NKR 55 Demens og medicin PICO 3 Melatonin versus placebo

Review information

Authors

Sundhedsstyrelsen[1]

[1][Empty affiliation]

Citation example: S. NKR 55 Demens og medicin PICO 3 Melatonin versus placebo. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Characteristics of studies

Characteristics of included studies

Asayama 2003

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention ● *Mean age (SD)*: 78.9 (7.3) ● *MMSE mean (SD)*: 12.6 (7.0) ● *No of males (%)*: 9,1 Control ● *Mean age (SD)*: 79.4 (5.3) ● *MMSE mean (SD)*: 10.3 (7.59 ● *No of males (%)*: 22,2 **Included criteria:** Patients were diagnosed as Alzheimer type dementia with brain CT or brain MRI and EEG for physical examination, and Diagnostic StatisticalManual of Mental Disorders, Fourth Edition（DSMIV）and the Clinical Diagnosis of the National Institute of Neurological and CommunicativeDisorders and Stroke and the Alzheimer's disease and Related Disorders Association （ NINCDSADRDA）for diagnostic criteria. Those patients hadno severe physical

	diseases and had no disorders cause sleep disorders besides ATD. **Excluded criteria:** Not described **Pretreatment:** There are no tests for baseline differences
Interventions	**Intervention Characteristics** Intervention ● *Description*: Melatonin 3 mg. Patients weregiven the drug at 20: 30. Patients were given meals at 8: 00, 12: 00, 18: 00and lights were off at 21: 00, and given a bath twicea week at 11: 00. Patients were allowed to spend a time freely in geriatric ward besides mentioned above. We paid attention to avoid any factor toinfluence their daily life. ● *Duration*: 4 weeks ● *Dose*: Melatonin 3 mg Control ● *Description*: Placebo. Patients were given the drug at 20: 30. ● *Duration*: 4 weeks ● *Dose*: Placebo
Outcomes	*Antal natlige vågenperioder* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Scale**: Actigraph ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** Not reported **Country:** Japan **Setting:** Geriatric ward of S Hospital during 2000-2002 **Comments:** **Authors name:** Kentaro Asayama **Institution:** Department of Neuropsychiatry, Nippon Medical School **Email:** asayama@nms.ac.jp **Address:** 1-1-5 Sendagi,Bunkyo-ku, Tokyo 113-8603, Japan
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The drugs were administrated in a double blind design by randomized allocation." Judgement Comment: No information provided, in regard to how the randomization was performed
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Not reported
Blinding of participants and personnel (performance bias)	Unclear risk	Judgement Comment: Unclear if personnel were blinded to the intervention however they write it is a double blinded study.
Blinding of outcome assessment (detection bias)	Low risk	Judgement Comment: Outcome is sleep which is measured by an obejective method (Actigraph)
Incomplete outcome data (attrition bias)	Low risk	Quote: "We studied 20 patients（PLA 9, MLT 11）. We could finally measure sleep time and activity counts by Actigraph on 18 patients（PLA 8, MLT 10）. The reason of unsuccessful measurement of Actigraph was patients' resistance to wear watchtype Actigraph on their arm through the week under measurement."
Selective reporting (reporting bias)	Low risk	Judgement Comment: Not referring to any registered protocol.
Other bias	Low risk	Judgement Comment: No other sources of bias

Dowling 2008

Methods	
Participants	
Interventions	
Outcomes	
Identification	
Notes	Data obtained from: McCleery J.; Cohen D.A.; Sharpley, A. L. Pharmacotherapies for sleep disturbances in dementia.The Cochrane database of systematic reviews 2016;11(Journal

