G.7.3.3 Dementia with Lewy bodies – cholinesterase inhibitors

DLB – cholinesterase inhibitor vs. placebo: adverse events

Quality assessment						No of patients		Effect		Quality
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	ChI	Placebo	Relative (95% CI)	Absolute (95% CI)	
Any adverse events – cholinesterase inhibitors (probability of experiencing ≥1; follow-up 12 to 20 weeks)										
3[1–3]	RCT	not serious	not serious	not serious	serious[4]	201/260 (77.3%)	101/141 (71.6%)	RR 1.11 (0.98 to 1.25)	79 more per 1000 (from 14 fewer to 179 more)	⊕⊕⊕O MODERATE
Any adverse events – donepezil (probability of experiencing ≥1; follow-up 12 weeks)										
2[1,2]	RCT	not serious	not serious	not serious	serious[4]	147/201 (73.1%)	55/80 (68.8%)	RR 1.05 (0.88 to 1.25)	34 more per 1000 (from 83 fewer to 172 more)	⊕⊕⊕O MODERATE
Any adverse events – rivastigmine (probability of experiencing ≥1; follow-up 20 weeks)										
1[3]	RCT	not serious	N/A	not serious	not serious	54/59 (91.5%)	46/61 (75.4%)	RR 1.21 (1.03 to 1.43)	158 more per 1000 (from 23 more to 324 more)	⊕⊕⊕⊕ HIGH
Serious adverse events – cholinesterase inhibitors (probability of experiencing ≥1; follow-up 12 to 20 weeks)										
3[1–3]	RCT	not serious	not serious	not serious	serious[4]	23/260 (8.8%)	15/141 (10.9%)	RR 0.98 (0.53 to 1.82)	2 fewer per 1000 (from 51 fewer to 89 more)	⊕⊕⊕O MODERATE
Serious adverse events – donepezil (probability of experiencing ≥1; follow-up 12 weeks)										
2[1,2]	RCT	not serious	not serious	not serious	serious[4]	13/201 (6.5%)	7/80 (8.8%)	RR 0.73 (0.3 to 1.81)	24 fewer per 1000 (from 61 fewer to 71 more)	⊕⊕⊕O MODERATE
Serious adverse events – rivastigmine (probability of experiencing ≥1; follow-up 20 weeks)										
1[3]	RCT	not serious	N/A	not serious	serious[4]	10/59 (16.9%)	8/61 (13.1%)	RR 1.29 (0.55 to 3.05)	38 more per 1000 (from 59 fewer to 269 more)	⊕⊕⊕O MODERATE
Adverse events requiring treatment withdrawal – cholinesterase inhibitors (probability of experiencing; follow-up 12 to 20 weeks)										
3[1–3]	RCT	not serious	not serious	not serious	serious[4]	25/260 (9.6%)	16/141 (11.3%)	RR 0.9 (0.49 to 1.63)	11 fewer per 1000 (from 58 fewer to 71 more)	⊕⊕⊕O MODERATE
Adverse events requiring treatment withdrawal – donepezil (probability of experiencing; follow-up 12 weeks)										
2[1,2]	RCT	not serious	not serious	not serious	serious[4]	18/201 (9%)	9/80 (11.3%)	RR 0.82 (0.39 to 1.74)	20 fewer per 1000 (from 69 fewer to 83 more)	⊕⊕⊕O MODERATE

Quality assessment						No of patients		Effect		Quality
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Chl	Placebo	Relative (95% CI)	Absolute (95% CI)	
Adverse events requiring treatment withdrawal – rivastigmine (probability of experiencing; follow-up 20 weeks)										
1[3]	RCT	not serious	N/A	not serious	serious[4]	7/59 (11.9%)	7/61 (11.5%)	RR 1.03 (0.39 to 2.77)	3 more per 1000 (from 70 fewer to 203 more)	⊕⊕⊕O MODERATE

[1] Ikeda 2015; data for 2 active treatment groups were combined (donepezil 5mg and 10mg)
[2] Mori 2012; data for 3 active treatment groups were combined (donepezil 3mg, 5mg and 10mg)
[3] McKeith 2000
[4] At a 95% confidence level, data are consistent with appreciable harm, appreciable benefit or no difference

DLB – cholinesterase inhibitor vs. placebo: cognitive function

Quality assessment						No of patients		Effect	Quality
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Chl	Placebo	Mean difference (95% CI)	
MMSE – cholinesterase inhibitors (follow-up 12 to 20 weeks; range of scores: 0-30; higher is better)									
3[1–3]	RCT	not serious	serious[4]	not serious	not serious	256	136	1.77 higher (1.06 to 2.47 higher)	⊕⊕⊕O MODERATE
MMSE – donepezil (follow-up 12 weeks; range of scores: 0-30; higher is better)									
2[1,3]	RCT	not serious	serious[4]	not serious	not serious	197	75	1.91 higher (1.11 to 2.71 higher)	⊕⊕⊕O MODERATE
MMSE – rivastigmine (follow-up 20 weeks; range of scores: 0-30; higher is better)									
1[2]	RCT	not serious	N/A	not serious	serious[5]	59	61	1.24 higher (0.28 lower to 2.76 higher)	⊕⊕⊕O MODERATE

[1] Ikeda 2015; data for 2 active treatment groups were combined (donepezil 5mg and 10mg)
[2] McKeith 2000; data for this outcome taken from a Cochrane review; data not reported in published paper
[3] Mori 2012; data for 3 active treatment groups were combined (donepezil 3mg, 5mg and 10mg)
[4] i^2 >40% between studies
[5] At a 95% confidence level, data are consistent with appreciable benefit, appreciable harm or no difference

