

Appendix Table 2. Study Characteristics and Effect Sizes for Outcomes Measured within Each Study\*

Author Year	1. Population 2. Interventions and treatment duration (TP) 3. # Randomized/# completing trial	1. Criteria for Diagnosis 2. Diagnosis 3. Disease Severity	Study Quality Funding Source Randomization Blinding Withdrawals	Cognitive Function		Global Assessment		Behavior/ Mood		Quality of Life/ ADL	
				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
<b>Donepezil versus Placebo (except otherwise stated)</b>											
Black 2003 (22) Pratt 2002 (97)	1. Community dwelling, mean age 73.9 years and 55.2% male  2. A: Donepezil 5mg/d B: Donepezil 10mg/d TP: 24 weeks  3. 603/478	1. NINCDS- AIREN  2. Vascular Dementia  3. Probable (70.5%) or possible (29.5%)	Industry Funded Rand – 2/2 Blind – 2/2 Withdraw – 1/1	ADAS-cog  ADAS-cog (for Probable VaD subgroup only)  MMSE (2 <sup>0</sup> )	A: -1.68 (-2.77,-0.59) B: -2.24 (-3.35,-1.13)  A: -1.67 (p=0.02) B: -2.60 (p<0.001)  A: 0.65 (0.04, 1.26) B: 1.10 (0.50, 1.70)	CIBIC+ (2 <sup>0</sup> ) RR improved or stabilized  CDR-SB (2 <sup>0</sup> )	A: 1.01 (0.88, 1.15) B: 1.14 (1.01, 1.29)  A: -0.12 (-0.45, 0.21) B: -0.36 (-0.68, -0.04)	NT	ADFACS (2 <sup>0</sup> )  IADL (2 <sup>0</sup> )	A: -0.80 (-1.88, 0.28) B: -0.91 (-2.02, 0.20)  A: -0.89 (-1.69,-0.09) B: -0.74 (-1.56, 0.08)	

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				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Burns 1999 (9)	1. Men and women, ≥ 50 years of age  2. A: Donepezil 5mg B: Donepezil 10mg TP: 24w k + 6w PB washout period 3. 818/632	1. DSM-III-R NINCDS- ADRDA  2. Alzheimer's disease  3. Probable (mild to moderate)	Industry Funded  Rand – 1/2 Blind – 1/2 Withdraw – 1/1	ADAS-cog	A: -1.00 (-1.74,-0.26) B: -2.80 (-3.40,-2.20)	CIBIC+  CIBIC+ RR improved  CDR-SB (2 <sup>0</sup> )	A: -0.20 (-0.42, 0.02) B: -0.40 (-0.54, -0.26)  A: 1.49 (0.98, 2.26) B: 1.78 (1.19, 2.67)  A: -0.27 (-0.43, -0.11) B: -0.40 (-0.54,-0.26)	NT	IDDD QoL (2 <sup>0</sup> )	A: -0.20 (-1.31, 0.91) B: -2.00 (-3.11,-0.89)	
Courtney 2004 (24)	1. Community Dwelling, mean age 75 years and 41% male  2. Donepezil 5mg -10mg TP: 48wk 2y follow-up  3. 565/293 in phase 1 and 111 in phase 2 and	1. DSM IV  2. Alzheimer's disease  3. Mild to moderate	Not Industry Funded  Rand – 1/2 Blind – 2/2 Withdraw –1/1	MMSE (2 <sup>0</sup> )	0.83 (0.5, 1.2)			NPI (2 <sup>0</sup> )	0.31 (-0.9, 1.5)	BADLS	1.02 (0.5, 1.6)



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				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Holmes 2004 (25)	1. Mean age 80.9 years and 38.5% male  2. Donepezil 5mg-10mg TP: 24 weeks  3. 96/80	1. NINCDS ADRDA  2. Alzheimer's disease  3. Probable (mild to moderate)	Industry Funded Rand – 2/2 Blind – 2/2 Withdraw – 1/1	MMSE (2 <sup>0</sup> )	1.70 (0.17, 3.23)	NT	NPI	-6.20 (-11.37,- 1.03)		NT	
Kemp 2003 (26)	1. Community dwelling, mean age 72 years  2. Donepezil 5mg-10mg TP: 4 months  3. 12/11	1. NINCDS- ADRDA  2. Alzheimer's disease  3. Probable (mild to moderate)	Not Industry Funded  Rand – 1/2 Blind – 1/2 Withdraw – 1/1	ADAS-cog	NR	NT		NT		NT	

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				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Krishnan 2003 (27)	1. Women ( $\geq 2$ years postmenopausal) and men $\geq 50$ years of age  2. Donepezil 5mg - 10mg TP: 24 weeks  3. 67/51	1. NINCDS DSM IV  2. Alzheimer's disease  3. Probable (mild to moderate)	Industry Funded  Rand – 2/2 Blind – 1/2 Withdraw – 1/1	ADAS-cog	4 ( $p < 0.02$ )		NT		NT		NT
Leroi 2003 (28)	1. Community dwelling, man age 68.5 y, 44.4% male in placebo group and 85.7% male in donepezil group  2. Donepezil 2.5mg - 10mg TP: 18 weeks  3. 16/10	1. DSM IV  2. Parkinson's disease  3. Mild to moderate	Partially Funded by industry Rand – 1/2 Blind – 1/2 Withdraw – 1/1	MMSE	-1.11 (-2.92, 0.7)	DRS-total	-0.68 (-7.63, 6.28)	NPI	-0.06 (-11.49, 11.38)		NT
				DRS- Memory	3.33 (0.35, 6.3)						
				HVLT-R	0.72 (-4.37, 5.81)						

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				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Mazza 2006 (31)	1. Mean age 68.5 years and 46% male  2. A: Donepezil 5mg B: Donepezil 5mg vs. Ginkgo biloba 160 mg/d TP: 24 weeks  3. 76/60	1. DSM IV  2. Alzheimer's disease  3. Mild to moderate	Industry Funded Rand – 2/2 Blind – 2/2 Withdraw – 1/1	MMSE	A: 1.45 (-1.96,4.86) B: 0.60 (-2.79, 3.99)	CGI	A: -1.05 (-1.43,-0.67) B: 0.00 (-0.49, 0.49)		NT		NT
Mohs 2001 (15)	1. mean age 75.4 years (range: 50-93y), 37% male, 92.15% white, 2.75% black, and 5.1% other  2. Donepezil 5mg-10mg TP: 54 weeks  3. 431/111	1. NINCDS DSM IV  2. Alzheimer's disease  3. probable (mild to moderate)	Industry Funded Rand – 1/2 Blind – 1/2 Withdraw – 1/1	MMSE(2 <sup>0</sup> )	(p<0.001)		NT		NT	ADFACS (2 <sup>0</sup> ) Instrumental ADL (p=0.001) Basic ADL (p=0.007)	