	Article):009178United Kingdom 2016

Risk of bias table

Gehrman 2009

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** **Included criteria:** A neurologist conducted a brief examination and reviewed medical records to confirm the diagnosis of probable AD,using NINCDS-ADRDA diagnostic criteria. **Excluded criteria:** No exclusion criteria are described in the study **Pretreatment:** No baseline differences are tested in the study
Interventions	**Intervention Characteristics** Intervention ● *Description*: Melatonin consisted of a combined dosing formulation containing 8.5mg immediate release (Regis Technologies) and 1.5 mg time release (PAR Pharmaceuticals). Capsules were administered by nursing staff at 10:00PM each night during the treatment period. ● *Duration*: 10 days ● *Dose*: 8.5 mg immediate release and 1.5 mg sustained release Control ● *Description*: Patients in the placebo group received capsules containing inactive compound that were identical in appearance to the melatonin capsules. Capsules were administered by nursing staff at 10:00PM each night during the treatment period ● *Duration*: 10 days ● *Dose*: capsules containing inactive compound that were identical inappearance to the melatonin capsules
Outcomes	*Længde af nattesøvn* ● **Outcome type**: ContinuousOutcome

Identification	**Sponsorship source:** This study was supported by NIA AG08415 (SAI), P50 AG05131, NIA K23 AG028452 (JLM) and the ResearchService of the Veterans Affairs San Diego Healthcare System. **Country:** USA **Setting:** Nursing homes in San Diego metropolitan area. **Comments:** **Authors name:** Sonia Ancoli-Israel **Institution:** Department of Psychiatry 0603; University of California, San Diego **Email:** sancoliisrael@ucsd.edu. **Address:** 9500 Gilman Drive, La Jolla, CA 92093-0603
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Subjects were randomized to receive either placebo or melatonin." Judgement Comment: No describtion how how the randomization was performed
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Not described
Blinding of participants and personnel (performance bias)	Unclear risk	Quote: "Patients in the placebo group received capsules containing inactive compound that were identical in appearance to the melatonin capsules." Judgement Comment: Participants were blinded - however it is unsure if the nurses were blinded.
Blinding of outcome assessment (detection bias)	Low risk	Quote: "Measurements—Sleep was measured continuously using actigraphy." Quote: "rater. Raters were blind to treatment condition." Judgement Comment: Objective measure of sleep
Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: Complete information however they do not described how many fullfilles the inclusion criteria and no flowchart
Selective reporting (reporting bias)	Low risk	Judgement Comment: No protocol is provided, however all outcomes seem to be reported
Other bias	Low risk	Judgement Comment: No other sources of bias

Riemersma vanderLek 2008

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention1 ● *Mean age (SD)*: 86 (5) ● N*o of males (%)*: 74 Intervention 2 ● *Mean age (SD)*: 87 (6) ● N*o of males (%)*: 72 Control 1 ● *Mean age (SD)*: 85 (5) ● N*o of males (%)*: 76 Control 2 ● *Mean age (SD)*: 85 (6) ● N*o of males (%)*: 74 **Included criteria:** For recruitment, all 253 residents living in the facilities were asked for verbal consent and the patients' responsible relatives were asked to provide written informed consent. Consent was obtained from 189. No other inclusion criteria were applied **Excluded criteria:** Exclusion criteria werethe use of monoamine oxidase inhibi-tors, long-term use of nonsteroid anti-inflammatory drugs, severe liver orkidney dysfunction, and aphakia.None of the potential participants hadto be excluded. **Pretreatment:** Randomization was balanced in thatnone of the individual or environmen-tal characteristics, use of medication,or pretreatment outcome variable lev-els differed significantly between the 4groups
Interventions	**Intervention Characteristics** Intervention1 ● *Description*: Inactive light facilities and Melatonin. Inactive light were installed, using equal number of fixtures as in the intervention groups, but these contained only half of the tubes, accommodated concealed band-stop filters, and were installed at a greater distance from the eyes

