (de Oliveira 2019, Oliveira 2021)	**MD -6.05 (-10.46, -1.64), I^2 0%**	75	Moderate
NPI-Aggressive	2 RCT (de Oliveira 2019, Oliveira 2021)	**MD -3.48 (-5.80, -1.15), I^2 0%**	75	Moderate
NPI-Anxiety	2 RCT (de Oliveira 2019, Oliveira 2021)	**MD -5.06 (-9.58, -0.53), I^2 0%**	75	Moderate
NPI-Aggr+anxiety	1 RCT (Gitlin 2021)	MD 2.39 (-13.41, 18.19), I^2 n.a.	206	Very Low[b,c]
NPI total	1 RCT (Novelli 2018)	MD -10.07 (-25.73, 5.59), I^2 n.a.	30	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

de Oliveira 2018: people with dementia and the presence of a caregiver for at least 4 hours a day, presence of at least 3 types of neuropsychiatric symptoms; outpatient clinic setting from university hospital in Brazil; TAP home version intervention; the TAP had 3 different phases: an initial phase of assessment of cognitive and functional abilities and characterisation of the person's previous skills, abilities and interests; implementation of the planned activities and instruction of the caregiver to perform the intervention at home; generalisation of daily activity techniques and methods to simplify activities as the disease progresses.

Gitlin 2021: people with dementia with agitated/aggressive behaviour (NPI-C frequency or severity ≥ 2), stable treatment with antidementia drugs, psychotropics, antidepressants (also caregivers); TAP for a duration of 3 months with 1h-1.5h sessions.

Novelli 2018: people with dementia and at least one BPSD, and caregivers; community-based; TAP for a duration of 4 months with a total of 8 sessions.

Oliveira 2021: people with moderate-severe dementia, one caregiver, and at least 3 BPSD; outpatients setting; in-home TAP for a duration of 3 months in 8 sessions.

ANIMAL ASSISTED THERAPY

Animal assisted therapy for people with dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
BARS*	1 RCT (Olsen 2016)	MD -3.64 (-7.62, 0.34), I^2 n.a.	51	Very Low[b,c]
CSDD	1 RCT (Olsen 2016)	MD 0.62 (-7.02, 8.26), I^2 n.a.	51	Very Low[b,c]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Olsen 2016: people with dementia; nursing homes setting; intervention with dogs for a duration of 12 weeks with follow up at 3 months.

***** Brief Agitation Rating Scale

DOLL THERAPY

Doll therapy for people with dementia				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
CMAI	1 RCT (Yilmaz 2021)	MD -17.10 (-39.64, 5.44), I^2 n.a.	29	Very Low[b,c]
CMAI-SF*	1 RCT (Moyle 2019)	MD 0.01 (-3.18, 3.30), I^2 n.a.	35	Very Low[b,c]
NPI	2 RCT (Molteni 2022, Yilmaz 2021)	MD -18.95 (-41.64, 3.75), I^2 75%	158	Very Low[b,c,d]

CI: confidence interval; SMD: standardized mean difference; MD: mean difference; AE: adverse events; SAE: serious adverse events; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Yilmaz 2020: people with moderate-severe dementia (very high mean age); nursing homes setting; intervention with DT for 8 weeks

Moyle 2018: women with dementia and documented presence of anxiety, aggression, agitation; setting nursing homes; intervention with DT 3 times a week for 3 weeks

Molteni 2022: women with moderate-severe dementia and at least one BPSD in addition to depression and apathy; nursing home setting; DT intervention for a duration of 30 days

***** CMAI-short form

Review question 22a (RQ NICE). Are there effective methods for assessing intercurrent illness in people living with dementia that are different from those already in use for people who do not have dementia?

Pain assessment				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
PAINAD VS NRS				
Presence of pain (PAINAD)	1 cohort study (Mosele 2012)	**MD 0.70 (0.26, 1.14), I^2 n.a.**	600	Low
Presence of pain (NRS)	1 cohort study (Mosele 2012)	MD 0.30 (-0.25, 0.85), I^2 n.a.	600	Low[b]
Prevalence of pain (PAINAD)	1 cohort study (Mosele 2012)	**RR 1.39 (1.20, 1.62), I^2 n.a.**	600	Low[b]
Prevalence of pain (NRS)	1 cohort study (Mosele 2012)	**RR 1.19 (1.00, 1.41), I^2 n.a.**	600	Low[b]
Correlation PAINAD-NRS	1 correlational (De Waters 2008)	CI group p<0.001; non-CI group p<0.001	25	Very Low[b]
NOPPAIN VS NRS E VDS				
Correlation NOPPAIN-NRS-VDS	1 cross-sectional (Horgas 2007)	CI group p=NS; non-CI group p<0.001	40	Low[b]
Correlation NOPPAIN-total number of pain indicators	1 cross-sectional (Horgas 2007)	CI group p<0.001; non-CI group p<0.001	40	Low[b]
REPOS VS PAINAD E NRS				
Correlation REPOS-PAINAD-NRS	1 case-control (Van Herk 2009)	CI group PAINAD rs=0.75 (0.66, 0.82); NRS rs= 0.19 (0.01, 0.35) non-CI group PAINAD rs=0.61 (0.40, 0.76); NRS rs=0.36 (0.09, 0.58)	174	Very Low[b]
Pain	1 case-control (Van Herk 2009)	CI group=5 (IQR 3 - 5); non-CI group=4 (IQR 3 - 5); p=0.0002)	174	Very Low[b]
ABBEY VS PAINAD AND NOPPAIN VS SELF-REPORT				
corr. observation-self-report	1 cohort study (Lukas 2013)	CI group Abbey, PAINAD, NOPPAIN all p<0.001 non-CI group Abbey (p=0.01), PAINAD (p=0.06), NOPPAIN (p=0.01)	125	Moderate
Agreement scales and self-report	1 cohort study (Lukas 2013)	CI group Abbey 78.3%, PAINAD 73.3%, NOPPAIN 80.0% non-CI group Abbey 66.1%, PAINAD 66.1%, NOPPAIN 69.2%	125	Moderate
PIMD VS MOBID				
Correlation PIMD-MOBID	1 cohort study (Ersek 2019)	pain intensity: at rest p=0.02, at movement p<0.001	190	Low[b]
Correlation PIMD-ECPIR	1 cohort study (Ersek 2019)	pain intensity: at rest p=0.8, at movement p<0.001	190	Low[b]

CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%
PAINAD: Pain Assessment in Advanced Dementia; NRS: numerical rating scale; VDS: verbal descriptor scale; CI: cognitively impaired; NOPPAIN: Non-Communicative Patient's Pain Assessment Instrument; Abbey: Abbey pain scale for dementia patients; PIMD: pain intensity measure for persons with dementia; ECPIR: Expert clinician pain intensity rating

Fall risk assessment				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Performance of BBS (Berg Balance Scale) for fall risk assessment				
BBS performance	1 case-control (Kato-Narita 2011)	**MD -1.80 (-3.06, -0,54), I^2 n.a.**	88	Low
Correlation between BBS scores and the number of falls	1 case-control (Kato-Narita 2011)	CI group p=0.045; non-CI group p=0.015	88	Low[b]
CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%				

Delirium assessment				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
DRS VS STANDARD CRITERIA				
AUC DRS vs DSM-5	1 cross-sectional (Sepulveda 2015)	CI group 87.03%; non-CI group 98.86%; MD 11.83 (3.07, 20.59)	125	Low
AUC DRS vs ICD-10	1 cross-sectional (Sepulveda 2015)	CI group 86.69%; non-CI group 97.37%; MD 10.68 (1.62, 19.74)	125	Low
AUC DRS vs DSM-III-R	1 cross-sectional (Sepulveda 2015)	CI group 88.55%; non-CI group 100%; MD 11.45 (3.02, 19.88)	125	Low
AUC DRS vs DSM-IV	1 cross-sectional (Sepulveda 2015)	CI group 88.29%; non-CI group 100%; MD 11.71 (3.44, 19.98)	125	Low
FAM-CAM* VS CAM IN setting di emergenza**				
Accuracy vs CAM – total sample	1 cohort study (Mailhot 2020)	se 56.7% (39-74), sp 83.3% (75-92), PPV 56.7% (37-75), NPV 83.3% (73-91)	108	Low
Accuracy in people with dementia	1 cohort study (Mailhot 2020)	se 60.8% (41-81), sp 74.3% (59-88), PPV 60.8% (41-81), NPV 74.3% (60-89)	55	Low
Accuracy in people without dementia	1 cohort study (Mailhot 2020)	se 42.8% (6-80), sp 90.7% (82-99), PPV 42.8% (6-80), NPV 90.7% (82-99)	53	Low
CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75% * Family Confusion Assessment Method; ** Confusion Assessment Method				

Review question 22b (RQ NICE). Are there effective methods for treating intercurrent illness in people living with dementia that are different from those already in use for people who do not have dementia?

Pain management				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Pain Assessment Checklist for Seniors with Limited Ability to Communicate (PACSLAC) vs stardard assessment				
PRN (*Pro Re Nata*) for quantifying the number of drugs	1 RCT (Fuchs-Lacelle 2008)	**MD 0.005, *p* = 0.00, I^2 n.a.**	173	Low[e]
Decrease in stress related to care activities	1 RCT (Fuchs-Lacelle 2008)	**MD -6.10, p = 0.04, I^2 n.a.**	173	Low[e]
Stepwise Protocol of Treating Pain (SPTP) vs standard treatment				
NPI	1 RCT (Husebo 2014)	**MD -9.60 (-15.68, -3.52), I^2 n.a.**	241	Moderate
MOBID-2 part 1 tot*	1 RCT (Sandvik 2014)	**MD -3.40 (-6.42, -0.38), I^2 n.a.**	327	Moderate
MOBID-2 part 2 tot**	1 RCT (Sandvik 2014)	**MD -2.60 (-4.37, -0.83), I^2 n.a.**	327	Moderate
MOBID-2 general	1 RCT (Sandvik 2014)	**MD -1.40 (-2.17, -0.63), I^2 n.a.**	327	Moderate
Pain Recognition and Treatment (PRT) vs training intervention on pain management				
PAINAD	1 RCT (Chen 2016)	MD -0.35 (-0.72, 0.02), I^2 n.a.	195	Low[a,b]
Number of weekly pharmacological interventions	1 RCT (Chen 2016)	MD 0,03 (-0.24, 0.30), I^2 n.a.	195	Low[a,b]
Number of weekly non-pharmacological interventions	1 RCT (Chen 2016)	**MD -1.05 (-1.46, -0.64), I^2 n.a.**	195	Low[a,b]
CMAI	1 RCT (Chen 2016)	MD -0.10 (-2.46, 2.26), I^2 n.a.	195	Low[a,b]
Observational Pain Management Protocol (OPMP) vs standard treatment				
Mean frequency of pharmacological treatments	1 RCT (Liu 2017)	**MD 8.62 (7.28, 9.96), I^2 n.a.**	162	Low
PAINAD	1 RCT (Liu 2017)	**MD -1.69 (-2.57, -0.81), I^2 n.a.**	162	Low
MSQ***	1 RCT (Liu 2017)	MD -0.52 (-7.76, 6.72), I^2 n.a.	162	Low[b]
Psychotropic agents	1 RCT (Liu 2017)	MD 4.28 (-9.32, 17.88), I^2 n.a.	162	Low[b]
Trans Cutaneous Electrical Nerve Stimulation (TENS)				
Algometry	1 RCT (Hahm 2019)	MD 0.30 (-0.26, 0.86), I^2 n.a.	32	Low[b]

CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
* musculoskeletal pain
** internal organs, head, skin
*** Medication Quantification Scale

Management of delirium				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Cognitive stimulation based on the participation to personalized recreational activities				
Barthel Index	1 RCT (Kolanowski 2011)	**MD 4.33 (-12.64, 21.3), group x time interaction, p = 0.001**	16	Very Low

