APPENDIX

Search terms and MeSH used in the literature search #1:

Sleep disorders, circadian rhythm"[MeSH Terms] OR ("sleep"[All Fields] AND "disorders"[All Fields] AND "circadian"[All Fields] AND "rhythm"[All Fields]) OR "circadian rhythm sleep disorders"[All Fields] OR ("circadian"[All Fields] AND "rhythm"[All Fields] AND "sleep"[All Fields] AND "disorder"[All Fields]) OR "circadian rhythm sleep disorder"[All Fields] OR (free[All Fields] AND "running"[All Fields] AND "disorder"[All Fields]) OR (irregular[All Fields] AND sleep-wake[All Fields] AND rhythm[All Fields]) OR (non[All Fields] AND 24-hour[All Fields] AND ("sleep disorders"[MeSH Terms] OR ("sleep"[All Fields] AND "disorders"[All Fields]) OR "sleep disorders"[All Fields] OR ("sleep"[All Fields] AND "disorder"[All Fields]) OR "sleep disorder"[All Fields])) OR (("Blindness"[Mesh] OR ("blindness"[MeSH Terms] OR "blindness"[All Fields] OR nonsighted[All Fields])) AND ("sleep disorders"[MeSH Terms] OR ("sleep"[All Fields] AND "disorders"[All Fields]) OR "sleep disorders"[All Fields])) AND (Meta-Analysis[ptyp] OR Practice Guideline[ptyp] OR systematic[sb]).

Terms for the literature search #2 in PubMed database

(((((circadian rhythm sleep disorders[tw] OR circadian rhythm sleep disorder[tw] OR "Sleep Disorders, Circadian Rhythm"[Mesh:noexp] OR "chronobiology disorders"[tw] OR "Chronobiology Disorders"[Mesh:noexp] OR hypernychthemeral[tw] OR circadian misalignment[tw] OR circadian dysregulation[tw]) OR ((irregular[tw] OR non 24 hour[tw]) AND (sleep wake[tw] OR sleep-wake[tw])) OR ((advanced[tw] OR delayed[tw]) AND sleep phase[tw]) OR (idiopathic[tw] AND chronic[tw] AND (sleep-onset[tw] OR sleep onset[tw]) AND insomnia[tw]) OR ((nonentrained[tw] OR non-entrained[tw]) AND (sleep[tw] OR "sleep"[mesh] OR "Sleep Disorders"[Mesh:noexp] OR circadian[tw] OR "Circadian Rhythm"[MeSH Terms])) OR ((DSPS[tw] OR ASPS[tw] OR early morning awakening[tw] OR (phase advance[All Fields] OR phase advance/delay[All Fields] OR phase advanced[All Fields] OR phase advancement[All Fields] OR phase advancements[All Fields] OR phase advances[All Fields]) OR (phase delay[All Fields] OR phase delay/arrest[All Fields] OR phase delayed[All Fields] OR phase delaying[All Fields] OR phase delays[All Fields]) OR (phase shift[All Fields] OR phase shifted[All Fields] OR phase shifter[All Fields] OR phase shifter/modulator[All Fields] OR phase shifters[All Fields] OR phase shifting[All Fields] OR phase shiftkeying[All Fields] OR phase shiftmeasurement[All Fields] OR phase shifts[All Fields])) AND (sleep[tw] OR "sleep"[mesh] OR "Sleep Disorders"[Mesh:noexp] OR circadian[tw] OR "Circadian Rhythm"[MeSH Terms])) OR ((free running[tw] AND (disorder[tw] OR rhythm[tw])) AND (sleep[tw] OR "sleep"[mesh] OR "Sleep Disorders"[Mesh:noexp] OR circadian[tw] OR "Circadian Rhythm"[MeSH Terms])) OR ((dark therapy[tw] OR light therapy[tw] OR amber lenses[tw] OR Blue light[tw] OR bright light[tw] AND blue blockers[tw] OR blue-blocker[tw] OR blue blocker[tw] OR blue-blocker[tw] OR eyewear[tw] OR Phototherapy[tw] OR

