

**Table 1: Baseline demographics and clinical characteristics of participants and carers**

	<b>Mirtazapine (n=102)</b>	<b>Placebo (n=102)</b>
<b>Participants</b>		
<b>Age (sd)</b>	82.2 (7.8)	82.8 (7.7)
<b>Sex</b>	n=102	n=102
Female	76 (75%)	59 (58%)
<b>Residence</b>	n=102	n=102
own household	55 (54%)	57 (56%)
care home	47 (46%)	45 (44%)
<b>Agitation</b>	n=102	n=102
CMAI (29-203)	71.1 (16.4)	69.8 (17.1)
<b>Cognition</b>	n=52	n=50
Standardised MMSE (0-30)	13.4 (8.1)	16.1 (6.7)
<b>Condition-specific quality of life</b>		
DEMQOL (28-122)	n=41	n=37
	92.4 (10.8)	95.8 (10.2)
DEMQOL-Proxy (31-124)	n=100	n=99
	92.3 (15.0)	90.9 (14.4)
<b>Generic quality of life</b>	n=100	n=101
EQ-5D (proxy report by carer) (0-1)	0.46 (0.34)	0.50 (0.32)
<b>Neuropsychiatric symptoms</b>		
NPI total score (0-144)	n=98	(n=102)
	32.7 (16.7)	34.9 (18.2)
NPI agitation/aggression subscore (0–12)	n=99	n=102
	5.6 (3.2)	5.6 (3.4)
NPI depression/anxiety/irritability subscore (0–36)	n=99	n=102
	9.9 (6.2)	10.5 (7.0)
<b>Suicidality</b>		
CSSRS	n=102	n=102
Suicidal ideation (lifetime)	18 (18%)	13 (13%)
Suicidal ideation (past month)	11 (11%)	11 (11%)
Suicidal behaviour (lifetime)	4 (4%)	0
Suicidal behaviour (past 3 months)	2 (2%)	0
<b>Carers</b>		
<b>Carer</b>		
Paid	39 (38%)	31 (30%)
Family	63 (62%)	71 (70%)
<b>Family carer relationship</b>		
Partner or spouse	34 (54%)	35 (49%)
Son or daughter	21 (33%)	31 (44%)
Sibling	1 (2%)	0
Other relative	5 (8%)	3 (4%)
Friend	1 (2%)	2(3%)
Other	1 (2%)	0
<b>Family carer occupation (pre-retirement)</b>		
Professional	13 (21%)	13 (18%)
Managerial and Technical	23 (37%)	22 (31%)
Skilled Non-manual	9 (14%)	11 (15%)
Skilled Manual	11 (17%)	8 (11%)

Partly Skilled	2 (3%)	8 (11%)
Unskilled	3 (5%)	0
Unemployed or Unwaged	2 (3%)	5 (7%)
Unanswered	0	4 (6%)
<b>Carer mental health (family carers only)</b>	n=61	n=66
GHQ-12	15.0 (5.8)	14.5 (4.9)
<b>Carer burden</b>	n=58	n=66
Zarit Carer Burden Inventory <sup>1</sup>	33.8 (15.7)	34.1 (13.9)
<b>Carer generic quality of life</b>	n=61	n=66
EQ-5D <sup>3</sup>	0.79 (0.21)	0.81 (0.22)
<b>NPI carer distress subscore (0-60)</b>	n=94	n=99
	14.1 (8.6)	15.5 (9.0)

CMAI Cohen Mansfield Agitation Inventory, MMSE Mini Mental State Examination, EQ-5D EuroQOL 5 dimension, NPI Neuropsychiatric Inventory, CSSRS Columbia Suicide Severity Rating Scale.

**Table 2: Comparisons of participant primary outcomes at 12 weeks and secondary outcomes at 6 weeks and 12 weeks**

	<b>Mirtazapine (n=102)</b>	<b>Placebo (n=102)</b>	<b>Difference</b>	<b>(95% CI)</b>	<b>Adjusted difference<sup>1</sup></b>	<b>(95% CI)</b>	<b>p-value</b>
<b>12 week primary outcome</b>							
Agitation (CMAI)	n=79 61.4 (sd 22.6)	n=87 60.8 (sd 21.8)	0.59	(-6.22, 7.40)	-1.74 -0.93 <sup>2</sup>	(-7.17, 3.69) -6.42, 4.56	0.530 0.739
<b>6 week secondary outcomes</b>							
Agitation (CMAI)	n=84 61.4 (23.5)	n=88 60.0 (19.9)	1.39	(-5.15, 7.93)	-0.55	(-6.18, 5.08)	0.848
Cognition (sMMSE)	n=33 14.9 ( 6.9)	n=30 16.5 ( 7.3)	-1.59	(-5.17, 1.99)	-0.14	(-1.46, 1.18)	0.838
Quality of life (DEMQOL)	n=32 95.1 (10.2)	n=32 96.8 ( 8.4)	-1.69	(-6.38, 3.00)	1.12	(-2.74, 4.97)	0.570
Quality of life (DEMQOL-Proxy)	n=79 96.6 (14.7)	n=86 94.6 (16.2)	2.03	(-2.74, 6.79)	0.80	(-3.18, 4.77)	0.694
Quality of life EQ-5D (proxy report by carer)	n=82 0.48 (0.33)	n=87 0.56 (0.30)	-0.08	(-0.17, 0.02)	-0.07	(-0.13, 0.00)	0.061
Neuropsychiatric symptoms	n=84	n=88					
NPI total score	27.1 (20.0)	24.8 (20.0)	2.29	(-3.73, 8.31)	2.03	(-2.89, 6.95)	0.419
NPI agitation/aggression subscore	n=84 4.0 (3.6)	n=88 4.2 (3.5)	-0.20	(-1.28, 0.87)	-0.34	(-1.30, 0.62)	0.490
NPI depression/anxiety/irritability subscore	n=84 7.9 (7.7)	n=88 7.2 (8.2)	0.68	(-1.72, 3.07)	0.70	(-1.24, 2.63)	0.482
<b>12 week secondary outcomes</b>							
Cognition (sMMSE)	n=24 16.9 ( 7.1)	n=26 15.0 (7.7)	1.84	(-2.29, 6.06)	1.36	(-0.30, 3.01)	0.108
Quality of life (DEMQOL)	n=24 94.3 ( 7.1)	n=24 97.1 (8.4)	-2.83	(-7.35, 1.68)	-1.36	(-5.82, 3.10)	0.549
Quality of life (DEMQOL-Proxy)	n=71 98.4 (14.5)	n=82 97.5 (12.4)	0.93	(-3.37, 5.23)	0.44	(-3.09, 3.96)	0.809
Quality of life EQ-5D (proxy report by carer)	n=77 0.46 (0.35)	n=84 0.50 (0.33)	-0.04	(-0.14, 0.07)	-0.01	(-0.08, 0.07)	0.822
Neuropsychiatric symptoms	n=75	n=84					
NPI total score	23.9 (17.8)	25.7 (19.6)	-1.80	(-7.69, 4.09)	-2.02	(-6.67, 2.62)	0.393
NPI agitation/aggression subscore	n=76 4.1 (3.4)	n=84 4.5 (3.6)	-0.40	(-1.49, 0.70)	-0.52	(-1.52, 0.47)	0.305