CAM	1 RCT (Kolanowski 2011)	MD -0.17 (-0.70, 0.36), group x time interaction, p = 0.1128	16	Very Low[b]
Dementia Rating Scale	1 RCT (Kolanowski 2011)	MD -1.80 (-11.74, 8.14), group x time interaction, p = 0.0842	16	Very Low[b]
MMSE	1 RCT (Kolanowski 2011)	MD 0.59 (-10.13, 11.31), group x time interaction, p = 0.0298	16	Very Low[b]
CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Management of people with dementia undergoing rehabilitation after hip fracture				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Multidimensional management vs standard care				
Incidence of falls	1 RCT (Stenvall 2007)	**tot: IRR 0.38 (0.20, 0.76); dementia: IRR 0.07 (0.01, 0.57)**	199	Moderate
Intervention of enhancement of in-hospital care vs standard care				
Independence in ADL	1 RCT (Stenvall 2012)	RR 4.35 (0.19, 101.46), I^2 n.a.	64	Very Low[b,c]
Mortality	1 RCT (Stenvall 2012)	RR 2.25 (0.73, 6.93), I^2 n.a.	64	Very Low[b,c]
Intervention of enhancement of in-hospital and home care vs standard care				
Mortality rate during hospitalisation	3 RCT (Freter 2017, Stenvall 2012, Uy 2008)	RR 0.63 (0.21, 1.91), I^2 17%	152	Very Low[b,c]
Mortality at 12 months	2 RCT (Huusko 2000, Shyu 2012)	RR 1.06 (0.53, 2.13), I^2 n.a.	177	Very Low[b,c]
Incidence of falls	1 RCT (Shyu 2012)	RR 0.22 (0.01, 4.33), I^2 n.a.	36	Very Low[b,c]
Chinese BI	1 RCT (Shyu 2012)	**MD 25.40 (10.89, 39.91), I^2 n.a.**	36	Very Low
In-hospital care management led by a geriatrician vs an in-hospital care management led by an orthopedist				
Incidence of delirium during hospitalisation	2 RCT (Marcantonio 2001, Wyller 2012)	RR 0.99 (0.83, 1.17), I^2 0%	212	Very Low[b,c]
Interdisciplinary home-based rehabilitation vs in-hospital standard care				
Incidence of falls	1 RCT (Karlsson 2020)	RR 0.90 (0.62, 1.31), I^2 n.a.	103	Very Low[b,c]
Mortality after discharge	1 RCT (Karlsson 2020)	RR 0.81 (0.42, 1.57), I^2 n.a.	103	Very Low[b,c]
CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Physical exercise for the prevention of falls				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Interventions based on physical exercise for fall prevention				
Risk of falls	7 RCT (Lord 2003, Moseley 2009, Pitkälä 2013, Rolland 2007, Rosendahl 2008, Toulotte 2003, Zieschang 2013)	RR 0.68 (0.51, 0.92), I^2 79%	688	Very Low[b,c,d]

Risk of hip fracture	2 RCT (Pitkälä 2013, Rolland 2007)	RR 1.46 (0.58, 3.70), I^2 0%	304	Very Low[b,c]
Physical rehabilitation through home-based exercises compared to standard care				
Number of falls	2 RCT (Pitkälä 2013, Wesson 2013)	**MD -1.08 (-1.79, -0.37)**	148	Low
Risk of falls	2 RCT (Pitkälä 2013, Wesson 2013)	**RR 0.69 (0.51, 0.93)**	148	Low
Risk of falls	1 RCT (Pitkälä)	**IR: IG 1.35 (1.07, 1.67) vs CT 3.0 (2.63, 3.57)**	133	Low
Hip fracture	1 RCT (Pitkälä)	IR: IG 0.05 (0.01, 0.14) vs CT 0.05 (0.01, 0.15)	133	Low[b]
Overall fractures	1 RCT (Pitkälä)	IR: IG 0.06 (0.02, 0.17) vs CT 0.07 (0.02, 0.18)	133	Low[b]
Physical rehabilitation based on personalized exercised				
At least 1 fall	1 RCT (Pitkälä 2013)	**RR 0.68 (0.50, 0.94), I^2 n.a.**	123	Low
Falls	1 RCT (Pitkälä 2013)	**IR: IG 1.86 (1.51, 2.26) vs CT 3.07 (2.63, 3.57)**	123	Low
Number of falls	1 RCT (Pitkälä 2013)	MD -1.03 (-2.19, 0.13), I^2 n.a.	123	Low[b]
Hip fracture	1 RCT (Pitkälä 2013)	IR: IG 0.04 (0.00, 0.13) vs CT 0.05 (0.01, 0.15)	123	Low[b]
Overall fractures	1 RCT (Pitkälä 2013)	IR: IG 0.09 (0.03, 0.21) vs CT 0.07 (0.02, 0.18)	123	Low[b]
Multifactorial intervention, based on a multidisciplinary assessment and subsequent personalized intervention, in people referring to the ER after a fall				
Falls	1 RCT (Shaw 2003)	RR 0.92 (0.81, 1.05), I^2 n.a.	274	Very Low[b,c]
Femoral head fractures	1 RCT (Shaw 2003)	RR 0.55 (0.21, 1.43), I^2 n.a.	274	Very Low[b,c]
Fall-related hospitalisations	1 RCT (Shaw 2003)	RR 1.11 (0.61, 2.00), I^2 n.a.	274	Very Low[b,c]
Mortality	1 RCT (Shaw 2003)	RR 1.03 (0.65, 1.64), I^2 n.a.	274	Very Low[b,c]
Multimodal physical exercise in institutionalised people				
Falls	1 RCT (Puente-González 2021)	**RR 0.36 (0.16, 0.82), I^2 n.a.**	72	Low
POMA-T*	1 RCT (Puente-González 2021)	**MD 2.43 (1.07, 3.79), I^2 n.a.**	72	Low
POMA-balance	1 RCT (Puente-González 2021)	**MD 0.63 (0.12, 1.14), I^2 n.a.**	72	Low
POMA-gait	1 RCT (Puente-González 2021)	**MD 1.82 (0.86, 2.78), I^2 n.a.**	72	Low
TUG**	1 RCT (Puente-González 2021)	**MD -3.10 (-5.43, -0.77), I^2 n.a.**	72	Low
Home-based technologies intervention coupled with a tele-assistance service (including a nightlight path, an electronic bracelet and distance communication tools)				
Falls	1 RCT (Tchalla 2012)	**RR 0.51 (0.16, 0.81), I^2 n.a.**	96	Low

CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
* Tinetti's Performance-Oriented Mobility Assessment
** Timed Up and Go

Review question 23 (RQ NICE). How should people living with dementia be cared for when admitted to hospital?