"Phototherapy"[Mesh]) AND (sleep[tw] OR "sleep"[mesh] OR "Sleep Disorders"[Mesh:noexp] OR circadian[tw] OR "Circadian Rhythm"[MeSH Terms])) OR "sleep phase chronotherapy"[MeSH Terms] OR ((chronotherapy[tw] OR chronotype[tw] OR "Chronotherapy"[Mesh:noexp]) AND (sleep[tw] OR "sleep"[mesh] OR "Sleep Disorders"[Mesh:noexp] OR circadian[tw] OR "Circadian Rhythm"[MeSH Terms])) OR ((melatonin receptor agonists[tw] OR melatonin receptor agonist[tw] OR melatonin agonist[tw] OR melatonin agonists[tw] OR melatonin receptor antagonists[tw] OR melatonin receptor antagonist[tw] OR melatonin antagonist[tw] OR melatonin antagonists[tw] OR "Receptors, Melatonin/drug effects"[Mesh] OR "Receptors, Melatonin/agonists"[Mesh] OR "Receptors, Melatonin/antagonists and inhibitors"[Mesh]) AND (sleep[tw] OR "sleep"[mesh] OR "Sleep Disorders"[Mesh:noexp] OR circadian[tw] OR "Circadian Rhythm"[MeSH Terms])) OR ((melatonin[tw] OR "melatonin"[MeSH Terms] OR ramelteon[tw] OR "ramelteon"[Substance] OR tasimelteon[tw] OR "tasimelteon"[Supplementary Concept] OR agomelatine[tw] OR "S 20098"[Supplementary Concept]) AND (sleep[tw] OR "sleep"[mesh] OR "Sleep Disorders"[Mesh:noexp] OR circadian[tw] OR "Circadian Rhythm"[MeSH Terms])) OR ((dim light melatonin onset[tw] OR DLMO[tw]) AND (sleep[tw] OR "sleep"[mesh] OR "Sleep Disorders"[Mesh:noexp] OR circadian[tw] OR "Circadian Rhythm"[MeSH Terms])) OR ((Blindness[tw] OR blind person[tw] OR blind people[tw] OR blind subject[tw] OR blind subjects[tw] OR blind patient[tw] OR blind patients[tw] OR "Visually Impaired Persons"[Mesh] OR enucleated[tw] OR "Blindness"[Mesh] OR nonsighted[tw] OR (visual impairement[All Fields] OR visual impairment[All Fields] OR visual impairment/blindness[All Fields] OR visual impairments[All Fields]) OR visually impaired[tw]) AND (sleep[tw] OR "sleep"[mesh] OR "Sleep Disorders"[Mesh:noexp] OR circadian[tw] OR "Circadian Rhythm"[MeSH Terms])) OR (("dementia"[MeSH Terms] OR dementia[tw] OR "alzheimer disease"[MeSH Terms] OR alzheimer[tw] OR alzheimers's[tw]) AND (sleep[tw] OR "sleep"[mesh] OR "Sleep Disorders"[Mesh:noexp] OR circadian[tw] OR "Circadian Rhythm"[MeSH Terms])) OR ((owl[tw] OR owls[tw] OR lark[tw] OR larks[tw] OR morningness[tw] OR eveningness[tw] OR morning types[tw] OR morning type[tw] OR evening types[tw] OR evening type[tw]) AND (sleep[tw] OR "sleep"[mesh] OR "Sleep Disorders"[Mesh:noexp] OR circadian[tw] OR "Circadian Rhythm"[MeSH Terms]))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR "drug therapy"[Subheading] OR randomly[tiab] OR trial[tiab] OR groups[tiab]) NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms])) AND (English[la] AND ("2006/10/01"[PDAT] : "3000/12/31"[PDAT]) NOT (Comment[pt] OR Editorial[pt] OR News[pt] OR Newspaper Article[pt] OR Letter[pt] OR Case Reports[pt] OR Review[pt])))) NOT (((((circadian rhythm sleep disorders[tw] OR circadian rhythm sleep disorder[tw] OR "Sleep Disorders, Circadian Rhythm"[Mesh:noexp] OR "chronobiology disorders"[tw] OR "Chronobiology Disorders"[Mesh:noexp] OR hypernychthemeral[tw] OR circadian misalignment[tw] OR circadian dysregulation[tw])) OR (((irregular[tw] OR non 24 hour[tw]) AND (sleep wake[tw] OR sleep-wake[tw]))) OR (((advanced[tw] OR delayed[tw]) AND (sleep phase[tw]))) OR