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				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Petersen 2005 (32)	1. Mean age 72.9 years and 54 % male  2. A: Donepezil 10mg B: Donepezil 10mg vs. Vitamin 2000IU TP: 36 months  3. 790/769	1. Amnestic mild cognitive impairment Logical memory delayed recall score = 1.5 to 2 standard deviations CDR = 0.5 MMSE = 24- 30  2. Amnestic mild cognitive impairment  3. Amnestic	Public Funding (PF) Rand – 1/2 Blind – 1/2 Withdraw – 1/1	ADAS-cog (2 <sup>0</sup> )  MMSE (2 <sup>0</sup> )	A: -0.06 (-1.18,1.06) B: -0.91 (-1.99,0.17)  A: 0.44 (-0.23,1.11) B: -0.11 (-0.75,0.53)	GDS (2 <sup>0</sup> )  CDR-SB (2 <sup>0</sup> )	A: 0.03 (-0.13,0.19) B: -0.05 (-0.21,0.11)  A: -0.04 (-0.44,0.36) B: -0.07 (-0.44,0.30)	ADL (2 <sup>0</sup> )	A: 0.13 (-1.40,1.66) B: -0.63 (-2.14,0.88)		NT
Prasher 2002 (12)	1. Community dwelling, mean age 54 years and 50.0% male  2. Donepezil 5mg - 10mg TP: 24 weeks  3. 31/27	1. ICD -10  2. Alzheimer's and Down's Syndrome  3. Mild to Moderate	Industry Funded Rand – 2/2 Blind – 1/2 Withdraw – 1/1	DMR  SIB(2 <sup>0</sup> )	-5.4 (p=0.22)  10.8 (p=0.06)	NPI(2 <sup>0</sup> ) 2.2 (-3.88, 8.28)		ABS(2 <sup>0</sup> ) 7.6 (p = 0.51)			

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				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Rogers 1996 (19)	1. mean age 71.8 years (range: 54 -85y), 40% male and 99% white	1. DSM-III-R NINCDS	Industry Funded	ADAS-Cog	A: -1.60 (-3.84,0.64) B: -2.10 (-4.35,0.15) C: -3.20 (-5.09,-1.31)	CGIC(2 <sup>0</sup> ) RR improved	A: 1.04 (0.84,1.28) B: 1.03 (0.84,1.27) C: 1.12 (0.93,1.35)	NT	ADL (2 <sup>0</sup> )	A:2.50(- 8.40, 13.40) B:-0.90(- 8.62,6.82) C:-4.60(- 12.34,3.14)	
Auxiliary: Rogers 2000 (100)	2. A: Donepezil 1mg/d	2. Alzheimer's disease	Rand – 1/2 Blind – 1/2 Withdraw – 1/1	MMSE (2 <sup>0</sup> )	A: -0.60 (-1.86,0.66) B: -0.30 (-1.62,1.02) C: 0.80 (-0.36,1.96)	CDR-SB(2 <sup>0</sup> )	A: 0.08 (-0.53,0.69) B: 0.13 (-0.61,0.87) C: -0.21 (-0.72,0.30)		QoL-P (2 <sup>0</sup> )	A: 2.00(- 13.11,17.11) B: 3.90(- 13.52,21.32) C: 10.10(- 11.23,31.43)	
Neumann 1999 (101)	B: Donepezil 3mg/d	3. Mild to moderate							QoL-C (2 <sup>0</sup> )	A:-9.00(- 28.20,10.20) B:-3.70(- 21.81,14.41) C:-3.40(- 25.71,18.91)	
Rogers 1998 (102)	C: Donepezil 5mg/d TP: 12 weeks + 2 weeks Placebo washout period 3. 161/141										

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				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Rogers 1998a (18)	1. Mean age 73.7 years (range: 50-94), Auxiliary: Doody 2001 (103) Steele 1999 (104)	1. NINCDS DSM-III-R  2. Alzheimer's disease  3. Mild to moderate	Industry Funded Rand – 1/2 Blind – 1/2 Withdraw – 1/1	ADAS-cog	A: -3.10 (-4.29,-1.91) B: -2.50 (-3.69,-1.31)	CIBIC +	A: -0.40 (-0.61,-0.19) B: -0.30 (-0.51,-0.09)	NT	QoL (2 <sup>0</sup> )	A: -8.30(- 15.78,-0.82) B: 1.70(- 5.78,9.18)	
	2. A: Donepezil 10mg B: Donepezil 5mg TP: 12weeks + 3 weeks Placebo washout period  3. 468/412			ADAS-cog ≥ 4 point change  MMSE (2 <sup>0</sup> )	PB = 30% DPZ 10 mg = 60%  A: 1.26 (0.58,1.94) B: 0.96 (0.27,1.65)	CIBIC + RR improved  CDR-SB (2 <sup>0</sup> )	A: 2.12 (1.43, 3.15) B: 1.78 (1.18, 2.69)  A: -0.17 (-0.47,0.13) B: 0.04 (-0.27,0.35)				

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				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Rogers 1998b (17)	1. Mean age 73.6 years (range: 51-94 years), 38% male and 95% white	1. NINCDS DSM-III-R	Industry Funded Rand – 1/2 Blind – 1/2 Withdraw – 1/1	ADAS-cog	A: -2.88 (-4.27,-1.49) B: -2.49 (-3.88,-1.10)	CIBIC +	A: -0.44 (-0.65,-0.23) B: -0.36 (-0.60,-0.12)	NT	QoL (2 <sup>0</sup> )	A: (p>0.05) B: (p=0.05)	
Auxiliary: Doody 2001 (103) Sparano 1998 (105)	2. A: Donepezil 10mg B: Donepezil 5mg TP: 24 weeks 3. 473/367	2. Alzheimer's disease 3. Mild to moderate		ADAS-cog ≥ 4 point change	PB = 26.8%, DPZ 5 mg = 37.8% DPZ 10 mg = 53.5%	CIBIC + RR improved	A: 2.22 (1.31, 3.76) B: 2.34 (1.39, 3.95)				
				ADAS-cog ≥ 7 point change	PB = 7.8%, DPZ 5mg = 15.4% DPZ 10 mg = 25.2%	CDR-SB (2 <sup>0</sup> )	A: -0.60 (-0.99, -0.21) B: -0.59 (-0.98, -0.20)				
				MMSE (2 <sup>0</sup> )	A: 1.36 (0.57, 2.15) B: 1.21 (0.42, 2.00)						



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				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Seltzer 2004 (10)	1. Generally healthy ambulatory patients aged 50 to 92 years, mean age of 74.1 years and 46.4% male  2. Donepezil 5mg - 10mg TP: 24 weeks  3. 153/116	1. DSM IV  2. Alzheimer's disease  3. Probable	Industry Funded Rand – 1/2 Blind – 1/2 Withdraw – 1/1	ADAS-cog -2.30 (-4.11,-0.49)  ADAS-cog ≥ 4 point change PB = 16% DPZ = 37%  ADAS-cog ≥ 7 point change PB = 7% DPZ = 10%  MMSE (2 <sup>0</sup> ) -1.20 (-2.73, 0.33)	CDR-SB(2 <sup>0</sup> ) (p > 0.05)		Apathy Scale (2 <sup>0</sup> ) (p > 0.05)				
Tariot 2001 (16)	1. Institution dwelling, mean age 85.7y (range: 65-100y) and 18% male  2. Donepezil 5mg - 10mg TP: 24 weeks  3. 208/162	1. NINCDS  2. Alzheimer's disease  3. Probable or possible or with cerebro- vascular disease (moderate to severe)	Industry Funded Rand – 2/2 Blind – 2/2 Withdraw – 1/1	MMSE (2 <sup>0</sup> ) 0.70 (0.14, 1.26)  MMSE ≥ 3 point change PB = 36% DPZ = 51% (p<0.05)	CDR-SB (2 <sup>0</sup> ) -0.80 (-1.12, -0.48)		NPI-NH 2.60 (-2.67, 7.87)		PSMS (2 <sup>0</sup> ) (p>0.05)		