DLB – cholinesterase inhibitor vs. placebo: global assessment

Quality assessment						No of patients		Effect (95% CI)	Quality
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Chl	Placebo		
CIBIC+ – donepezil (follow-up 12 weeks; range of scores: 1-7; lower is better)[1]									
1[2]	RCT	not serious	N/A	not serious	not serious	91	30	MD 1.17 lower (1.66 to 0.68 lower)	⊕⊕⊕⊕ HIGH
CIBIC+ – donepezil (at least minimal improvement; follow-up 12 weeks; higher is better)									
1[2]	RCT	not serious	N/A	not serious	not serious	62/91 (68.1%)	10/30 (33.3%)	RR 2.04 (1.21 to 3.46) 347 more per 1000 (from 70 more to 820 more)	⊕⊕⊕⊕ HIGH

[1] Mean and SD calculated from data presented in paper
[2] Mori 2012; data for 3 active treatment groups were combined (donepezil 3mg, 5mg and 10mg)

DLB – cholinesterase inhibitor vs. placebo: carer-reported outcomes

Quality assessment						No of patients		Effect	Quality
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	ChI	Placebo	Mean difference (95% CI)	
ZBI - donepezil (follow-up 12 weeks; lower is better)									
2[1,2]	RCT	not serious	not serious	not serious	not serious	191	77	4.49 lower (7.64 to 1.34 lower)	⊕⊕⊕⊕ HIGH

[1] Ikeda 2015; data for 2 active treatment groups were combined (donepezil 5mg and 10mg)
[2] Mori 2012; data for 3 active treatment groups were combined (donepezil 3mg, 5mg and 10mg)

DLB – cholinesterase inhibitor vs. placebo: Other non-cognitive outcomes

Quality assessment						No of patients		Effect	Quality
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	ChI	placebo	Mean difference (95% CI)	
NPI-10 item – cholinesterase inhibitors (follow-up 12 to 20 weeks; range of scores: 0-120; lower is better)[1]									
3[2–4]	RCT	not serious	serious[5]	not serious	serious[6]	243	129	2.06 lower (7.15 lower to 3.02 higher)	⊕⊕OO LOW
NPI-10 item – donepezil (follow-up 12 weeks; range of scores: 0-120; lower is better)[1]									
2[2,4]	RCT	not serious	serious[5]	not serious	serious[6]	196	76	1.54 lower (9.37 lower to 6.29 higher)	⊕⊕OO LOW
NPI-10 item – rivastigmine (follow-up 20 weeks; range of scores: 0-120; lower is better)									
1[3]	RCT	not serious	N/A	not serious	serious[6]	47	53	3.8 lower (9.25 lower to 1.65 higher)	⊕⊕⊕O MODERATE
NPI-4 item – cholinesterase inhibitors (follow-up 12 to 20 weeks; range of scores: 0-48; lower is better)[7]									
2[3,4]	RCT	not serious	not serious	not serious	not serious	161	93	2.49 lower (4.64 to 0.33 lower)	⊕⊕⊕⊕ HIGH
NPI-4 item – donepezil (follow-up 12 weeks; range of scores: 0-48; lower is better)[7]									
1[4]	RCT	not serious	N/A	not serious	not serious	102	32	3.59 lower (6.93 to 0.25 lower)	⊕⊕⊕⊕ HIGH
NPI-4 item – rivastigmine (follow-up 20 weeks; range of scores: 0-48; lower is better)[7]									
1[3]	RCT	not serious	N/A	not serious	serious[6]	59	61	1.7 lower (4.52 lower to 1.12 higher)	⊕⊕⊕O MODERATE
NPI-2 item – donepezil (follow-up 12 weeks; range of scores: 0-24; lower is better)[8]									
2[2,4]	RCT	not serious	serious[5]	not serious	serious[6]	196	76	2.3 lower (6.32 lower to 1.72 higher)	⊕⊕OO LOW

UPDRS III – cholinesterase inhibitors (follow-up 12 weeks; lower is better)[1]									
2[2,4]	RCT	serious[9]	not serious	not serious	not serious[10]	195	77	0.67 lower (2.08 lower to 0.73 higher)	⊕⊕⊕O MODERATE
UPDRS III – donepezil (follow-up 12 weeks; lower is better)[1]									
2[2,4]	RCT	not serious	not serious	not serious	not serious[10]	195	77	0.67 lower (2.08 lower to 0.73 higher)	⊕⊕⊕⊕ HIGH

[1] SD not reported for this outcome in Ikeda 2015; calculated from SE reported in paper
[2] Ikeda 2015; data for 2 active treatment groups were combined (donepezil 5mg and 10mg)
[3] McKeith 2000
[4] Mori 2012; data for 3 active treatment groups were combined (donepezil 3mg, 5mg and 10mg)
[5] i^2 >40% between studies
[6] At a 95% confidence level, data are consistent with appreciable benefit, appreciable harm or no difference
[7] NPI 4-item consists of 4 NPI domains – hallucinations, delusions, dysphoria and apathy
[8] NPI 2-item consists of 2 NPI domains – hallucinations and cognitive fluctuation
[9] Data for outcome not presented in McKeith 2000. Study reported no significant difference between groups
[10] CI do not cross MID between 3.25 (Horvath et al., 2015) and 5 points (Schrag et al., 2006)