

G.10.1.5 Sleep problems

Melatonin vs placebo

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
Total night-time sleep time (minutes)							
3 (Dowling, Singer, Wade)	Serious ¹	Not serious	Not serious	Serious ⁴	195	MD 12.59 (-12.56, 37.74)	Low
Ratio of daytime sleep to night-time sleep							
2 (Dowling, Singer)	Serious ²	Not serious	Not serious	Serious ⁴	184	MD -0.13 (-0.29, 0.03)	Low
Sleep efficiency							
1 (Singer)	Not serious	N/A	Not serious	Serious ⁴	151	MD -0.01 (-0.04, 0.03)	Moderate
Nocturnal time awake (minutes)							
1 (Singer)	Not serious	N/A	Not serious	Serious ⁴	151	MD 9.08 (-7.51, 25.66)	Moderate
Number of night-time awakenings							
1 (Singer)	Not serious	N/A	Not serious	Serious ⁴	151	MD 6.00 (-2.65, 14.65)	Moderate
Carer-rated sleep quality, change from baseline							
1 (Singer)	Not serious	N/A	Not serious	Serious ⁴	151	MD -0.01 (-0.21, 0.19)	Moderate
Activities of daily living							
1 (Singer)	Not serious	N/A	Not serious	Serious ⁴	151	MD 0.40 (-1.41, 2.22)	Moderate
Number of adverse events reported per person							
1 (Singer)	Not serious	N/A	Not serious	Serious ⁴	151	MD 0.20 (-0.72, 1.12)	Moderate
Pittsburgh Sleep Quality Index global score							

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
1 (Wade)	Serious ¹	N/A	Serious ³	Serious ⁴	11	MD -1.71 (-4.27,0.87)	Very Low
Pittsburgh Sleep Quality Index sleep latency (minutes)							
1 (Wade)	Serious ¹	N/A	Serious ³	Serious ⁴	11	MD 0.60 (-30.30, 31.50)	Very Low
<ol style="list-style-type: none"> 1. Very high risk of reporting bias for Wade study. 2. Potential problems with sequence generation, allocation concealment and attrition bias. 3. Mean MMSE baseline scores > 20 cut off – patients had mild dementia. 4. Non-significant result 							

Trazadone vs placebo

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
Total night-time sleep time (minutes)							
1 (Camargos)	Not serious	N/A	Not serious	Not serious	30	MD 42.46 (0.9, 84.0)	High
Sleep efficiency							
1 (Camargos)	Not serious	N/A	Not serious	Not serious	30	MD 8.53 (1.9, 15.1)	High
Nigh-time waking after sleep onset (minutes)							
1 (Camargos)	Not serious	N/A	Not serious	Serious ¹	30	MD -20.41 (-60.4, 19.6)	Moderate
Number of nocturnal awakenings							
1 (Camargos)	Not serious	N/A	Not serious	Serious ¹	30	MD -3.71 (-8.2, 0.8)	Moderate
Total daytime sleep time (minutes)							
1 (Camargos)	Not serious	N/A	Not serious	Serious ¹	30	MD 5.12 (-28.2, 38.4)	Moderate
Number of daytime naps							
1 (Camargos)	Not serious	N/A	Not serious	Serious ¹	30	MD 0.84 (-2.6, 4.3)	Moderate
Activities of daily living (Katz Index)							
1 (Camargos)	Not serious	N/A	Not serious	Serious ¹	30	MD 0.5 (-0.8, 1.8)	Moderate
<ol style="list-style-type: none"> 1. Non-significant result. 							

Memantine vs placebo

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
Epworth Sleepiness Scale (Scale goes from 0 to 24, higher scores worse)							
1 (Larsson)	Serious ¹	N/A	Not serious	Serious ²	60	MD -0.35 (-3.26, 2.56)	Low
Stavanger Sleep Questionnaire							
1 (Larsson)	Serious ¹	N/A	Not serious	Not serious	55	MD 0.48 (0.06, 0.90)	Moderate
<ol style="list-style-type: none"> Unclear whether study personnel, medical staff and patients were blinded to treatment and whether placebo and intervention groups were treated equally apart from the intervention. Non-significant result 							