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				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Thomas 2001 (20)	1. Mean age 66.5 years (range: 58-73y) and 46% male  2. Donepezil 5mg - 10mg TP: 6 months  3. 60/54	1. NINCDS  2. Alzheimer's disease  3. Mild to moderate	Not reported Rand -2/2 Blind - 1/2 Withdraw - 1/1	ADAS-cog MMSE WAIS	-7.12 (p<0.001)  1.00 (p=0.06)  4.00 (p=0.43)	NT		NT		NT	
Tune 2003 (29)	1. Mean age 72.2 years (placebo), 73.7 years (donepezil), 28.6% male (placebo) and 21.4% male (donepezil)  2. Donepezil 5mg -10mg TP: 24 weeks  3. 28/26	1. NINCDS- ADRDA  2. Alzheimer's disease  3. Probable (Mild to moderate)	Industry Funded Rand - 1/2 Blind - 1/2 Withdraw - 1/1	ADAS-cog (2 <sup>0</sup> )	-2.09 (-4.96, 0.78)	NT	NPI (2 <sup>0</sup> )	2.75 (-9.29, 14.79)		NT	

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				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Wilkinson 2003 (106) Pratt 2002 (107)	1. Mean age 75.0 years and 59.9% male  2. A: Donepezil 5mg B: Donepezil 10mg TP: 24 weeks  3. 616/491	1. NINCDS- AIREN  2. Vascular dementia  3. Probable or possible	Partially Funded by industry Rand – 2/2 Blind – 2/2 Withdraw – 1/1	ADAS-cog  MMSE (2 <sup>0</sup> )	A: -1.44 (-2.52,-0.36) B: -2.07 (-3.32,-0.82)  A: 1.29 (0.60,1.98) B: 1.09 (0.40,1.78)	CIBIC + RR improved  CDR-SB (2 <sup>0</sup> )	A: 1.56 (1.16, 2.11) B: 1.29 (0.94, 1.77)  A: -0.27 (-0.66,0.12) B: -0.44 (-0.83,-0.05)	NT	ADFACS (2 <sup>0</sup> )	A: -0.62 (-1.81,0.57) B: -0.65 (-1.79,0.49)	
Winblad 2001 (13)  Winblad 2006 (108)	1. Mean age 72.5y (range: 50 – 87 years), 36% male, and 100% white  2. Donepezil 5mg - 10mg TP: 52 weeks  3. 286/192	1. DSM IV NINCDS  2. Alzheimer's disease  3. Mild to Moderate	Industry Funded Rand – 2/2 Blind – 1/2 Withdraw – 1/1	MMSE(2 <sup>0</sup> )	1.43 (0.98, 1.88)	GBS total score  GBS-I  GDS (2 <sup>0</sup> )	-6.20 (-12.02,-0.38)  -3.70 (-6.75,-0.65)  (p=0.047)	NPI (2 <sup>0</sup> )  (p > 0.05)	A-PDS (2 <sup>0</sup> )	(p<0.05)	

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Winblad 2006 (33)	1. Institution dwelling, mean age 84.9 years and 24% male  2. Donepezil 5mg - 10mg TP: 6 months  3. 249/194	1. DSM IV NINCDS  2. Alzheimer's disease  3. Severe	Industry Funded  Rand – 2/2 Blind – 1/2 Withdraw – 1/1	SIB  MMSE (2 <sup>0</sup> )	4.50 (1.17, 7.83)  1.00 (0.17, 1.83)	CGI-I (2 <sup>0</sup> )	-0.30 (-3.49, 2.89)	NPI (2 <sup>0</sup> )	-1.70 (-4.75, 1.35)	ADCS- ADL-severe (2 <sup>0</sup> )	1.40 (0.14, 2.66)

#### Donepezil versus Galantamine

Wilcock, 2003 (34)	1. Mean age 73.5 years, 37.9% male, 100% white (galantamine) and 98.9% white (donepezil)  2. Donepezil 10mg vs. Galantamine 24mg TP: 52 weeks  3. 188/149	1. NINCDS- ADRDA  2. Alzheimer's Disease, Dementia Alzheimer's type, Senile dementia of the Alzheimer's type.  3. Probable	Industry Funded  Rand – 1/2 Blind – 1/2 Withdraw – 1/1	MMSE (2 <sup>0</sup> )  MMSE ≥ 0 at 12 months  ADAS- cog/11 (2 <sup>0</sup> )	-1.68 (-2.82,-0.54)  DPZ = 32.5% GAL = 55.2% (p<0.005)  1.21 (-0.97, 3.39)	NT	NPI (2 <sup>0</sup> )  (p>0.05)	BrADL	0.21 (-1.80, 2.22)
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Ancoli- Israel 2005 (35)	1. Community dwelling, mean age 77.5 years, 68.6 years (caregivers), 38% male and 81% white  2. Donepezil (5 – 10mg/d) vs. Galantamine (8- 16mg/d) TP: 52 weeks  3. 63/54	1. NINCDS- ADRDA  2. Alzheimer's disease  3. Mild to moderate	Industry Funded Rand – 1/2 Blind – 1/2 Withdraw – 1/1	NT		CIBIC+ RR improved or stabilized	0.86 (0.74, 1.01)	NT		NT	

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<b>Donepezil versus Rivastigmine</b>											
Bullock 2005 (37)	1. Mean age 75.9 years,	1. NINCDS- ADRDA	Industry Funded Rand – 2/2	SIB	-0.61 (-3.66, 2.44)	GDS (2 <sup>0</sup> )	0.11 (0.00, 0.22)	NPI (2 <sup>0</sup> )	0.54 (-1.68, 2.76)	ADCS-ADL (2 <sup>0</sup> )	-2.08 (-4.58, 0.42)
Bullock 2006 (36)	31.3% male and 98.8% white  2. Donepezil (5 - 10mg/d) vs. Rivastigmine (3 - 12mg/d)  TP: 24 months  3. 998/578	2. Alzheimer's disease  3. Moderate to moderately severe	Blind – 2/2 Withdraw – 1/1	MMSE (2 <sup>0</sup> )	-0.50 (-1.33, 0.33)						
<b>Galantamine versus Placebo (except otherwise stated)</b>											
Brodsky 2005 (39)	1. Mean age 76.5 years and	1. NINCDS- ADRDA	Industry Funded Rand – 2/2	ADAS-cog	A: -2.50 (-3.39,-1.61)	CIBIC+ (2 <sup>0</sup> )	A: 1.08 (0.94, 1.23)	NPI (2 <sup>0</sup> )	A: -1.20 (-2.97,0.57)	ADCS-ADL (2 <sup>0</sup> )	A: 2.40 (0.80,4.00)
Dunbar 2006 (49)	36% male  2. A: Galantamine PRC B: Galantamine TP: 26 weeks 3. 971/768	2. Alzheimer's disease  3. Probable (mild to moderate)	Blind – 2/2 Withdraw – 1/1		B: -2.80 (-3.76,-1.84)	RR improved or stabilized	B: 1.10 0.97, 1.25)		B: -1.50 (-3.38,0.38)		B: 1.40 (-0.22,3.02)