((idiopathic[tw] AND chronic[tw] AND (sleep-onset[tw] OR sleep onset[tw]) AND insomnia[tw])) OR (((nonentrained[tw] OR non-entrained[tw]) AND (sleep[tw] OR "sleep"[mesh] OR "Sleep Disorders"[Mesh:noexp] OR circadian[tw] OR "Circadian Rhythm"[MeSH Terms]))) OR ((((DSPS[tw] OR ASPS[tw] OR phase advance* OR phase delay* OR phase shift*) AND (sleep[tw] OR "sleep"[mesh] OR "Sleep Disorders"[Mesh:noexp] OR circadian[tw] OR "Circadian Rhythm"[MeSH Terms]))) OR (((free running[tw] AND (disorder[tw] OR rhythm[tw])) AND (sleep[tw] OR "sleep"[mesh] OR "Sleep Disorders"[Mesh:noexp] OR circadian[tw] OR "Circadian Rhythm"[MeSH Terms]))) OR (((dark therapy[tw] OR light therapy[tw] OR amber lenses[tw] OR Blue light[tw] OR bright light[tw] OR eyewear[tw] OR Phototherapy[tw] OR "Phototherapy"[Mesh]) AND (sleep[tw] OR "sleep"[mesh] OR "Sleep Disorders"[Mesh:noexp] OR circadian[tw] OR "Circadian Rhythm"[MeSH Terms]))) OR ((Sleep Phase Chronotherapy[Mesh])) OR (((chronotherapy[tw] OR "Chronotherapy"[Mesh:noexp]) AND (sleep[tw] OR "sleep"[mesh] OR "Sleep Disorders"[Mesh:noexp] OR circadian[tw] OR "Circadian Rhythm"[MeSH Terms]))) OR ((((melatonin receptor agonists[tw] OR melatonin receptor agonist[tw] OR melatonin agonist[tw] OR melatonin agonists[tw] OR melatonin receptor antagonists[tw] OR melatonin receptor antagonist[tw] OR melatonin antagonist[tw] OR melatonin antagonists[tw] OR melatonin receptor inhibitor[tw] OR melatonin receptor inhibitors[tw] OR melatonin inhibitor[tw] OR melatonin inhibitors[tw] OR "Receptors, Melatonin/drug effects"[Mesh] OR "Receptors, Melatonin/agonists"[Mesh] OR "Receptors, Melatonin/antagonists and inhibitors"[Mesh]) AND (sleep[tw] OR "sleep"[mesh] OR "Sleep Disorders"[Mesh:noexp] OR circadian[tw] OR "Circadian Rhythm"[MeSH Terms]))) OR (((melatonin[tw] OR "melatonin"[MeSH Terms] OR ramelteon[tw] OR "ramelteon"[Substance] OR tasimelteon[tw] OR "tasimelteon"[Supplementary Concept] OR agomelatine[tw] OR "S 20098"[Supplementary Concept]) AND (sleep[tw] OR "sleep"[mesh] OR "Sleep Disorders"[Mesh:noexp] OR circadian[tw] OR "Circadian Rhythm"[MeSH Terms]))) OR (((dim light melatonin onset[tw] OR DLMO[tw]) AND (sleep[tw] OR "sleep"[mesh] OR "Sleep Disorders"[Mesh:noexp] OR circadian[tw] OR "Circadian Rhythm"[MeSH Terms]))) OR (((Blindness[tw] OR "Blindness"[Mesh] OR nonsighted[tw] OR (visual impair*) OR (visually impaired[tw])) AND (sleep[tw] OR "sleep"[mesh] OR "Sleep Disorders"[Mesh:noexp] OR circadian[tw] OR "Circadian Rhythm"[MeSH Terms]))) OR ((("dementia"[MeSH Terms] OR dementia[tw] OR "alzheimer disease"[MeSH Terms] OR alzheimer[tw] OR alzheimers's[tw]) AND (sleep[tw] OR "sleep"[mesh] OR "Sleep Disorders"[Mesh:noexp] OR circadian[tw] OR "Circadian Rhythm"[MeSH Terms]))) OR (((owl[tw] OR owls[tw] OR lark[tw] OR larks[tw] OR morningness[tw] OR eveningness[tw] OR morning types[tw] OR morning type[tw] OR evening types[tw] OR evening type[tw]) AND (sleep[tw] OR "sleep"[mesh] OR "Sleep Disorders"[Mesh:noexp] OR circadian[tw] OR "Circadian Rhythm"[MeSH Terms]))))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR "drug therapy"[Subheading] OR randomly[tiab] OR trial[tiab] OR groups[tiab]) NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms])) AND (English[la]

AND ("2006/10/01"[PDAT] : "3000/12/31"[PDAT]) NOT (Comment[pt] OR Editorial[pt] OR News[pt] OR Newspaper Article[pt] OR Letter[pt] OR Case Reports[pt] OR Review[pt])))