	● *Duration*: 6 months ● *Dose*: Dim light ± 300 lux and by participant to evening melatonin (2.5 mg) Intervention 2 ● *Description*: light exposure and melatonin. Light exposure was manipulated byinstalling a large number of ceiling-mounted fixtures with Plexiglas diffus-ers containing an equal amount of Phil-ips TLD 840 and 940 fluorescent tubes(Philips Lighting BV, Eindhoven, theNetherlands) in the common livingroom. Lights were on daily between ap-proximately 9AMand 6PM. The aim wasan exposure of ± 1000 lux, measuredbefore the eyes in the gaze direction ● *Duration*: 6 months ● *Dose*: Whole-day bright ±1000 lux and by participant to evening melatonin (2.5 mg) Control 1 ● *Description*: Inactive light facilities and Placebo. Inactive light were installed, using equal number of fixtures as in the intervention groups, but these contained only half of the tubes, accommodated concealed band-stop filters, and were installed at a greater distance from the eyes ● *Duration*: 6 months ● *Dose*: Dim light ± 300 lux and placebp Control 2 ● *Description*: LIght exposure only and placebo. Light exposure was manipulated byinstalling a large number of ceiling-mounted fixtures with Plexiglas diffus-ers containing an equal amount of Phil-ips TLD 840 and 940 fluorescent tubes(Philips Lighting BV, Eindhoven, theNetherlands) in the common livingroom. Lights were on daily between ap-proximately 9AMand 6PM. The aim wasan exposure of ± 1000 lux, measuredbefore the eyes in the gaze direction ● *Duration*: 6 months ● *Dose*: Whole-day bright ±1000 lux and placebo
Outcomes	*Længde af nattesøvn* ● **Outcome type**: ContinuousOutcome *BPSD_NPI Q* ● **Outcome type**: ContinuousOutcome

Identification	**Sponsorship source:** Financial and material support were provided by the Netherlands Organization for Health Research, the Hague, by grants 0028-300-30 and 907-00-012; the Netherlands Organisation for Scientific Research, the Hague, by grants 016.025.041 and 051.04.010; the Stichting De Drie Lichten, Leiden; Stichting RVVZ; Zeist by grant 01-220; Japan Foundation for Aging and Health; Hersenstichting Nederland by grant 11F04-2.47; Internationale Stichting Alzheimer Onderzoek by grant 05511. Philips Lighting BV, Braun, and Cambridge Neurotechnology supplied material for this study at reduced cost **Country:** Netherland **Setting:** Care facilities **Comments:** **Authors name:** Rixt F. Riemersma-van der Lek **Institution:** Netherlands Institute for Neuro-science, **Email:** e.van.someren@nin.knaw.nl **Address:** Royal Netherlands Academy of Arts and Sciences, Amsterdam
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The 12 homes for the elderly were randomly assigned to active (6 facili- ties, n = 98) or placebo (6 facilities, n=91) light exposure. Forty-nine par- ticipants were assigned to light only, 46 to melatonin only, 49 to their combi- nation, and 45 to neither light nor mela- tonin (double placebo). The mean (SD) ratio of participants assigned to the ac- tive melatonin group within each fa- cility was 0.50 (0.06)." Quote: "In a 2 2 factorial design, facilities were randomly assigned using the Micro- soft Excel (Redmond, Washington) ran- dom number function to 1 of the 2 light conditions and participants to double- blind daily intake of melatonin (2.5 mg, Terafarm, Brielle, the Netherlands, n = 95) or placebo (n = 94), given"
Allocation concealment (selection bias)	Low risk	Quote: "Randomization was performed by a re- search assistant not involved in the study (J. van Heerikhuize, Netherlands Insti- tute for Neuroscience, Amsterdam) and kept concealed. Codes were revealed to the researchers only after completion of the study and subsequent"