Multicomponent strategies aimed at mental health				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
GDS (6-8 weeks)	1 RCT (Baldwin 2004)	MD -2.20 (-5.09, 0.69), I^2 n.a.	153	Low[b]
MMSE (6-8 weeks)	1 RCT (Baldwin 2004)	MD -0.90 (-3.91, 2.11), I^2 n.a.	153	Very Low[b,c]
Length of stay (days)	1 RCT (Baldwin 2004)	MD -1.70 (-11.00, 7.60), I^2 n.a.	153	Very Low[b,c]
Psychotropic drugs prescriptions at discharge	1 RCT (Baldwin 2004)	RR 1.04 (0.70, 1.57), I^2 n.a.	123	Very Low[b,c]
readmission at 3 months	1 RCT (Baldwin 2004)	RR 0.89 (0.52, 1.52), I^2 n.a.	153	Very Low[b,c]
Mortality	1 RCT (Baldwin 2004)	RR 1.29 (0.67, 2.47), I^2 n.a.	153	Very Low[b,c]
CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Family-centred function focused care models				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Barthel index	1 study (Boltz 2015)	MD 13.50 (-1.64, 28.64), I^2 n.a.	86	Very Low[b,c]
Gait and balance (Tinetti Scale)	1 study (Boltz 2015)	MD 0.0 (-5.23, 5.23), I^2 n.a.	86	Very Low[b,c]
Delirium severity (DSS)	1 study (Boltz 2015)	MD -2.70 (-6.31, 0.91), I^2 n.a.	86	Very Low[b,c]
Discharge to nursing homes	1 study (Boltz 2015)	RR 1.04 (0.52, 2.10), I^2 n.a.	86	Very Low[b,c]
Readmission after 30 days	1 study (Boltz 2015)	**RR 0.29 (0.08, 0.97), I^2 n.a.**	86	Low[b]
Length of stay	1 study (Boltz 2015)	MD -0.40 (-1.27, 0.47), I^2 n.a.	86	Low[b]
HADS-A	1 study (Boltz 2015)	MD -2.40 (-5.03, 0.23), I^2 n.a.	86	Very Low[b,c]
HADS-D	1 study (Boltz 2015)	MD -1.60 (-3.87, 0.67), I^2 n.a.	86	Very Low[b,c]
CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Proactive case finding with palliative care service				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Length of stay (days)	1 study (Campbell 2004)	**MD -4.70 (-8.87, -0.53), I^2 n.a.**	52	Low[b]
Length of stay – days in ICU	1 study (Campbell 2004)	**MD -3.30 (-5.46, -1.14), I^2 n.a.**	52	Low[b]
Reason for discharge (mortality)	1 study (Campbell 2004)	RR 1.21 (0.77, 1.91), I^2 n.a.	52	Very Low[b,c]
Reason for discharge (istitutionalitation rate)	1 study (Campbell 2004)	RR 0.60 (0.26, 1.41), I^2 n.a.	52	Very Low[b,c]

CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations

Management of mental health in specialist units				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Discharge at home	1 RCT (Goldberg 2013)	RR 1.06 (0.95, 1.17), I^2 n.a.	600	Low[b]
Mortality	1 RCT (Goldberg 2013)	RR 0.90 (0.67, 1.20), I^2 n.a.	600	Low[b]
Readmission	1 RCT (Goldberg 2013)	RR 0.92 (0.73, 1.15), I^2 n.a.	600	Low[b]
Institutionalization	1 RCT (Goldberg 2013)	RR 0.72 (0.51, 1.00), I^2 n.a.	600	Low[b]
Caregiver satisfaction in care	1 RCT (Goldberg 2013)	**RR 1.10 (1.03, 1.18), I^2 n.a.**	600	Moderate
CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Follow-up individualized care plan				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Readmission to ER at 30 days	1 RCT (Villars 2013)	RR 0.91 (0.49, 1.69), I^2 n.a.	558	Very Low[b,c]
Readmission to other hospital ward at 30 days	1 RCT (Villars 2013)	RR 0.81 (0.52, 1.23), I^2 n.a.	558	Very Low[b,c]
Readmission to ER at 3 months	1 RCT (Villars 2013)	RR 0.80 (0.58, 1.09), I^2 n.a.	558	Very Low[b,c]
Readmission to other hospital ward at 3 months	1 RCT (Villars 2013)	RR 0.76 (0.48, 1.21), I^2 n.a.	558	Very Low[b,c]
CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Multidimensional nutritional assessment				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
AHN	1 RCT (Arahata 2017)	**RR 2.07 (1.47, 2.90), I^2 n.a.**	214	Low
Survival rate without AHN	1 RCT (Arahata 2017)	**RR 2.57 (1.46, 4.53), I^2 n.a.**	214	Low[c]
People without AHN	1 RCT (Arahata 2017)	**RR 1.77 (1.25, 2.51), I^2 n.a.**	214	Low
Nasogastric tube and PEG insertions	1 RCT (Arahata 2017)	**RR 0.21 (0.08, 0.59), I^2 n.a.**	214	Low
Central or peripheral venous catheter insertions	1 RCT (Arahata 2017)	RR 0.90 (0.67, 1.19), I^2 n.a.	214	Low[b]
Lenght of stay	1 RCT (Arahata 2017)	MD 14.00 (-0.11, 28.11), I^2 n.a.	214	Low[b]
Mortality at discharge	1 RCT (Arahata 2017)	RR 0.95 (0.65, 1.40), I^2 n.a.	214	Low[b]

CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations
AHN: Artificial hydration and/or nutrition; PEG: Percutaneous Endoscopic Gastrostomy.