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				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Bullock 2004 (45)	1. Mean 76.5 years and 48.3% male 2. Galantamine (24 mg/d) TP: 6 months double blind and then 6 months open-label extension 3. 285/238	1. NINCDS- ADRDA NINCDS- AIREN 2. Alzheimer's Disease and Cerebrovascul ar disease 3. Probable vascular dementia, possible Alzheimer's disease	Not reported Rand – 1/2 Blind – 2/2 Withdraw – 1/1	ADAS- cog/11 (at 6 months – end of double-blind phase)	-3.10 (-4.59,-1.61)	NT	NPI	N/A	DAD	N/A	
Erkinjuntti 2002 (43)	1. Mean age 75.1 years (range: 40 – 90 years), 53% male and 99.9% white 2. Galantamine (24 mg/d) TP: 6 months  3. 592/457	1. NINDS NINCDS 2. Vascular dementia and Alzheimer's disease 3. Probable	Partially Funded by industry Rand – 2/2 Blind – 2/2 Withdraw – 1/1	ADAS- cog/11  ADAS-cog ≥ 4 point change	-2.70 (-3.95,-1.45)  PB = 22.2% GAL = 35.3% (p = 0.005)	CIBIC+- RR improved or stabilized	1.25 (1.08, 1.45)	NPI (2 <sup>0</sup> )	-2.20 (-4.83, 0.43)	DAD (2 <sup>0</sup> )	4.60 (1.50, 7.70)

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				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Koontz 2005 (47)	1. Community dwelling, mean age 71 years, 100% male  2. Galantamine (4 -12 mg/d) TP: 16 weeks  3. 19/10	1. Peterson Criteria MMSE.26 living independently  2. Mild cognitive impairment  3. N/A	Industry Funded  Rand – 1/2 Blind – 1/2 Withdraw – 1/1	CANTAB- SOC  CANTAB- PRM  CVLT (immediate recall only)	2.80 (p=0.023)  1256 (p=0.001)  1256 (p=0.050)	NT	NT	FAQ	(p=0.029)		
Raskind 2000 (41)	1. mean age 75.4 years, 38% male and 91.5% white  2. A: Galantamine 24mg/d B: Galantamine 32mg/d TP: 6 months  3. 636/438	1. NINCDS  2. Alzheimer's Disease  3. Mild to moderate	Industry Funded  Rand – 2/2 Blind – 2/2 Withdraw – 2/1	ADAS- cog/11	A: -0.10 (-1.23,1.03) B: -3.40 (-4.63,-2.17)	CIBIC+ RR improved or stabilized	A: 1.29 (1.11, 1.50) B: 1.22 (1.04, 1.43)	ADAS- cog/13 (2 <sup>0</sup> )	A: 4.5 (p< 0.001) B: 4.1 (p< 0.001)	DAD (2 <sup>0</sup> )	(p>0.05)

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				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Rockwood 2001 (40)	1. mean age 74.9 years, 44% male  2. Galantamine 24 -32mg TP: 3 months  3. 386/288	1. NINCDS  2. Alzheimer's Disease  3. Probable (mild to moderate)	Industry Funded Rand – 2/2 Blind – 2/2 Withdraw – 1/1	ADAS- cog11  ADAS- cog13 (2 <sup>0</sup> )  ADAS-cog ≥ 4 point change	-1.70 (-2.79,-0.61)  -1.90 (-3.15,-0.65)  PB = 22%, GAL 24-32 mg = 28.3%	CIBIC+ RR improved or stabilized	1.29 (1.11, 1.50)	NPI (2 <sup>0</sup> )  -0.80 (-2.67, 1.07)	DAD (2 <sup>0</sup> )  4.80 (2.05, 7.55)		

Author Year	1. Population  2. Interventions and treatment duration (TP)  3. # Randomized/# completing trial	1. Criteria for Diagnosis  2. Diagnosis  3. Disease Severity	Study Quality  Funding Source Randomization Blinding Withdrawals	Cognitive Function		Global Assessment		Behavior/ Mood		Quality of Life/ ADL	
				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Tariot 2000 (39)	1. Mean age 76.8 years. 36% male and 93% white  2. A: Galantamine 8mg/d B: Galantamine 16mg/d C: Galantamine 24mg/d TP: 5 months  3. 978/679	1. NINCDS  2. Alzheimer's Disease  3. Probable (mild to moderate)	Not reported Rand – 2/2 Blind – 2/2 Withdraw – 1/1	ADAS-Cog	A: -1.30 (-2.57,-0.03) B: -3.10 (-4.13,-2.07) C: -3.10 (-4.18,-2.02)	CIBIC+ RR improved or stabilized	A: 1.08 (0.88,1.33) B: 1.35 (1.16,1.57) C: 1.31 (1.12,1.52)	NPI (2 <sup>0</sup> )	A: 0.30 (-2.09,2.69) B: -2.10 (-4.04,-0.16) C: -2.00 (-4.08,0.08)	ADCS/ADL (2 <sup>0</sup> )	A: 0.60 (-1.36,2.56) B: 3.10 (1.57,4.63) C: 2.30 (0.64,3.96)
				ADAS-cog ≥ 4 point change(2 <sup>0</sup> )	PB = 19.6% *GAL 16mg = 35.6% *GAL 24mg = 37% (*p<0.01)						
				ADAS-cog ≥ 7 point change(2 <sup>0</sup> )	PB = 7.6% +GAL 16mg = 15.9% +GAL 24mg = 22.3% (+ p<0.001)						

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				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Wilcock 2000 (42) Wilcock 2001 (109)	1. Mean age 72.2 years, 37% male 2. A: Galantamine 24mg/d B: Galantamine 32mg/d TP: 6 months  3. 653/525	1. NINCDS  2. Alzheimer's Disease  3. mild to moderate	Non-industry Funding source Rand -2/2 Blind - 2/2 Withdraw - 1/1	ADAS-cog	A: -2.90 (-4.00, -1.80) B: -3.20 (-4.36, -2.04)	CIBIC	A: 1.08 (0.70, 1.65) B: 1.49 (1.00, 2.22)	NT	DAD (2 <sup>0</sup> )	A: 2.80 (-0.11, 5.71) B: 3.50 (0.52, 6.48)	
				ADAS-cog ≥ 4 point change(2 <sup>0</sup> )	PB = 15 %, +GAL 24mg = 29% +GAL 32mg = 32% (+p < 0.001)	CIBIC+ RR improved or stabilized	A: 1.24 (1.04, 1.48) B: 1.32 (1.11, 1.57)				
Wilkinson 2001 (44)	1. Community dwelling, mean age 73.8 years, 42% male 2. A: Galantamine (18mg/d) B: Galantamine (24mg/d) C: Galantamine (36mg/d) TP: 12 weeks  3. 285/206	1. NINCDS DSM-III-R  2. Alzheimer's Disease  3. mild to moderate	Industry Funded Rand - 2/2 Blind - 2/2 Withdraw - 1/1	ADAS-Cog	A: -1.70 (-3.64, 0.24) B: -3.00 (-5.23, -0.77) C: -2.30 (-4.24, -0.36)	CGIC(2 <sup>0</sup> )	A: 1.32 (0.84, 2.08) B: 1.02 (0.59, 1.77) C: 1.15 (0.67, 1.98)	NT	PDS-1(2 <sup>0</sup> )	A: 0.72 (0.41, 1.27) B: 0.42 (0.18, 0.98) C: 0.88 (0.47, 1.63)	