Blinding of participants and personnel (performance bias)	Low risk	Quote: "Caregivers were blinded to ran- domization and were asked to guess their facility's light status." Quote: "random number function to 1 of the 2 light conditions and participants to double- blind daily intake of melatonin (2.5 mg, Terafarm, Brielle, the Netherlands, n = 95) or placebo (n = 94),"
Blinding of outcome assessment (detection bias)	Low risk	Quote: "Codes were revealed to the researchers only after completion of the study and subsequent data reduc- tion and processing steps. The"
Incomplete outcome data (attrition bias)	Low risk	Quote: "Because,particularlyafter1.5years,many cases were lost to follow-up, it was im- portant to determine whether treatment effectsobtainedfromanalysesonthecom- plete 3.5-year data set were present when only the first 1.5 years of follow-up were included in the analysis." Quote: "participants eventu- ally lost to follow-up. Drop out was pri- marily due to logistic limitations (ie, discontinuation of facilities) and sec- ondarily related to the very nature of the population under study, which is at high risk of death and transfer to a nursing home. We verified that the treatment effects were not modulated by dropout pattern and were robust in a sensitivity analysis limiting the data set to the first 1.5 years of follow-up."
Selective reporting (reporting bias)	High risk	Quote: "Trial Registration controlled-trials.com/isrctn Identifier: ISRCTN93133646" Judgement Comment: The trial was pre-registred at Trial Registration controlled-trials.com/isrctn Identifier: ISRCTN93133646.The pre-sepcified primary outcome measures 24-hour salvatory melatonin and cortisol levels were not reported in the study
Other bias	Low risk	Judgement Comment: Non-Commercial funding

Serfaty 2002

Methods	
Participants	
Interventions	
Outcomes	
Identification	
Notes	Data obtained from: McCleery J.; Cohen D.A.; Sharpley, A. L. Pharmacotherapies for sleep disturbances in dementia.The Cochrane database of systematic reviews 2016;11(Journal

	Article):009178United Kingdom 2016

Risk of bias table

Singer 2003

Methods	
Participants	
Interventions	
Outcomes	
Identification	
Notes	Data obtained from: McCleery J.; Cohen D.A.; Sharpley, A. L. Pharmacotherapies for sleep disturbances in dementia.The Cochrane database of systematic reviews 2016;11(Journal Article):009178United Kingdom 2016

Risk of bias table

Wade 2014

Methods	
Participants	
Interventions	
Outcomes	
Identification	
Notes	Data obtained from: McCleery J.; Cohen D.A.; Sharpley, A. L. Pharmacotherapies for sleep disturbances in dementia.The Cochrane database of systematic reviews 2016;11(Journal Article):009178United Kingdom 2016

Risk of bias table

Footnotes

Characteristics of excluded studies

Cardinali 2002

Reason for exclusion	Wrong study design

Cardinali 2011

Reason for exclusion	Wrong study design

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

References to studies

Included studies

Asayama 2003

Asayama, K.; Yamadera, H.; Ito, T.; Suzuki, H.; Kudo, Y.; Endo, S.. Double blind study of melatonin effects on the sleep-wake rhythm, cognitive and non-cognitive functions in Alzheimer type dementia. Journal of Nippon Medical School = Nippon Ika Daigaku zasshi 2003;70(4):334-341. [DOI:]

Dowling 2008

Dowling, G. A.; Burr, R. L.; Van Someren, E. J.; Hubbard, E. M.; Luxenberg, J. S.; Mastick, J.; Cooper, B. A.. Melatonin and bright-light treatment for rest-activity disruption in institutionalized patients with Alzheimer's disease. Journal of the American Geriatrics Society 2008;56(2):239-246. [DOI: JGS1543 [pii]]

Gehrman 2009

Gehrman, P. R.; Connor, D. J.; Martin, J. L.; Shochat, T.; Corey-Bloom, J.; Ancoli-Israel, S.. Melatonin fails to improve sleep or agitation in double-blind randomized placebo-controlled trial of institutionalized patients with Alzheimer disease. The American Journal of Geriatric Psychiatry : Official Journal of the American Association for Geriatric Psychiatry 2009;17(2):166-169. [DOI: 10.1097/JGP.0b013e318187de18 [doi]]

Riemersma vanderLek 2008

Riemersma-van der Lek, R. F.; Swaab, D. F.; Twisk, J.; Hol, E. M.; Hoogendijk, W. J.; Van Someren, E. J.. Effect of bright light and melatonin on cognitive and noncognitive function in elderly residents of group care facilities: a randomized controlled trial. Jama 2008;299(22):2642-2655. [DOI: 10.1001/jama.299.22.2642 [doi]]