Physical activity				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
NPI	1 RCT (Fleiner 2017)	MD -5.90 (-12.46, 0.66), I^2 n.a.	85	Low[b]
CMAI	1 RCT (Fleiner 2017)	MD -3,90 (-10.63, 2.83), I^2 n.a.	85	Low[b]
CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Involvement of a pharmacist or pharmacologist in the hospital team				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Readmission due to issues related to the pharmacological treatment after 30 days	1 RCT (Gustafsson 2017)	**RR 0.47 (0.24, 0.93), I^2 n.a.**	429	Moderate
Readmission at 30 days	1 RCT (Gustafsson 2017)	RR 0.79 (0.52, 1.22), I^2 n.a.	429	Low[b]
Mortality at 30 days	1 RCT (Gustafsson 2017)	RR 1.32 (0.88, 1.99), I^2 n.a.	429	Low[b]
CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Review question 24 (RQ NICE). What models of palliative care are effective for people with dementia?

QUANTITATIVE EVIDENCE

Specialist palliative care team				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Development of a palliative care plan	1 RCT (Ahronheim 2000)	**RR 5.84 (1.37, 25.02), I^2 n.a.**	99	Low[c]
Frequency of new feeding tubes	1 RCT (Ahronheim 2000)	RR 1.06 (0.68, 1.65), I^2 n.a.	99	Low[b]
Total number of feeding tubes	1 RCT (Ahronheim 2000)	RR 1.06 (0.81, 1.39), I^2 n.a.	99	Low[b]
Frequency of mechanical ventilation	1 RCT (Ahronheim 2000)	RR 0.53 (0.10, 2.77), I^2 n.a.	99	Low[b]
tracheostomy	1 RCT (Ahronheim 2000)	RR 0.35 (0.01, 8.48), I^2 n.a.	99	Low[b]
Cardiopulmonary resuscitation	1 RCT (Ahronheim 2000)	RR 0.15 (0.01, 2.86), I^2 n.a.	99	Low[b]
Mortality rate during hospitalisation	1 RCT (Ahronheim 2000)	RR 1.06 (0.53, 2.13), I^2 n.a.	99	Low[b]
CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Decision aids on feeding options				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Decisional conflict at 3 months	1 RCT (Hanson 2011)	**MD -0.47, p<0.001**	254	Low
Need for any modified diet	1 RCT (Hanson 2011)	RR 1.08 (0.92, 1.26), I^2 n.a.	254	Low[b]
Specialised dysphagia dieta at 3 months	1 RCT (Hanson 2011)	RR 1.17 (0.98, 1.41), I^2 n.a.	254	Low[b]
Specialised staff assistance at 3 months	1 RCT (Hanson 2011)	RR 2.00 (0.98, 4.10), I^2 n.a.	254	Low[b]
Need for specialised utensils at 3 months	1 RCT (Hanson 2011)	RR 0.60 (0.22, 1.60), I^2 n.a.	254	Low[b]
Head and body positioning	1 RCT (Hanson 2011)	RR 2.00 (0.18, 21.78), I^2 n.a.	254	Low[b]
New feeding tubes at 9 months	1 RCT (Hanson 2011)	RR 0.33 (0.03, 3.12), I^2 n.a.	201	Low[b]
Do-not-feed orders at 9 months	1 RCT (Hanson 2011)	RR 1.98 (0.37, 10.57), I^2 n.a.	201	Low[b]
Mortality at nine months	1 RCT (Hanson 2011)	RR 0.92 (0.59, 1.44), I^2 n.a.	201	Low[b]
Weight loss at nine months	1 RCT (Hanson 2011)	**RR 0.37 (0.15, 0.91), I^2 n.a.**	201	Low
CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations; * Indicates less conflict in the decision (difference in mean change from baseline no 95%CI available)				

Goals of Care (GOC) interventions				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Family-healthcare provider concordance in primary care goals	1 RCT (Hanson 2017)	**RR 3.12 (1.68, 5.78), I^2 n.a.**	299	Moderate
Quality of general communication	1 RCT (Hanson 2017)	MD -0.40 (-1.02, 0.23), I^2 n.a.	299	Low[b]
SM-EOLD*	1 RCT (Hanson 2017)	MD -0.30 (-3.14, 2.54), I^2 n.a.	299	Low[b]
SWC-EOLD**	1 RCT (Hanson 2017)	MD -1.30 (-3.03, 0.43), I^2 n.a.	299	Low[b]
PCTPD***	1 RCT (Hanson 2017)	MD 0.30 (-0.35, 0.95), I^2 n.a.	299	Low[b]
CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations; * Symptom Management at the End of Life in Dementia; ** Satisfaction With Care at the End of Life in Dementia; *** Palliative care treatment plan domain score				

Facilitated case conferencing				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
family-rated CAD-EOLD*	1 RCT (Agar 2017)	MD -0.80 (-2.82, 1.22), I^2 n.a.	131	Low[b]
family-rated SM-EOLD**	1 RCT (Agar 2017)	MD -2.70 (-5.61, 0.21), I^2 n.a.	131	Low[b]
family-rated SWC-EOLD***	1 RCT (Agar 2017)	MD 0.70 (-0.93, 2.33), I^2 n.a.	131	Low[b]
nurse-rated CAD-EOLD*	1 RCT (Agar 2017)	MD -1.20 (-3.22, 0.82), I^2 n.a.	131	Low[b]
nurse-rated SM-EOLD**	1 RCT (Agar 2017)	MD -0.80 (-3.87, 2.27), I^2 n.a.	131	Low[b]
CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations; * Comfort Assessment in Dying with Dementia; ** Symtoms management the End of Life in Dementia; *** Satisfaction With Care at the End of Life in Dementia				