Author Year	1. Population  2. Interventions and treatment duration (TP)  3. # Randomized/# completing trial	1. Criteria for Diagnosis  2. Diagnosis  3. Disease Severity	Study Quality  Funding Source Randomization Blinding Withdrawals	Cognitive Function		Global Assessment		Behavior/ Mood		Quality of Life/ ADL	
				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Wilkinson 2005 (48)	1. Mean age 75 years  2. Galantamine TP: 4 weeks, 48 wk open label  3. 285/206	1. NR  2. Alzheimer's Disease  3. mild to moderate	Industry Funded Rand – 1/2 Blind – 1/2 Withdraw – 1/1	ADAS-cog	(p>0.05)						

Author Year	1. Population 2. Interventions and treatment duration (TP) 3. # Randomized/# completing trial	1. Criteria for Diagnosis 2. Diagnosis 3. Disease Severity	Study Quality Funding Source Randomization Blinding Withdrawals	Cognitive Function		Global Assessment		Behavior/ Mood		Quality of Life/ ADL	
				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*

**Rivastigmine versus Placebo (except otherwise stated)**

Agid 1998 (50)	1. mean age 69.4 years (range: 50 – 90 years) and 44% male  2. A: Rivastigmine (6mg/d) B: Rivastigmine (4mg/d) TP: 13 weeks  3. 402/357	1. DSM-III-R NINCDS  2. Alzheimer's Disease  3. Probable (mild to moderate)	Industry Funded Rand –2/2 Blind – 2/2 Withdraw – 2/1	MMSE	A: 0.30 (-0.46, 1.06) B: 0.00 (-0.77, 0.77)	CGIC RR Successful outcome	A: 1.43 (1.00, 2.04) B: 1.05 (0.71, 1.56)	NOSGER - Mood	A: 0.00 (-0.74,0.74) B: 0.10 (-0.67,0.87)	NOSGER - IADL	A: -0.50(- 1.40,0.40) B: 0.20(- 0.66,1.06)
				Digit Symbol Substitution	A: 2.30 (0.30, 4.30) B: 1.20 (-0.37, 2.77)						
				Trail Making	A: -7.80 (-18.58, 2.98) B: -2.10 (-11.03, 6.83)						
				FULD Object- Memory Evaluation (TS)	A: 1.60 (0.04, 3.16) B: 1.30 (-0.22, 2.82)						
				FULD Object- Memory Evaluation (TR)	A: 1.00 (-0.12, 2.12) B: 0.70 (-0.46, 1.86)						

Author Year	1. Population  2. Interventions and treatment duration (TP)  3. # Randomized/# completing trial	1. Criteria for Diagnosis  2. Diagnosis  3. Disease Severity	Study Quality  Funding Source Randomization Blinding Withdrawals	Cognitive Function		Global Assessment		Behavior/ Mood		Quality of Life/ ADL	
				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Ballard 2005 (57)	1. Institutions Dwelling, mean age 83.8 years, 20% male  2. A: Rivastigmine B: Rivastigmine vs. Quetiapine TP: 26 weeks  3. 93/74	1. NINCDS- ADRDA  2. Alzheimer's Disease  3. moderate to severe	Industry provided supplies Rand – 2/2 Blind – 1/2 Withdraw – 1/1	SIB (2 <sup>0</sup> )	A: -6.40 (-19.43, 6.63) B: 8.20 (-4.88, 21.28)		NT	Agitation Inventory	A: -1.80 (-11.71, 8.11) B: -2.70 (-11.99, 6.59)		NT
Corey- Bloom 1998 (51) <u>Auxiliary:</u> Farlow 2001 (110) Farlow 2000 (111) Kumar 2000 (112) Del Ser 2000 (113) Doraiswamy 2002 (114)	1. Mean age 74.5 years, (range: 45 – 89 years), 39% male and 95% White  2. A: Rivastigmine (6 -12 mg) B: Rivastigmine (1 - 4 mg) TP: 26 weeks  3. 699/545	1. DSM-IV NINCDS  2. Alzheimer's Disease  3. mild to moderate severe	Industry Funded Rand – 2/2 Blind – 2/2 Withdraw – 2/1	ADAS-Cog	A: -3.78 (-4.87,-2.69) B:-1.73 (-2.82,-0.64)	CIBIC+	A: -0.29 (-0.52,-0.06) B: -0.26 (-0.49,-0.03)	NT		PDS (2 <sup>0</sup> )	A: 3.38 (1.51,5.25) B: -0.29 (-2.16,1.58)
				ADAS-cog ≥ 4 point change (2 <sup>0</sup> )	RIV 6-12mg =25%	CIBIC+ RR improved	A: 1.51 (1.03, 2.19) B: 1.57 (1.09, 2.28)				
						GDS (2 <sup>0</sup> )	A: 0.19 (0.06,0.32) B: 0.16 (0.03,0.29)				

Author Year	1. Population 2. Interventions and treatment duration (TP) 3. # Randomized/# completing trial	1. Criteria for Diagnosis 2. Diagnosis 3. Disease Severity	Study Quality Funding Source Randomization Blinding Withdrawals	Cognitive Function		Global Assessment		Behavior/ Mood		Quality of Life/ ADL	
				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Emre 2005 (52) <u>Auxillary:</u> Wesnes 2005 (115) Dujardin 2006 (108) Tekin 2006 (117) Willan 2006 (118)	1. Mean age 72.7y, 64.9% male, 99.6% White 2. Rivastigmine (3 -12 mg/d) TP: 24 weeks 3. 541/410	1. DSM-IV 2. Dementia associated with Parkinson's disease 3. mild to moderate- severe	Industry Funded Rand – 2/2 Blind – 2/2 Withdraw – 1/1	ADAS-cog MMSE (2 <sup>0</sup> ) DRS (2 <sup>0</sup> )	-2.80 (-4.26,-1.34) 1.00 (0.33,1.67) (P<0.05)	ADCS- CGIC	-0.50 (-0.77,-0.23)	NPI (2 <sup>0</sup> ) -2.00 (-3.91,-0.09)	ADCS-ADL (2 <sup>0</sup> ) 2.50 (0.43,4.57)		
Forette 1999 (11)	1. Mean age 70.6 years 2. A: Rivastigmine b.i.d B: Rivastigmine t.i.d TP: 18 weeks 3. 114/85	1. NINCDS DSM-III-R 2. Alzheimer's Disease 3. Mild to moderate	Industry Funded Rand – 1/2 Blind – 1/2 Withdraw – 1/1	ADAS-Cog Wechsler logical memory test ADAS-cog improved	A: -4.80 (-6.04,-3.56) B: -1.60 (-2.78,-0.42) A vs B 1.7 (p=0.012) A: (p=0.054)	NOSGER Self-care NOSGER Memory CIBIC+ RR Improved	A: -0.10 (-1.49, 1.29) B: -0.30 (-1.74, 1.14) A: -2.00 (-4.04, 0.04) B: -2.30 (-4.25, -0.35) A: 3.58 (1.19, 10.74) B: 2.26 (0.72, 7.15)	NOSGER Disturbing behavior NOSGER Mood NOSGER Social behavior	A: -0.40 (-2.04, 1.24) B: -0.80 (-2.69, 1.09) A: 1.30 (-0.59, 3.19) B: 0.20 (-1.73, 2.13) A: -0.30 (-2.13, 1.53) B: -1.40 (-3.46, 0.66)	IADL	A: -0.40 (-2.60, 1.80) B: -1.50 (-3.85, 0.85)