Serfaty 2002

Serfaty, M.; Kennell-Webb, S.; Warner, J.; Blizard, R.; Raven, P.. Double blind randomised placebo controlled trial of low dose melatonin for sleep disorders in dementia. International journal of geriatric psychiatry 2002;17(12):1120-1127. [DOI: 10.1002/gps.760 [doi]]

Singer 2003

Singer, C.; Tractenberg, R. E.; Kaye, J.; Schafer, K.; Gamst, A.; Grundman, M.; Thomas, R.; Thal, L. J.; Alzheimer's Disease Cooperative Study. A multicenter, placebo-controlled trial of melatonin for sleep disturbance in Alzheimer's disease. Sleep 2003;26(7):893-901. [DOI:]

Wade 2014

Wade, A. G.; Farmer, M.; Harari, G.; Fund, N.; Laudon, M.; Nir, T.; Frydman-Marom, A.; Zisapel, N.. Add-on prolonged-release melatonin for cognitive function and sleep in mild to moderate Alzheimer's disease: a 6-month, randomized, placebo-controlled, multicenter trial. Clinical interventions in aging 2014;9(Journal Article):947-961. [DOI: 10.2147/CIA.S65625 [doi]]

Excluded studies

Cardinali 2002

Cardinali, D. P.; Brusco, L. I.; Liberczuk, C.; Furio, A. M.. The use of melatonin in Alzheimer's disease. Neuro endocrinology letters 2002;23 Suppl 1(Journal Article):20-23. [DOI: NEL230702R04 [pii]]

Cardinali 2011

Cardinali, D. P.; Furio, A. M.; Brusco, L. I.. The use of chronobiotics in the resynchronization of the sleep/wake cycle. Therapeutical application in the early phases of Alzheimer's disease. Recent patents on endocrine, metabolic & immune drug discovery 2011;5(2):80-90. [DOI: BSP/EMI/E-Pub/0012 [pii]]

Other references

Additional references

Other published versions of this review

Classification pending references

Data and analyses

1 Melatonin vs placebo

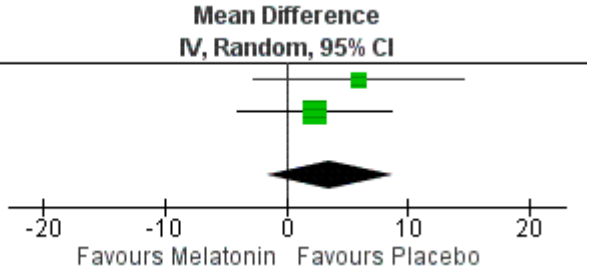
Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Antal natlige vågenperioder_Længst mulig behandlingstid_Total	2	58	Mean Difference (IV, Random, 95% CI)	3.61 [-1.54, 8.76]
1.4 Længde af nattesøvn (timer)_Længst mulig behandlingstid_total	6	397	Mean Difference (IV, Random, 95% CI)	0.36 [-0.16, 0.89]
1.8 Søvnkvalitet vurderet af omsorgsgiver_Total	2	140	Std. Mean Difference (IV, Random, 95% CI)	-0.18 [-0.78, 0.42]
1.11 BPSD_NPI_Længst mulig behandlingstid_Total	2	278	Std. Mean Difference (IV, Random, 95% CI)	-0.34 [-0.60, -0.08]
1.14 Bivirkninger (antal per person)_Længst mulig behandlingstid_Total	2	127	Mean Difference (IV, Random, 95% CI)	0.69 [-0.60, 1.99]
1.17 Livskvalitet_Længst mulig behandlingstid	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable

Figures

Figure 1 (Analysis 1.1)

Study or Subgroup	Melatonin Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Dowling 2008	40	15	15	34	9	18	35.4%	6.00 [-2.65, 14.65]
Serfaty 2002	14	6.59	11	11.7	9.7	14	64.6%	2.30 [-4.10, 8.70]
Total (95% CI)			**26**			**32**	**100.0%**	**3.61 [-1.54, 8.76]**

Heterogeneity: Tau² = 0.00; Chi² = 0.45, df = 1 (P = 0.50); I² = 0%
Test for overall effect: Z = 1.37 (P = 0.17)