Generic and patient-specific feedback strategies				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
family-rated CAD-EOLD*patient specific vs control	1 RCT (Boogaard 2018)	**MD 2.20 (0.04, 4.36), I^2 n.a.**	287	Moderate
family-rated CAD-EOLD* Generic vs control	1 RCT (Boogaard 2018)	MD 1.00 (-1.12, 3.12), I^2 n.a.	266	Low[b]
family-rated SWC-EOLD patient specific vs control	1 RCT (Boogaard 2018)	MD -0.20 (-1.88, 1.48), I^2 n.a.	255	Low[b]

family-rated SWC-EOLD generic vs control	1 RCT (Boogaard 2018)	**MD -1.70 (-3.24, -0.16), I^2 n.a.**	266	Moderate
CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations; * Comfort Assessment in Dying with Dementia; ** Symtoms management the End of Life in Dementia; *** Satisfaction With Care at the End of Life in Dementia				

Triggered palliative care by hospitalisation				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
family-rated CAD-EOLD	1 RCT (Hanson 2018)	MD 0.80 (-1.27, 2.87), I^2 n.a.	62	Low[b]
PCDI (0-10)	1 RCT (Hanson 2018)	**MD 4.90 (3.83, 5.97), I^2 n.a.**	62	Moderate
Frequency of documented discussions about prognosis	1 RCT (Hanson 2018)	**RR 28.80 (4.17, 198.97), I^2 n.a.**	62	Low[c]
Frequency of documented discussions about care goals	1 RCT (Hanson 2018)	**RR 3.60 (1.95, 6.64), I^2 n.a.**	62	Moderate
Decisions not to tube feed	1 RCT (Hanson 2018)	**RR 8.53 (2.14, 34.02), I^2 n.a.**	62	Low[c]
Frequency of decisions not to re-hospitalise	1 RCT (Hanson 2018)	RR 9.58 (0.54, 170.73), I^2 n.a.	62	Very Low[b,c]
CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations; PDCI: Palliative Care Domain Index				

Decision support tools				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Decisional conflict – administering antibiotics				
Clinicians	1 RCT (Loizeau 2019)	MD -5.80 (-14.59, 2.99), I^2 n.a.	64	Very Low[b,c]
Family members	1 RCT (Loizeau 2019)	MD -6.10 (-16.90, 4.70) I^2 n.a.	100	Very Low[b,c]
Formal caregiver	1 RCT (Loizeau 2019)	**MD -12.10 (-23.86, -0.34) I^2 n.a.**	68	Low[c]
Decisional conflict – artificial hydration				
Clinicians	1 RCT (Loizeau 2019)	MD -5.50 (-15.33, 4.33), I^2 n.a.	64	Very Low[b,c]
Family members	1 RCT (Loizeau 2019)	MD -6.40 (-15.77, 2.97) I^2 n.a.	100	Very Low[b,c]
Formal caregiver	1 RCT (Loizeau 2019)	MD -0.40 (-12.90, 12.10) I^2 n.a.	68	Very Low[b,c]
CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Programmes based on multicomponent interventions				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
family-rated CAD-EOLD	1 RCT (van den Block 2020)	MD -0.14 (-1.89, 1.61), I^2 n.a.	913	Low[b]
QoL-LTC	1 RCT (van den Block 2020)	MD 2.21 (-1.09, 5.51) I^2 n.a.	940	Moderate
CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations; QoL-LTC: Quality of Dying in Long Term Care				

Specific training programmes				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Unplanned hospitalisations at 6 months	1 RCT (Tropea 2022)	RR 1.11 (0.89, 1.38), I^2 n.a.	1.304	Very Low[b,c]
Unplanned hospitalisations at 12 months	1 RCT (Tropea 2022)	RR 1.12 (0.95, 1.31) I^2 n.a.	1.304	Very Low[b,c]
Hospital mortality at 6 months	1 RCT (Tropea 2022)	RR 1.14 (0.55, 2.38), I^2 n.a.	1.304	Very Low[b,c]
Hospital mortality at 12 months	1 RCT (Tropea 2022)	RR 0.90 (0.52, 1.56), I^2 n.a.	1.304	Very Low[b,c]
CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Multidimensional and multidisciplinary training interventions for end-of-life care				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
Family Perception of Care Scale (FPCS)	2 RCT (Brazil 2017, Verrault 2018)	**MD 9.37 (3.42, 15.31), I^2 0%**	254	Low[c]
CAD-EOLD	1 RCT (Verrault 2018)	**MD 2.70 (0.55, 4.85), I^2 n.a.**	124	Low[c]
SM-EOLD	1 RCT (Verrault 2018)	**MD 4.90 (1.15, 8.65), I^2 n.a.**	124	Low[c]
Total Decisional Conflict Scale (DCS)	1 RCT (Brazil 2017)	MD -6.00 (-15.95, 3.95), I^2 n.a.	142	Very Low[b,c]
General Health Questionnaire (GHQ)	1 RCT (Brazil 2017)	MD -0.50 (-3.18, 2.18), I^2 n.a.	143	Low[b]
CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

Advance care planning				
Outcomes	**No. of Studies**	**Observed effect (95% CI), I^2**	**No. of participants**	**Certainty of evidence (GRADE)**
No hospitalization directives	1 RCT (Mitchell 2018)	RR 1.02 (0.89, 1.17), I^2 n.a.	400	Low[b]
No tube feeding directives	1 RCT (Mitchell 2018)	**RR 1.19 (1.05, 1.36), I^2 n.a.**	400	Moderate
No intravenous hydration directives	1 RCT (Mitchell 2018)	RR 1.20 (0.94, 1.53), I^2 n.a.	400	Low[b]
Goal-of-care discussions	1 RCT (Mitchell 2018)	RR 1.34 (0.99, 1.83), I^2 n.a.	400	Low[b]
CI: confidence interval; MD: mean difference; RR: risk ratio; a. I2 >40%; b. non-significant results; c. 95% CI ratio crosses both ends of a defined MID interval; d. I2>75%; e: methodological limitations				