Author Year	1. Population  2. Interventions and treatment duration (TP)  3. # Randomized/# completing trial	1. Criteria for Diagnosis  2. Diagnosis  3. Disease Severity	Study Quality  Funding Source Randomization Blinding Withdrawals	Cognitive Function		Global Assessment		Behavior/ Mood		Quality of Life/ ADL	
				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Karaman 2005 (53)	1. History of cognitive decline that was gradual in onset and progressive over a period of at least 6 months MMSE score of 14. Mean age 73.8 years (range: 60 - 90 years), 45.5% male  2. Rivastigmine (3 -12 mg/d) TP: 12 months  3. 44/41	1. NINCDS- ADRDA DSM IV  2. Alzheimer's Disease  3. Moderate to severe	Not reported Rand – 1/2 Blind – 1/2 Withdraw – 1/1	ADAS-cog	-5.27 (-5.73,-4.81)	CIBIC+	-0.18 (-0.28, -0.08)	NT	PDS	3.52 (3.40, 3.64)	
				ADAS-cog Decline ≥ 4 points	PB = 45% RIV = 18.3%	GDS	4.30 (3.81, 4.79)		DAD	-1.00 (-1.06,-0.94)	
				MMSE	-0.35 (-0.46,-0.24) PB = deteriorated by 1.2 points RIV = improved by 0.20 points	ADCS-ADL	0.24 (0.14,0.34)				

Author Year	1. Population  2. Interventions and treatment duration (TP)  3. # Randomized/# completing trial	1. Criteria for Diagnosis  2. Diagnosis  3. Disease Severity	Study Quality  Funding Source Randomization Blinding Withdrawals	Cognitive Function		Global Assessment		Behavior/ Mood		Quality of Life/ ADL	
				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
McKeith 2000 (54)	1. Mean age 73.9 years (range: 57 – 87 years) and 56% male  2. Rivastigmine (3.0 - 12 mg/d) TP: 20 weeks  3. 102/92	1. Consensus criteria  2. Lewy-body dementia  3. mild to moderate	Industry Funded  Rand – 2/2 Blind – 2/2 Withdraw – 1/1	MMSE (2 <sup>0</sup> ) 1.4 (p=0.072)  CCASSS (p< 0.05)		CGC+ (2 <sup>0</sup> ) (p > 0.05)		NPI-4 1.70 (-1.12, 4.52)  NPI-10 (2 <sup>0</sup> ) 3.80 (-1.65, 9.25)			NT
Potkin 2001 (55)	1. Mean age 75.9 years, (range: 64 – 89 years)  2. Rivastigmine (3, 6 or 9 mg/d) TP: 26 weeks  3. 27/27	1. DSM-IV NINCDS  2. Alzheimer's Disease  3. mild to moderate severe	Partially Funded by industry Rand – 1/2 Blind – 2/2 Withdraw – 0/1	Picture Naming task (p > 0.05)		CIBIC+ RR improved or stabilized 2.63 (0.79, 8.70)		NT			NT

Author Year	1. Population 2. Interventions and treatment duration (TP) 3. # Randomized/# completing trial	1. Criteria for Diagnosis 2. Diagnosis 3. Disease Severity	Study Quality Funding Source Randomization Blinding Withdrawals	Cognitive Function		Global Assessment		Behavior/ Mood		Quality of Life/ ADL	
				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Rösler 1999 (56)	1. Community dwelling. Comorbidity: diabetes, hypertension, arthritis. Mean age 72 years (range: 45 – 95 years), and 41% male	1. DSM-IV NINCDS 2. Alzheimer's Disease 3. mild to moderate severe	Industry Funded Rand – 2/2 Blind – 2/2 Withdraw – 1/1	ADAS- Cog	A: -1.60 (-2.84,-0.36) B: 0.03 (-1.22, 1.28)	CIBIC+	A: -0.47 (-0.73,-0.21) B: -0.14 (-0.39,0.11)	NT	PDS (2 <sup>0</sup> )	A: 2.23 (-0.16,4.62) B: -1.19 (-3.59,1.21)	
<u>Auxiliary:</u> Rösler 2001 (119) Rösler 1998 (120) Del Ser 2000 (113)				ADAS-cog ≥ 4 point change	PB = 16% +RIV 1-4 mg/d = 15% *RIV 6-12 mg/d = 24% (+p>0.05; *p<0.01)	CIBIC+ RR improved GDS (2 <sup>0</sup> )	A: 1.83 (1.34, 2.50) B: 1.48 (1.07, 2.05) A: 0.20 (0.06 ,0.34) B: 0.04 (-0.10, 0.18)				
Farlow 2000 (111) Doraiswamy 2002 (114)	2. A: Rivastigmine (6-12mg/d) B: Rivastigmine (1-4mg/d) TP: 14 weeks  3. 725/581			MMSE (2 <sup>0</sup> )	A: 0.68 (0.04, 1.32) B: -0.15 (-0.79, 0.49)						

Tacrine versus Placebo (except otherwise stated)

Author Year	1. Population  2. Interventions and treatment duration (TP)  3. # Randomized/# completing trial	1. Criteria for Diagnosis  2. Diagnosis  3. Disease Severity	Study Quality  Funding Source Randomization Blinding Withdrawals	Cognitive Function		Global Assessment		Behavior/ Mood		Quality of Life/ ADL	
				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Knapp 1994b (58) Auxiliary: Farlow 1998 (121) Gracon 1996 (122) Henke 1997 (123) Knapp 1994a (124) Knopman 1996 (125) Raskind 1997 (126) Schneider 1997 (127) Schneider 1996 (128) Smith 1996 (129)	1. mean age 72.8 years (range: 49 – 95 years) and 48% male  2. A: Tacrine 80mg/d B: Tacrine 120mg/d C: Tacrine 160mg/d TP: 30 weeks  3. 663/279	1. NINCDS  2. Alzheimer's Disease  3. Probable (mild to moderate)	Industry Funded Rand – 2/2 Blind – 2/2 Withdraw – 0/1	ADAS-Cog  ADAS-cog ≥ 4 point change  MMSE (2 <sup>0</sup> )  MMSE ≥ 3.0 point change	A: -1.40 (-3.50, 0.70) B: -2.00 (-3.50,-0.50) C: -2.20 (-3.50,-0.80)  PB= 25% TA 160 mg = 40%  A: 0.60 (-0.60,1.70) B: 0.40 (-0.40,1.20) C: 0.90 (0.10,1.60)  P = 20% TA 160 mg = 42%	CIBI  FCCA  GDS (2 <sup>0</sup> )  ADAS-Total (2 <sup>0</sup> )	A: -0.10 (-0.40, 0.10) B: -0.20 (-0.40, -0.01) C: -0.20 (-0.40, -0.01)  A: -0.30 (-0.80,0.10) B: -0.40 (-0.80,-0.10) C: -0.60 (-0.90,-0.30)  A: 0.07 (-0.10,0.30) B: -0.05 (-0.20,0.08) C: -0.20 (-0.30,-0.04)  A: -2.40 (-5.20, 0.40) B: -2.20 (-4.20, -0.30) C: -3.00 (-4.80, -1.10)	ADAS- Noncog (2 <sup>0</sup> )  A: -0.80 (-2.20,0.60) B: -0.30 (-1.30,0.70) C: -0.70 (-1.60,0.20)	IADL (2 <sup>0</sup> )  (p>0.05)		