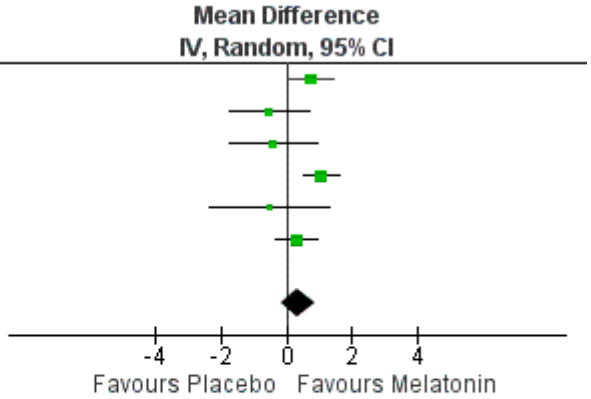


Forest plot of comparison: 1 Melatonin vs placebo, outcome: 1.1 Antal natlige vågenperioder_Længst mulig behandlingstid_Total.

Figure 4 (Analysis 1.4)

Study or Subgroup	Melatonin Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Asayama 2003 (1)	7.12	0.49	11	6.38	0.98	9	21.6%	0.74 [0.04, 1.44]
Dowling 2008	8.15	1.75	15	8.68	1.8	18	12.2%	-0.53 [-1.74, 0.68]
Gehrman 2009 (2)	7.5	2	24	7.9	2.3	17	10.5%	-0.40 [-1.75, 0.95]
Riemersma vanderLek 2008 (3)	8.8079	1.8073	76	7.7514	1.4996	74	25.8%	1.06 [0.53, 1.59]
Serfaty 2002 (4)	5.74	2.2	11	6.26	2.5	14	6.6%	-0.52 [-2.37, 1.33]
Singer 2003 (5)	6.12	1.23	104	5.82	1.47	24	23.2%	0.30 [-0.33, 0.93]
Total (95% CI)			**241**			**156**	**100.0%**	**0.36 [-0.16, 0.89]**

Heterogeneity: Tau² = 0.20; Chi² = 10.59, df = 5 (P = 0.06); I² = 53%
Test for overall effect: Z = 1.35 (P = 0.18)



Footnotes

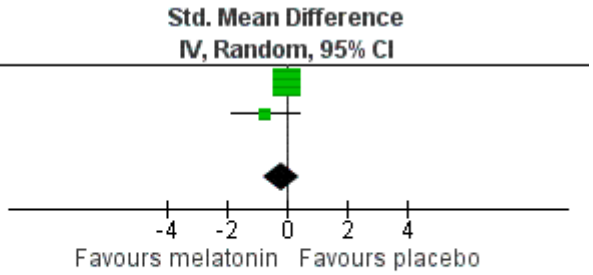
(1) Data var opgivet i minutter, som er omregnet til timer
(2) Det fremgår ikke hvorvidt variansen er afrapporteret i SD eller SE. Vi har angivet det som en SD. Da interventionen var kombineret slow-release og immediate...
(3) Vi har poolet Interventionsgrupperne (Melatonin+aktivt lys og Melatonin only). Vi har poolet kontrolgrupperne (Aktivt lys only og Dobbelt placebo (intet aktivt lys og...
(4) Data var opgivet som Median og Interquartile range. Disse er omregnet, hvor median=mean og SD= (upper IQR-lower IQR)/1.35. Data var opgivet i minutter, som er...
(5) Data for Interventionsgrupperne er poolet (Melatonin 2.5 mg slow release og Melatonin 10 mg). Data omregnet fra minutter til timer.

Forest plot of comparison: 1 Melatonin vs placebo, outcome: 1.4 Længde af nattesøvn (timer)_Længst mulig behandlingstid_total.