QUALITATIVE EVIDENCE

Themes identified by caregivers			
No. of Studies	**Study design**	**Description**	**Confidence (CERQual)**
Bereaved carer – meeting physical care needs			
1 (Lawrence 2011)	Structured interviews	Ensuring adequate food and fluid intake, hygiene, toileting, dressing.	Moderate
Bereaved carer – going beyond task-focused care			
3 (Crowther 2013, Lawrence 2011, Moore 2017)	Structured and non-structured interviews	End-of-life care was evaluated positively if it was felt that the professionals cared about their dying relative.	Moderate
2 (Crowther 2013, Treloar 2009)	Non-structured interviews, mixed methods	Getting to know individual's interests, sensitivities and preferences (including food preferences).	Moderate
Bereaved carer –planning			
2 (Dening 2012, Lawrence 2011)	Structured interviews	Advance directives and advance statements.	Moderate
1 (Lawrence 2011)	Structured interviews	Discussing treatment planning with families and the wider care team.	Moderate
1 (Lawrence 2011)	Structured interviews	Enabling family members to be present at the time of death.	Moderate
1 (Dening 2012)	Semi-structured interviews, focus group	Family carers described how little happened routinely; they had to initiate and then "push" for services to be provided, these were unpredictable and fragmented.	Moderate
Bereaved carer – impact of hospitalisation			

3 (Dening 2012, Treloar 2009, Poole 2018)	Semi-structured interviews, focus group	Not liking the hospital environment.	Moderate
1 (Crowther 2013)	Non-structured interviews	Dying on an open ward rather than finding a side room in a hospital.	Moderate
1 (Dening 2012)	Semi-structured interviews, focus group	Carers described how acute hospital staff struggled to provide basic care. Carers perceived a lack of understanding, little compassion and low staffing levels.	Moderate
Bereaved carer - Knowing the person well and having a sense of their personal and social identity was said to enable carers and health-care professionals to make better informed best interests decisions on behalf of a person with dementia			
1 (Lamahewa 2017)	Semi-structured interviews, focus group	This was thought to be particularly pertinent at the end of life, when the person with dementia may not always able to verbally express themselves.	High
Bereaved carer – Knowledge of dementia provides insight for decision making			
1 (Lamahewa 2017)	Semi-structured interviews, focus group	A sense of preparedness, understanding and insight into the impact of dementia on the end of life seemed likely to have resulted in a greater level of acceptance amongst some carers, which was said to have a powerful influence on decision making between families and practitioners.	High
Current carer - Lack of familiarity of the person with dementia by health-care providers inadvertently leads to disease labelling			
1 (Lamahewa 2017)	Semi-structured interviews, focus group	Lack of familiarity of the person with dementia by health-care providers inadvertently leads to disease labelling, whereby the individuality and identity of the person is lost and they are defined by their disease. This was considered to be particularly relevant when a person with dementia is admitted to hospital where staff have no information about them.	High
Current carer - When healthcare professionals do not communicate with carers because of poor communication or lack of time to involve the family, this can complicate decision making			
1 (Lamahewa 2017)	Semi-structured interviews, focus group	When healthcare professionals do not communicate with carers because of poor communication or lack of time to involve the family, this can complicate decision making.	High
Current carer - Family carers reported often having to retell the same narrative to different health-care professionals			
1 (Lamahewa 2017)	Semi-structured interviews, focus group	There was a sense of frustration due to the lack of continuity in some settings, even within the same care setting.	High
Current carer – Carers sometimes have doubts making decisions, particularly if there was not an up-to-date living will			
2 (Lamahewa 2017, Poole 2018)	Semi-structured interviews, focus group	Often decisions were based on the family member's insight about/or knowledge of the values or preferences of the person with dementia. However, they expressed feelings of uncertainty in how to best meet the needs of their relative. Further complications resulted if formal discussion had not taken place or if legal arrangements were not in place.	High
Carer - Carers often held strong views regarding the perceived quality of care			
1 (Moore 2017)	Interviews	Carers often held strong views regarding the perceived quality of care.	High

Carer - Carers valued continuity and receiving regular feedback about their relative's health condition and the progression of dementia			
1 (Moore 2017)	Interviews	Carers valued continuity and receiving regular feedback about their relative's health condition and the progression of dementia.	Moderate
Carer – Planning - Being able to monitor services was important and reflected poor levels of trust in service providers			
2 (Moore 2017, Dening 2012)	Interviews	The standards of social service staff would drop if they felt they were not being monitored by the family. (Family carers described how little happened routinely; they had to initiate and then "push" for services to be provided, these were unpredictable and fragmented).	High
Carer – Carers were rarely informed about the dementia from diagnosis onwards through to the palliative stages			
1 (Moore 2017)	Interviews	Carers' capacity to understand the progression of dementia and be involved and informed during advanced dementia relied on information provision throughout the different stages of dementia. At diagnosis, carers were rarely informed about the likely progression of dementia.	Moderate
Carer - The unpredictable course of dementia made it very challenging for carers to prepare for the end of life			
1 (Moore 2017)	Interviews	Some were unsure about the value of early information about advanced stages of disease given the potentially unnecessary anxiety this might create.	Moderate
Carer – Carers valued timely and sensitive information provided by a knowledgeable professional and that was reinforced in writing			
1 (Moore 2017)	Interviews	Some felt that the lack of basic information left them struggling to adapt to changes and feeling ill-prepared for symptoms that they later discovered were common in advanced dementia.	Moderate
Carer – End of life (EOL) plans were not started early enough			
1 (Moore 2017)	Interviews	End of life plans were rarely initiated during the early stages of dementia preventing the person with dementia being involved in decision making. Sometimes the person with dementia was never informed of their diagnosis. EOL planning often occurred after admission to a care home or after a critical health event usually involving hospitalisation in the advanced stages of dementia. Carers often appreciated these conversations as they could be involved in care and feel that they had contributed to a plan to promote comfort care at EOL.	Moderate
Carer – Some carers were satisfied with EOL care if they felt adequately informed and involved, even when EOL care was not in accordance with advance care plans			
1 (Moore 2017)	Interviews	Some carers were satisfied with EOL care if they felt adequately informed and involved, even when EOL care was not in accordance with advance care plans.	Moderate
Carer – Enabling family members to be present at the time of death			
3 (Moore 2017, Lawrence 2011, Poole 2018)	Interviews	For most, but not all, being present at EOL was important and some described vigils from hours to weeks, being with the person before they died.	High
Carer – Carers often grieve for their relative before the person dies			