Light therapy

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
Total sleep duration (minutes, 6-50 days)							
1 (Dowling)	Serious ¹	N/A	Not serious	Serious ³	35	MD 9.00 (-67.14, 85.14)	Low
Number of night-time awakenings at endpoint							
1 (Dowling)	Serious ¹	N/A	Not serious	Serious ³	35	MD -4.00 (-11.06, 3.06)	Low
Sleep latency at endpoint (after 3 weeks of treatment)							
1 (Gasio)	Serious ²	N/A	Not serious	Serious ³	13	MD -79.00 (-327.17, 169.17)	Low
Sleep latency at follow-up (3 weeks after treatment)							
1 (Gasio)	Serious ²	N/A	Not serious	Serious ³	13	MD -62.00 (-216.55, 92.55)	Low
Total sleep duration (minutes) at endpoint (after 3 weeks of treatment)							
1 (Gasio)	Serious ²	N/A	Not serious	Serious ³	13	MD 143.00 (-637.66, 923.66)	Low
Total sleep duration (minutes) at follow-up (3 weeks after treatment)							
1 (Gasio)	Serious ²	N/A	Not serious	Serious ³	13	MD 110 (-77.22, 297.22)	Low
Night-time activity counts (per night) at endpoint (after 3 weeks of treatment)							
1 (Gasio)	Serious ²	N/A	Not serious	Serious ³	13	MD -20.60 (-46.52, 5.32)	Low
Night-time activity counts (per night) at follow-up (3 weeks after treatment)							

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
1 (Gasio)	Serious ²	N/A	Not serious	Serious ³	13	MD -24.70 (-52.70, 3.30)	Low
<ol style="list-style-type: none"> 1. Potential problems with sequence generation, allocation concealment and attrition bias. 2. Potential problems with allocation concealment and blinding of assessors. 3. Non-significant result. 							

Slow-stroke back massage

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
Total night-time sleep time (NTST)							
1 (Harris)	Not serious	N/A	Not serious	Serious ¹	40	MD 35.78 (-12.04, 83.60)	Moderate
Sleep efficiency							
1 (Harris)	Not serious	N/A	Not serious	Serious ¹	40	MD 4.10 (-4.58, 12.78)	Moderate
1. Non-significant result.							

Multicomponent non-pharmacological interventions vs usual care

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
Total night-time sleep time (minutes)							
2 (Alessi 2005, McCurry 2011)	Not serious	Not serious	Not serious	Not serious	184	MD 23.72 (0.73, 46.70)	High
Total night-time awake time (minutes)							
2 (McCurry 2005, McCurry 2011)	Not serious	Not serious	Not serious	Not serious	89	MD -38.89 (-65.49, -12.29)	High
Number of night-time awakenings							
3 (Alessi 2005, McCurry 2005, McCurry 2011)	Not serious	Not serious	Not serious	Serious ¹	207	MD -2.20 (-4.83, 0.43)	Moderate
Total daytime sleep time (minutes)							
1 (McCurry 2011)	Not serious	N/A	Not serious	Serious ¹	66	MD -7.30 (-46.82, 32.22)	Moderate
Sleep disorders inventory							
1 (McCurry 2011)	Not serious	N/A	Not serious	Not serious	66	MD -0.90 (-1.45, -0.35)	High

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
RMBPC - depression							
1 (McCurry 2005)	Not serious	N/A	Not serious	Serious ¹	23	MD -0.22 (-0.48, 0.04)	Moderate
1. Non-significant result. 2. Subgroup analyses carried out post-hoc.							

Individualised activities

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
Daytime minutes slept							
1 (Richards 2005)	Serious ¹	N/A	Not serious	Not serious	50	MD -45.12 (-72.45, -17.79)	Moderate
Night-time minutes to sleep onset							
1 (Richards 2005)	Serious ¹	N/A	Not serious	Serious ²	50	MD 9.87 (-18.28, 38.02)	Low
Night-time minutes slept							
1 (Richards 2005)	Serious ¹	N/A	Not serious	Serious ²	50	MD -4.67 (-74.6, 65.26)	Low
Night-time minutes awake							
1 (Richards 2005)	Serious ¹	N/A	Not serious	Serious ²	50	MD -21.85 (-94.28, 50.58)	Low
Night-time sleep efficiency							
1 (Richards 2005)	Serious ¹	N/A	Not serious	Serious ²	50	MD -0.35 (-10.35, 9.65)	Low
Day/night sleep ratio							
1 (Richards 2005)	Serious ¹	N/A	Not serious	Serious ²	50	MD -0.17 (-0.73, 0.39)	Low
1. Subgroup analyses carried out post-hoc. 2. Non-significant result.							