Figure 7 (Analysis 1.8)

Study or Subgroup	Melatonin Mean	Melatonin SD	Melatonin Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
Singer 2003 (1)	-0.309	0.5826	104	-0.3	0.6	23	77.0%	-0.02 [-0.47, 0.44]
Wade 2014 (2)	-5.29	3.45	7	-2.83	2.56	6	23.0%	-0.74 [-1.89, 0.40]
Total (95% CI)			**111**			**29**	**100.0%**	**-0.18 [-0.78, 0.42]**

Heterogeneity: Tau² = 0.07; Chi² = 1.35, df = 1 (P = 0.25); I² = 26%
Test for overall effect: Z = 0.60 (P = 0.55)



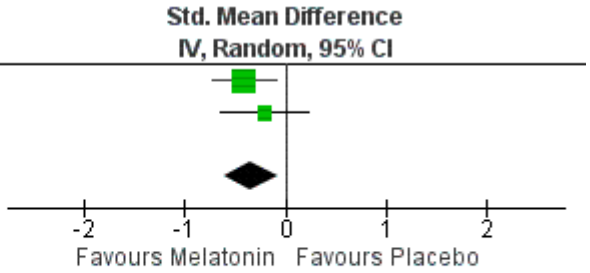
Footnotes
(1) Sleep Quality Rating
(2) PSQI (Pittsburgh Sleep Quality Index)

Forest plot of comparison: 1 Melatonin vs placebo, outcome: 1.8 Søvnkvalitet vurderet af omsorgsgiver_Total.

Figure 10 (Analysis 1.11)

Study or Subgroup	Melatonin Mean	Melatonin SD	Melatonin Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
Riemersma vanderLek 2008 (1)	3.675	3.5426	76	5.4905	5.1682	74	65.4%	-0.41 [-0.73, -0.09]
Singer 2003 (2)	-3.1019	14.0198	104	-0.17	14.1	24	34.6%	-0.21 [-0.65, 0.24]
Total (95% CI)			**180**			**98**	**100.0%**	**-0.34 [-0.60, -0.08]**

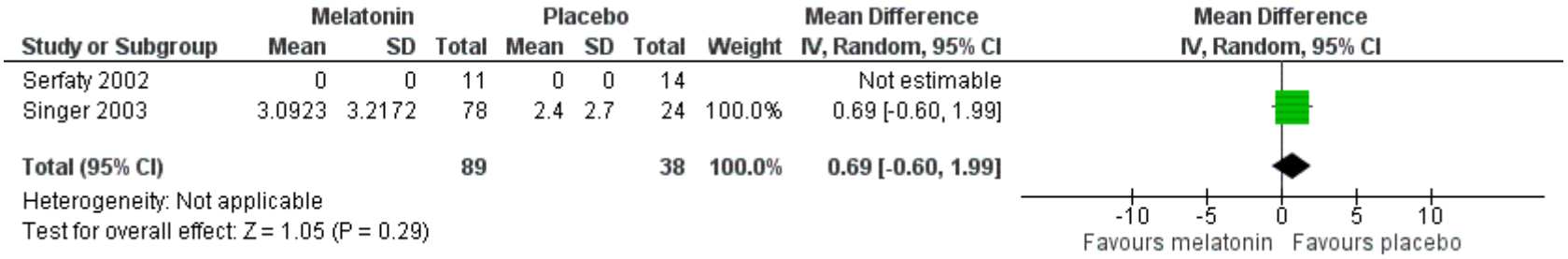
Heterogeneity: Tau² = 0.00; Chi² = 0.51, df = 1 (P = 0.47); I² = 0%
Test for overall effect: Z = 2.54 (P = 0.01)