Author Year	1. Population 2. Interventions and treatment duration (TP) 3. # Randomized/# completing trial	1. Criteria for Diagnosis 2. Diagnosis 3. Disease Severity	Study Quality Funding Source Randomization Blinding Withdrawals	Cognitive Function		Global Assessment		Behavior/ Mood		Quality of Life/ ADL	
				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Maltby 1994 (59)	1. Community dwelling, mean age 68.8 years (range: 52 – 84 years) and 51% male  2. Tacrine (25- 100 mg/d) TP: 36 weeks  3. 41/32	1. NINCDS DSM-III-R  2. Alzheimer's Disease  3. Probable (mild to moderate)	Non-industry Funding source Rand – 1/2 Blind – 1/2 Withdraw – 1/1	MMSE	-0.10 (p=0.944)	NT	LPRS	-0.50 (p=0.638)	NT		
				<u>Memory</u> <u>Tests:</u> Verbal (total words)	4.50 (p=0.200)						
				Visual (total objects)	1.50 (p=0.359)						
				Digit forward (6 months)	0.50 (p=0.723)						
				Verbal fluency (6 months)	3.80 (p=0.198)						
				Face recognition (6 months)	-0.10 (p=0.651)						

Author Year	1. Population  2. Interventions and treatment duration (TP)  3. # Randomized/# completing trial	1. Criteria for Diagnosis  2. Diagnosis  3. Disease Severity	Study Quality  Funding Source Randomization Blinding Withdrawals	Cognitive Function		Global Assessment		Behavior/ Mood		Quality of Life/ ADL	
				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Prentice 1996 (60)	1. Mean age 68.0 years, 13% male  2. Tacrine (40- 80mg/d) TP: 13 weeks  3. 23/19	1. DSM-III-R NINCDS  2. Alzheimer's Disease  3. Probable	Partially Funded by industry. Rand – 1/2 Blind – 1/2 Withdraw – 1/1	MMSE	0.10 (p>0.05)	NT		RPT	-2.00 (p>0.05)		NT
Wong 1999 (62)	1. Mean age 73.8 years, (range: 52 – 94 years), 50% male  2. Tacrine (30- 120mg/d) TP: 30 weeks  3. 100/56	1. NINCDS  2. Alzheimer's Disease  3. Probable (mild to moderate)	Industry provided supplies Rand – 1/2 Blind – 1/2 Withdraw – 1/1	CASI	2.75 (-1.31, 6.81)	CGIC investigator (2 <sup>0</sup> )	-0.03 (-0.49, 0.43)	ADS (2 <sup>0</sup> )	0.34 (-1.63, 2.31)		NT
				IQCODE	0.18 (-0.14, 0.50)						
				MMSE (2 <sup>0</sup> )	1.29 (-0.20, 2.78)						

Author Year	1. Population  2. Interventions and treatment duration (TP)  3. # Randomized/# completing trial	1. Criteria for Diagnosis  2. Diagnosis  3. Disease Severity	Study Quality  Funding Source Randomization Blinding Withdrawals	Cognitive Function		Global Assessment		Behavior/ Mood		Quality of Life/ ADL	
				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Wood 1994 (63)	1. Community dwelling, mean age 75 years, 54% male  2. Tacrine (20 – 120 mg/d) TP: 12 weeks  3. 154/131	1. NINCDS  2. Alzheimer's Disease  3. mild to moderate	Industry Funded Rand –1/2 Blind – 1/2 Withdraw – 1/1	MMSE  AMTS(2 <sup>0</sup> )	0.38 (p=0.55)  0.34 (p=0.18)	CGRS  RGRS(2 <sup>0</sup> )  Blessed(2 <sup>0</sup> )  GBS(2 <sup>0</sup> )	(p=0.012)  (p=0.03)  -0.16 (p=0.60)  -2.6 (p=0.53)	ADAS-non cog (2 <sup>0</sup> )  (p > 0.05)			NT
Weinstein 1991 (61) Goad 1991 (130)	1. Community Dwelling, mean age 74.6 years (range: 56-79 years), 50% male  2. Tacrine 100 mg/d TP: 12 weeks  3. 13/12	1. DSM-III-R  2. Alzheimer's Disease  3. Probable (mild to severe)	Non-Industry Funding source, industry provided supplies Rand – 2/2 Blind – 2/2 Withdraw – 1/1	CAMCOG	0.00 (-6.40, 6.40)		NT		NT	IDDD	3.33 (-7.49, 14.16)

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			Funding Source Randomization Blinding Withdrawals	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
<b>Tacrine versus others</b>											
Gutzmann 2002 (64)	1. Community dwelling, mean age 71.2 years (range: 44-90 years), 36% male, 100% white  2. Tacrine 160mg/d vs. Idebenone 360 mg/d TP: 60 weeks  3. 203/44	1. NINCDS DSM-III-R  2. Alzheimer's Disease, Progressive degenerated dementia  3. mild to moderate	Partially Funded by industry  Rand – 1/2 Blind – 1/2 Withdraw – 1/1	ADAS-cog (2 <sup>0</sup> )	-2.29 (p > 0.05)	CGI (2 <sup>0</sup> )	0.13 (p > 0.05)	ADAS-non cog (2 <sup>0</sup> )	-1.71 (p > 0.05)	NOSGER- IADL(2 <sup>0</sup> )	-0.53 (p > 0.05)

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				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
<b>Memantine vs. placebo</b>											
Orgogozo 2002 (65)	1. Mean age 76.4 years, 53% male, 100% white 2. Memantine (5 - 20mg/d) TP: 28 weeks 3. 321/234	1. NINDS- AIREN 2. Vascular dementia 3. mild to moderate	Industry Funded Rand – 1/2 Blind – 1/2 Withdraw –1/1	ADAS-Cog	-2.85 (-4.39,-1.31)	CIBIC+	-0.29 (-0.66, 0.08)	NOSGER (2 <sup>0</sup> )	-0.53 (-3.91, 2.85)		NT
				MMSE (2 <sup>0</sup> )	1.23 (0.23, 2.23)	RR improved or stabilized	1.15 (0.91, 1.45)				
						CGI-C Clinician (2 <sup>0</sup> )	-0.27 (-0.56, 0.02)				
						RR improved	1.40 (1.03, 1.90)				
						CGI-C Caregiver (2 <sup>0</sup> )	-0.30 (-0.63, 0.03)				
						RR improved	1.14 (0.84,1.55)				
						GBS (2 <sup>0</sup> )	-3.74 (-7.82, 0.34)				