Continuous positive air pressure

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
Epworth Sleepiness Scale 3 weeks (Scale goes from 0 to 24, higher scores worse)							
1 (Chong 2006)	Not Serious	N/A	Not serious	Serious ¹	39	MD -1.10 (-3.10, 0.90)	Moderate
1. Non-significant result.							

Non-pharmacological management of agitation, aggression and apathy

Sensory interventions

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
Agitation (CMAI) – lower numbers favour intervention							
5 (Ballard 2002, Yang 2015, Ridder 2013, Lin 2011, Burns 2009)	Not serious	Not serious	Not serious	Serious ¹	446	MD -0.83 (-2.52, 0.85)	Moderate
Negative affect – lower numbers favour intervention							
1 (O'Connor 2013)	Not serious	N/A	Not serious	Serious ¹	64	MD -0.20 (-2.11, 1.71)	Moderate
Positive affect – higher numbers favour intervention							
1 (O'Connor 2013)	Not serious	N/A	Not serious	Serious ¹	64	MD 0.40 (-4.49, 5.29)	Moderate
Agitated behaviours – lower numbers favour intervention							
3 (O'Connor 2013, Sung 2006, Burns 2009)	Not serious	Not serious	Not serious	Serious ²	141	SMD -0.26 (-0.59, 0.08)	Moderate
Quality of life (ADRQL) - higher numbers favour intervention							
1 (Ridder 2013)	Not serious	N/A	Not serious	Serious ¹	42	MD 17.60 (-24.66, 59.86)	Moderate
Depression (Cornell scale) – lower numbers favour intervention							
1 (Burns 2011)	Not serious	N/A	Not serious	Serious ¹	45	MD 0.50 (-1.15, 2.15)	Moderate
Behavioural pathology (MOUSEPAD, BEHAVE-AD) – lower numbers favour intervention							
2 (Burns 2011, Lyketsos 1999)	Not serious	Not serious	Not serious	Serious ¹	74	MD 0.18 (-0.27, 0.64)	Moderate
MMSE – higher numbers favour intervention							
1 (Burns 2011)	Not serious	N/A	Not serious	Serious ¹	46	MD 1.80 (-1.41, 5.01)	Moderate
1. Non-significant result. 2. 95% CI crosses one line of a defined MID interval.							

Social contact

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
Agitation – lower numbers favour intervention							
2 (Camberg 1999, Churchill 1999)	Not serious	Serious ¹	Not serious	Very serious ²	164	SMD -0.19 (-0.71, 0.33)	Very low
1. $I^2 > 40\%$. 2. 95% CI crosses two lines of a defined MID interval.							

Activities

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
Agitation – lower numbers favour intervention							
6 (C-M 2007, C-M 2012, Fitzsimmons 2002, Kolanowski 2001, van der Ploeg 2013, Watson 1998)	Serious ³	Serious ¹	Not serious	Serious ⁴	465	SMD -0.34 (-0.74, 0.05)	Very low
Negative affect – lower numbers favour intervention							
3 (C-M 2007, C-M 2012, van der Ploeg 2013)	Serious ³	Not serious	Not serious	Not serious	336	MD -0.02 (-0.04, -0.00)	Moderate
Pleasurable affect – higher numbers favour intervention							
3 (C-M 2007, C-M 2012)	Serious ³	Serious ¹	Not serious	Not serious	292	MD 0.29 (0.15, 0.42)	Low
Interested affect – higher numbers favour intervention							
3 (C-M 2007, C-M 2012, van der Ploeg 2013)	Serious ³	Serious ¹	Not serious	Not serious	336	SMD 0.57 (0.23, 0.90)	Low
Constructive engagement – higher numbers favour intervention							
1 (van der Ploeg 2013)	Serious ³	N/A	Not serious	Serious ²	44	MD 0.30 (-2.32, 2.92)	Low
Negative engagement – lower numbers favour intervention							

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
1 (van der Ploeg 2013)	Serious ³	N/A	Not serious	Serious ²	44	MD -0.20 (-5.46, 5.06)	Low
1. $i^2 > 40\%$. 2. Non-significant result. 3. Methods of randomisation unclear 4. 95% CI crosses one line of a defined MID interval.							