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NPI depression/anxiety/irritability subscore	n=75 6.9 (6.7)	n=84 7.3 (8.0)	-0.44	(-2.77, 1.88)	-0.58	(-2.43, 1.27)	0.541
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1. Adjusted for pre-specified factors: baseline CMAI, household status, and centre.
2. Adjusted for sex and pre-specified factors: baseline CMAI, household status, and centre.

**Table 3: Comparisons of carer secondary outcomes at 6 weeks and 12 weeks**

	<b>Mirtazapine (n=102)</b>	<b>Placebo (n=102)</b>	<b>Difference</b>	<b>95% CI</b>	<b>Adjusted difference<sup>1</sup></b>	<b>95% CI</b>	<b>p-value</b>
<b>6 Week Outcomes</b>							
Carer GHQ-12	n=50 12.8 (6.2)	n=54 12.1 (4.9)	0.69	(-1.46, 2.85)	0.61	(-1.21, 2.42)	0.512
Carer EQ-5D	n=50 0.83 (0.16)	n=55 0.83 (0.15)	0.00	(-0.06, 0.06)	0.01	(-0.04, 0.05)	0.821
Zarit Carer Burden Inventory	n=46 34.7 (16.3)	n=49 29.4 (13.9)	5.35	(0.82, 11.53)	3.76	(-0.30, 7.83)	0.069
NPI carer distress subscore	n=78 11.5 (1.1)	n=84 10.2 (8.8)	1.37	(-1.45, 4.19)	1.48	(-0.78, 3.73)	0.199
<b>12 Week Outcomes</b>							
Carer GHQ-12	n=44 13.1 (6.0)	n=52 12.2 (5.4)	0.88	(-1.43, 3.19)	0.36	(-1.58, 2.31)	0.714
Carer EQ-5D	n=46 0.80 (0.16)	n=49 0.82 (0.19)	-0.02	(-0.09, 0.06)	0.02	(-0.04, 0.07)	0.561
Zarit Carer Burden Inventory <sup>2</sup>	n=42 35.5 (17.2)	n=48 29.0 (15.8)	6.48	(-0.43, 13.39)	5.01	(0.80, 9.23)	0.020
NPI carer distress subscore	n=72 10.0 (8.6)	n=81 10.5 (8.3)	-0.52	(-3.22, 2.17)	-0.27	(-2.34, 1.80)	0.798

1. Adjusted for pre-specified factors: baseline CMAI, household status, and centre.

2. Asked of family carers only

**Table 4: Dose escalation and compliance with study medication**

	<b>Mirtazapine (n=102)</b>	<b>Placebo (n=102)</b>
<b>Dose escalation</b>		
<b>End of Week 4</b>	n=91	n=98
3 study meds/day	50 (55%)	59 (60%)
2 study meds/day	11 (12%)	16 (16%)
1 study med/day	9 (10%)	8 (8%)
0 study meds/day <sup>1</sup>	19 (21%)	15 (14%)
Dose information missing/inconsistent	2 (2%)	1 (1%)
<b>End of Week 6</b>	n=86	n=95
3 study meds/day	48 (56%)	49 (52%)
2 study meds/day	10 (12%)	23 (24%)
1 study med/day	9 (10%)	8 (8%)
0 study meds/day <sup>1</sup>	13 (15%)	7 (7%)
Dose information missing/inconsistent	1 (1%)	8 (8%)
<b>Compliance with study medication</b>		
<b>In trial at 6 weeks</b>	n=86	n=95
% Compliance <sup>2</sup> : mean (SD)	85 (16)	81 (16)
Compliance missing or inconsistent	n=44	n=45
<b>In trial at 12 weeks</b>	n=82	n=88
Taking trial medication at 12 weeks	n=68	n=76
% Compliance <sup>1</sup> : mean (SD)	75 (23)	74 (27)
Compliance missing or inconsistent	n=49	n=50

3. 1: Combining those reported on 0 tablets a day and those choosing or advised to stop

4. 2: Compliance: number of tablets taken/expected number of tablets taken x100 where: number of tablets taken is based upon expected number of tablets, minus number of tablets returned at 6 or 12 week visit; expected number of tablets calculated using prescribed number of tablets at each stage of trial