Footnotes
(1) NPI-Q
(2) NPI

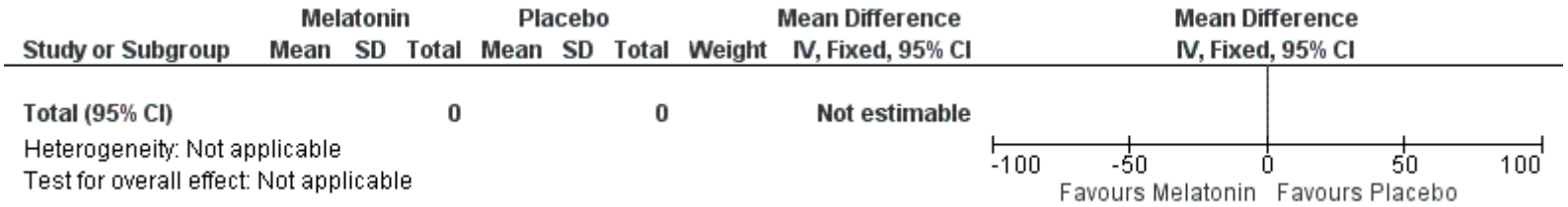
Forest plot of comparison: 1 Melatonin vs placebo, outcome: 1.11 BPSD_NPI_Længst mulig behandlingstid_Total.

Figure 13 (Analysis 1.14)



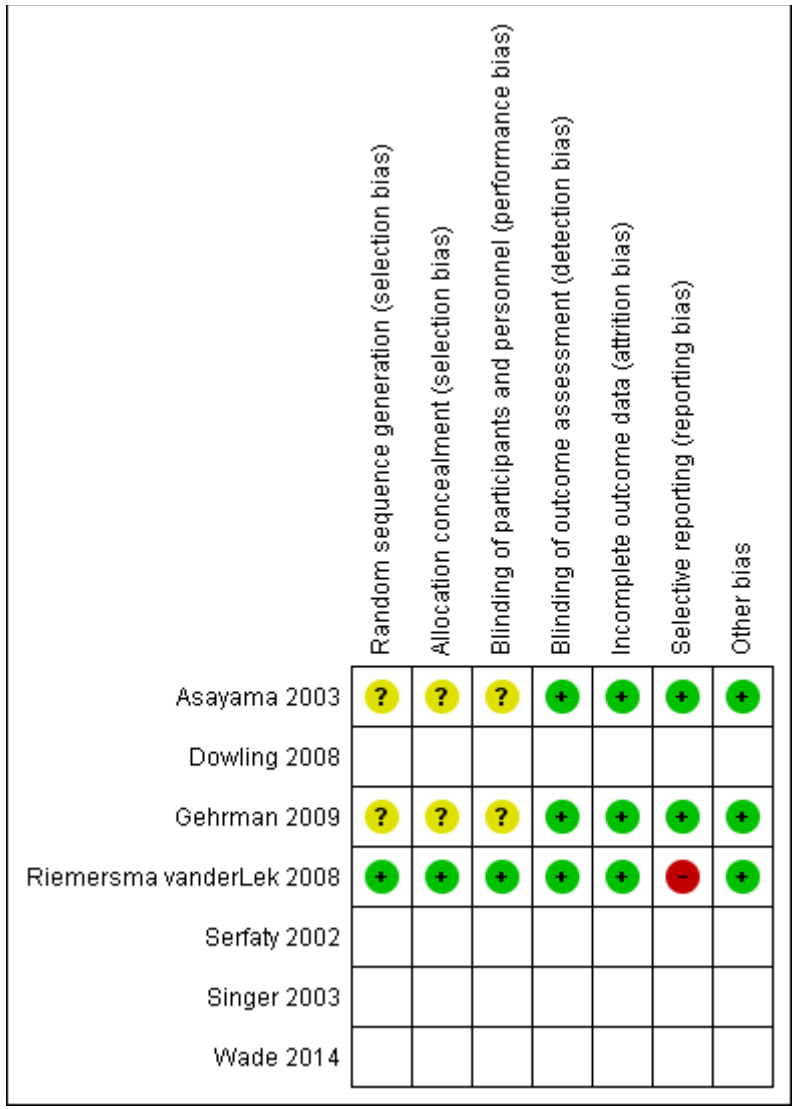
Forest plot of comparison: 1 Melatonin vs placebo, outcome: 1.14 Bivirkninger (antal per person)_Længst mulig behandlingstid_Total.

Figure 16 (Analysis 1.17)



Forest plot of comparison: 1 Melatonin vs placebo, outcome: 1.17 Livskvalitet_Længst mulig behandlingstid.

Figure 17



Risk of bias summary: review authors' judgements about each risk of bias item for each included study.