Care delivery interventions

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
Agitation (CMAI) – lower numbers favour intervention							
2 (Rapp 2013, Zwijsen 2014)	Not serious	Serious ¹	Not serious	Serious ²	701	MD -6.06 (-14.04, 1.92)	Low
Aggressive behaviours – lower numbers favour intervention							
2 (Rapp 2013, Zwijsen 2014)	Not serious	Serious ¹	Not serious	Very serious ³	701	SMD -0.30 (-0.99, 0.38)	Very low
Number of psychotropic prescriptions							
1 (Rapp 2013)	Not serious	N/A	Not serious	Serious ²	304	MD -0.03 (-0.13, 0.07)	Moderate
Number of antidepressant prescriptions							
1 (Rapp 2013)	Not serious	N/A	Not serious	Not serious	304	MD 0.04 (0.03, 0.05)	Moderate
Number of cholinesterase inhibitor prescriptions							
1 (Rapp 2013)	Not serious	N/A	Not serious	Not serious	304	MD 0.11 (0.10, 0.12)	Moderate
1. $i^2 > 40\%$. 2. Non-significant result. 3. 95% CI crosses two lines of a defined MID interval.							

Staff training

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
Agitation (CMAI) – lower numbers favour intervention							
1 (Deudon 2009)	Not serious	N/A	Not serious	Not serious	272	MD -5.69 (-9.85, -1.53)	High

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
Physically aggressive behaviours – lower numbers favour intervention							
1 (Deudon 2009)	Not serious	N/A	Not serious	Serious ¹	272	MD -0.08 (-0.39, 0.23)	Moderate
Verbally aggressive behaviours – lower numbers favour intervention							
1 (Deudon 2009)	Not serious	N/A	Not serious	Not serious	272	MD -0.16 (-0.32, -0.00)	High
1. Non-significant result.							

Gingko biloba

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
NPI total score – lower numbers favour intervention							
4 (Herrschaft 2012, Ihl 2011, Napryeyenko 2007, Nikolova 2013)	Not serious	Serious ¹	Not serious	Not serious	1,596	MD -3.86 (-7.62, -0.10)	Moderate
NPI distress score – lower numbers favour intervention							
4 (Herrschaft 2012, Ihl 2011, Napryeyenko 2007, Nikolova 2013)	Not serious	Serious ¹	Not serious	Not serious	1,596	MD -2.33 (-4.34, -0.33)	Moderate
Activities of daily living – lower numbers favour intervention							
4 (Herrschaft 2012, Ihl 2011, Napryeyenko 2007, Nikolova 2013)	Not serious	Serious ¹	Not serious	Serious ²	1,596	SMD -0.54 (-0.91, -0.18)	Low
Quality of life – higher numbers favour intervention							
2 (Herrschaft 2012, Ihl 2011)	Not serious	Not serious	Not serious	Not serious	806	MD 2.00 (0.88, 3.12)	High
Clinical global assessment – lower numbers favour intervention							
4 (Herrschaft 2012, Ihl 2011,	Not serious	Serious ¹	Not serious	Not serious	1,590	MD -0.75 (-1.34, -0.15)	Moderate

Number of RCTs	Risk of bias	Inconsistency	Indirectness	Imprecision	Sample size	Effect size (95% CI)	Quality
Napryeyenko 2007, Nikolova 2013)							
Cognition – lower numbers favour intervention							
4 (Herrschaft 2012, Ihl 2011, Napryeyenko 2007, Nikolova 2013)	Not serious	Serious ¹	Not serious	Serious ²	1,590	SMD -0.78 (-1.50, -0.05)	Low
1. $i^2 > 40\%$. 2. 95% CI crosses one line of a defined MID interval							