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				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Peskind 2006 (69)	1. Mean age 77.5, 41.2% male, 93.8 % White  2. Memantine 20mg/d TP: 24 weeks  3. 403/394	1. NINDS- ADRDA  2. Alzheimer's Disease  3. Probable (mild to moderate)	Industry Funded Rand – 2/2 Blind – 2/2 Withdraw – 1/1	ADAS-Cog	-1.00 (-2.72, 0.72)	CIBIC+	-0.28 (-3.16, 2.60)	NPI (2 <sup>0</sup> )	-2.10 (-5.59, 1.39)	ADCS-ADL (2 <sup>0</sup> )	0.00 (-2.31, 2.31)
Reisburg 2003 (68) Wimo 2003 (131)	1. Community dwelling, mean age 76 years, 33% male,  2. Memantine 20mg/d TP: 28 weeks  3. 252/181	1. NINDS- ADRDA DSM IV  2. Alzheimer's Disease  3. Moderate to severe	Industry Funded Rand – 2/2 Blind – 2/2 Withdraw – 1/1	SIB(2 <sup>0</sup> )	6.10 (2.99, 9.21)	CIBIC+	-0.30 (-0.58, -0.02)	NPI (2 <sup>0</sup> )	-3.30 (-7.33, 0.73)	ADCS-ADL	2.10 (0.46, 3.74)
				MMSE(2 <sup>0</sup> )	0.70 (0.02,1.38)	GDS (2 <sup>0</sup> )	-0.10 (-0.22,0.02)			FAST(2 <sup>0</sup> )	-0.40 (-0.73,-0.07)

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				Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Tariot 2004 (70)	1. Mean age 75.5 years, 35.0% male	1. NINDS- ADRDA	Industry Funded Rand – 2/2 Blind – 2/2	SIB	3.40 (1.51, 5.29)	CIBIC+ (2 <sup>0</sup> )	-0.25 (-0.46, -0.04)	NPI(2 <sup>0</sup> )	-3.80 (-6.53,-1.07)	ADCS-ADL	1.40 (0.00, 2.80)
Van Dick 2005 (132) Cummings 2006 (133)	2. Memantine (5-20mg/d) TP: 24 weeks  3. 404/322	2. Alzheimer's Disease  3. Moderate to severe	Withdraw – 1/1	SIB ≥8 points  SIB ≥12 points	ARR (%) 8.5 (1.5, 15.5)  ARR (%) 5.0 (0.3, 9.7)	RR improved or stabilized	1.23 (1.00, 1.50)				
Wilcock 2002 (66)	1. Community Dwelling, mean age 77.4 years, (range: 54 – 97 years), 51% male  2. Memantine (5 - 20mg/d) TP: 28 weeks  3. 579/464	1. DSM-III-R NINDS- AIREN  2. Vascular dementia  3. mild to moderate	Industry provided supplies Rand – 2/2 Blind – 2/2 Withdraw – 0/1	ADAS-Cog	-1.75 (-3.02, 0.48)	CGI-C	(p=0.1103)	NOSGER (2 <sup>0</sup> )	-1.13 (-3.57, 1.31)		NT
				MMSE (2 <sup>0</sup> )	-0.27 (-1.06, 0.52)	GBS (2 <sup>0</sup> )	-0.83 (-3.78, 2.12)				

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			Funding Source Randomization Blinding Withdrawals	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*	Measure	Result Effect Size*
Winblad 1999 (67)	1. Institution dwelling, mean age 71.2 years, (range: 60 – 80 years) and 42% male  2. Memantine (5 - 10mg/d) TP: 12 weeks  3. 166/151	1. DSM-III-R 2. Dementia of Alzheimer's type, Vascular dementia, progressive degenerative dementia  3. Moderate to severe	Not reported Rand –1/2 Blind – 1/2 Withdraw – 1/1	MMSE	NR	CGI-C RR improved	1.62 (1.24, 2.12)			BGP (Care Dependency subscale)	-2.00 (-5.65, 1.65)

\*Effect size estimate included 95% confidence interval OR end point mean difference. 2<sup>0</sup> = secondary outcome; ABS=Adaptive Behaviour Scale; ADAS-Cog=Alzheimer's Dementia Assessment Scale-Cognitive Component; ADCD-ADL=Alzheimer's Disease Co-operative Study-Activities of Daily Living; ADCS- ARR = adjusted relative risk; CGIC=Alzheimer's Disease Co-operative Study-Clinical, Global Impression of Change; ADFACS=Alzheimer's Disease Functional Assessment and Change Scale; AMTS=Abbreviated Mental Test Score; BADLS=Bristol Activities of Daily Living Scale; CAMTOT=CAMCOG Total Score, Cambridge Cognitive Schedule; CANTAB-PRM=Cambridge Automated Neuropsychological Test Assessment Battery-Patterns of Recognition; CANTAB-SOC=Cambridge Automated Neuropsychological Test Assessment Battery-Stockings of Cambridge; CASI=Cognitive Abilities Screening Instrument; CDR-SB=Clinical Dementia Rating-Sum of Boxes; CGI=Clinical Global Impression; CGIC=Clinical Global Impression of Change; CIBI=Clinician's Interview-Based Impression; CIBIC+=Clinician's Interview Based Impression of Change; CVLT=California Verbal Learning Test; DAD=Disability Assessment for Dementia; DMR=Dementia Rating Scale for Mentally Retarded; DPZ=Donepezil; DRS-Memory=Dementia Rating Scale-Memory; DRS-total=Dementia Rating Scale-total; DSM IV=Diagnostic and Statistical Manual of Mental Disorders, Edition IV; DSM-III-R=Diagnostic and Statistical Manual of Mental Disorders, Edition III-R; FAQ=Functional Activities Questionnaire; FCCA=Final Comprehensive Consensus Assessment; FRS=Functional Rating Scale test; GBS-1=Gottfries-Brane-Steen; GDS=Global Deterioration Scale; Ham-D=Hamilton Depression Rating Scale; HVLT-R=Hopkins Verbal Learning Test; IADL=Instrumental Activities of Daily Living Scale; IDDD=Interview for Deterioration in Daily Living Activities in Dementia-complex task; IQCODE=Informant Questionnaire on Cognitive Decline in the Elderly; MMSE=Mini-mental Status Exam; N/A=Not available; NINCDS=National Institute of Neurological and Communicative Disorders and Stroke; NINCDS-ADRDA=National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association; NINCDS-AIREN=National Institute of Neurological and Communicative Disorders and Stroke-Association Internationale pour la Recherche et l'Enseignement en Neurosciences; NINDS-AIREN=National Institute of Neurological Disorders and Stroke-Association Internationale pour la Recherche et l'Enseignement en Neurosciences; NOSGER-IADL=Nurses Observation Scale for Geriatric Assessment-Instrumental Activities of Daily Living subscale; NOSGER-Mood=Nurses Observation Scale for Geriatric Assessment-Mood; NPI-4=Neuropsychiatric Inventory-subscore 4; NPI-NH=Neuropsychiatric Inventory-Nursing Home Version; NT=not tested; PB=Placebo;

PDS=Progressive Deterioration Scale; PGA=Patient Global Assessment; PSMS=Physical Self-maintenance Scale; QoL=Quality of Life; RPT=Rivermead Profile Test; RR=Relative risk; SIB=Severe Impairment Battery; SKT=Syndrome Kurz Test, syndrome short test; TP=Toulouse Pieron; VaD=Vascular Dementia