1 (Moore 2017)	Interviews	Carers described grief as a staged process pre and post death with losses associated with dementia before death.	Moderate
Carer – There was evidence of links between satisfaction with EOL care, the carer's capacity to influence the care being provided, and emotional consequences			
1 (Moore 2017)	Interviews	Two carers who had not moved their relative from what they perceived as a poor quality care home, reported the lowest satisfaction. This was influenced by their guilt at not having done more to improve EOL care.	Moderate
Carer – Participants discussed the failure of services to acknowledge their grief or to provide information about obtaining support			
1 (Moore 2017)	Interviews	This was both prior to and after their relative's death.	Moderate
Carer - Despite high levels of grief, many carers felt they did not need formal support or counselling and did not seek it			
1 (Moore 2017)	Interviews	Instead they described the benefits of their social network including friends, family or faith community. Some carers could not face their grief or the fact that their relative had dementia	Moderate
Carer – Carers who felt well informed about how dementia progressed, were regularly updated on their relative's health condition and felt involved appeared more satisfied with EOL care			
1 (Moore 2017)	Interviews	Those who failed to influence care that they perceived as poor reported high levels of grief after death and experienced guilt and regret. Admission to a care home was often associated with a loss of control and a need for heightened vigilance.	Moderate

Themes identified by health professionals			
No. of Studies	**Study design**	**Description**	**Confidence (CERQual)**
Meeting physical care needs			
2 (Lawrence 2011, Poole 2018)	Structured interviews	Identifying and responding to the physical care needs of the person with dementia.	Moderate
2 (Lawrence 2011, Poole 2018)	Structured interviews	Pain control.	Moderate
1 (Lawrence 2011)	Structured interviews	Palliative care nurses were considered skilled in identifying and managing pain in patients with complex needs and were also sensitive to nausea and hallucinations in people with dementia at the end of life.	Moderate
Complex pathways of care			
1 (Dening 2012)	Semi-structured interviews, focus group	People with advanced dementia had complex medical and social needs requiring input from a number of agencies, but the coordination was poor.	Moderate
1 (Dening 2012)	Semi-structured interviews, focus group	Out of hours staff often felt unsupported and lacking in access to key information.	Moderate

Going beyond task-focused care			
1 (Lawrence 2011)	Structured interviews	Risk of becoming entirely task-focused with little empathy	Moderate
1 (Lawrence 2011)	Structured interviews	Getting to know individual's interests, sensitivities and preferences	Moderate
Planning			
2 (Lawrence 2011, Grisaffi 2010)	Structured and semi-structured interviews	People with dementia should be given the opportunity to plan for the future.	Moderate
1 (Lawrence 2011)	Structured interviews	Whether individuals should be transferred to hospital during the final stages of their life. Hospitalisation was a frequent occurrence despite agreement among care professionals that this was often inappropriate.	Moderate
1 (Lawrence 2011)	Structured interviews	Palliative care staff noted that professionals across care settings could be reluctant to withdraw active treatment in the absence of explicit planning or a clear consensus among the care team.	Moderate
1 (Grisaffi 2010)	Semi-structured interviews	Discontinuity of care.	Low
Flexibility			
1 (Davies 2014)	Semi-structured interviews	The growing number of guidelines, standards, rules and regulations placed upon professionals in health and social care makes palliative care standardised leaving no room for flexibility	Moderate
1 (Grisaffi 2010)	Semi-structured interviews	GP's prior knowledge of the person with dementia is important in informing decisions. To help the person overcome the communication and capacity issues, relatives and carers are seen as an expert source of information regarding the person's wishes	Low
1 (Davies 2014)	Semi-structured interviews	NHS Primary Care Trusts have no duty of care for people who are self-funding their care home	Moderate
Systemisation			
2 (Davies 2014, Grisaffi 2010)	Semi-structured interviews	Some routines are useful, such as certain meetings, pain assessment, when to stop pursuing certain treatments.	Moderate
Staff training to reduce the need to call for specialist help			
1 (Davies 2014)	Semi-structured interviews	Syringe driver training, checks when prescribing.	Moderate
1 (Davies 2014)	Semi-structured interviews, focus group	Many, particularly hospice, ambulance staff and district nurses acknowledged they had received little or no training in dementia, in particular concerning communication and managing behavioural problems.	Moderate
In some cases, the lack of palliative care skills is not seen as a gap to be filled by the generalist, rather the responsibility of a specialist service			
1 (Davies 2014)	Semi-structured interviews	Some district nurses and GPs feel that palliative care should be left to specialists.	Moderate
Lack of trust, fear of litigation, fear of blame and threats to speciality			

1 (Davies 2014)	Semi-structured interviews	Managing both real and perceived risks can be a difficult challenge.	Moderate
Difficulty in deciding when to start end-of-life care			
1 (Grisaffi 2010)	Semi-structured interviews	The typically slow erratic decline and the indicators for starting the pathway could lead to either a person being on it for a long time or 'yo-yoing' on and off as their state fluctuated.	Moderate
Holistic view of confort			
1 (Poole 2018)	Interviews, focus group	Importance of psychosocial elements such as emotional comfort, compassion and spirituality.	Low
Specialized training			
1 (Poole 2018)	Interviews, focus group	Staff providing end-of-life dementia care should have additional or specialist training to ensure a good standard of care.	Low