Terms for the literature search #2 in Embase database

('circadian rhythm sleep disorders':de,ab,ti OR 'circadian rhythm sleep disorder':de,ab,ti OR 'circadian rhythm sleep disorder'/exp OR 'chronobiology disorders':de,ab,ti OR 'hypernychthemeral':de,ab,ti OR 'circadian misalignment':de,ab,ti OR 'circadian dysregulation':de,ab,ti) OR(('advanced':de,ab,ti OR 'delayed':de,ab,ti) AND ('sleep phase':de,ab,ti)) OR (('irregular':de,ab,ti OR 'non 24 hour':de,ab,ti) AND ('sleep wake':de,ab,ti OR 'sleep-wake':de,ab,ti)) OR (('idiopathic':de,ab,ti AND 'chronic':de,ab,ti AND ('sleep-onset':de,ab,ti OR 'sleep onset':de,ab,ti) AND 'insomnia':de,ab,ti)) OR (('nonentrained':de,ab,ti OR 'non-entrained':de,ab,ti) AND ('sleep':de,ab,ti OR 'sleep'/exp OR 'sleep disorder'/de OR 'circadian':de,ab,ti OR 'circadian rhythm'/exp)) OR (('DSPS':de,ab,ti OR 'ASPS':de,ab,ti OR 'early morning awakening':de,ab,ti OR phase advance* OR phase delay* OR phase shift*) AND ('sleep':de,ab,ti OR 'sleep'/exp OR 'sleep disorder'/de OR 'circadian':de,ab,ti OR 'circadian rhythm'/exp)) OR ((('free running':de,ab,ti AND ('disorder':de,ab,ti OR 'rhythm':de,ab,ti)) AND ('sleep':de,ab,ti OR 'sleep'/exp OR 'sleep disorder'/de OR 'circadian':de,ab,ti OR 'circadian rhythm'/exp))) OR (('dark therapy':de,ab,ti OR 'light therapy':de,ab,ti OR 'amber lenses':de,ab,ti OR 'blue blocker':de,ab,ti OR 'blue-blocker':de,ab,ti OR 'blue blockers':de,ab,ti OR 'blue-blockers':de,ab,ti OR 'Blue light':de,ab,ti OR 'bright light':de,ab,ti OR 'eyewear':de,ab,ti OR 'Phototherapy':de,ab,ti OR 'phototherapy'/exp) AND ('sleep':de,ab,ti OR 'sleep'/exp OR 'sleep disorder'/de OR 'circadian':de,ab,ti OR 'circadian rhythm'/exp)) OR (('chronotherapy':de,ab,ti OR 'chronotype':de,ab,ti OR 'chronotherapy'/exp) AND ('sleep':de,ab,ti OR 'sleep'/exp OR 'sleep disorder'/de OR 'circadian':de,ab,ti OR 'circadian rhythm'/exp OR 'sleep therapy'/exp)) OR (('melatonin receptor agonists':de,ab,ti OR 'melatonin receptor agonist':de,ab,ti OR 'melatonin agonist':de,ab,ti OR 'melatonin agonists':de,ab,ti OR 'melatonin receptor antagonists':de,ab,ti OR 'melatonin receptor antagonist':de,ab,ti OR 'melatonin antagonist':de,ab,ti OR 'melatonin antagonists':de,ab,ti OR 'melatonin receptor inhibitor':de,ab,ti OR 'melatonin receptor inhibitors':de,ab,ti OR 'melatonin inhibitor':de,ab,ti OR 'melatonin inhibitors':de,ab,ti OR 'melatonin receptor'/exp/dd_dt OR ('melatonin receptor'/exp AND 'agonist'/exp)) AND ('sleep':de,ab,ti OR 'sleep'/exp OR 'sleep disorder'/de OR 'circadian':de,ab,ti OR 'circadian rhythm'/exp)) OR (('melatonin':de,ab,ti OR 'melatonin'/exp OR 'ramelteon':de,ab,ti OR 'ramelteon'/exp OR 'tasimelteon':de,ab,ti OR 'tasimelteon'/exp OR 'agomelatine':de,ab,ti OR 'agomelatine'/exp) AND ('sleep':de,ab,ti OR 'sleep'/exp OR 'sleep disorder'/de OR 'circadian':de,ab,ti OR 'circadian rhythm'/exp)) OR (('dim light melatonin onset':de,ab,ti OR 'DLMO':de,ab,ti) AND ('sleep':de,ab,ti OR 'sleep'/exp OR 'sleep disorder'/de OR 'circadian':de,ab,ti OR 'circadian rhythm'/exp)) OR (('Blindness':de,ab,ti OR 'blindness'/exp OR 'blind person':de,ab,ti OR 'blind people':de,ab,ti OR 'blind subject':de,ab,ti OR 'blind subjects':de,ab,ti OR 'blind patient':de,ab,ti OR 'blind patients':de,ab,ti OR 'enucleated':de,ab,ti OR 'nonsighted':de,ab,ti OR (visual AND impair*) OR ('visually impaired':de,ab,ti)) AND

('sleep':de,ab,ti OR 'sleep'/exp OR 'sleep disorder'/de OR 'circadian':de,ab,ti OR 'circadian rhythm'/exp)) OR (('dementia'/exp OR 'dementia':de,ab,ti OR 'Alzheimer disease'/exp OR 'alzheimer':de,ab,ti OR alzheimer*) AND ('sleep':de,ab,ti OR 'sleep'/exp OR 'sleep disorder'/de OR 'circadian':de,ab,ti OR 'circadian rhythm'/exp)) OR (('owl':de,ab,ti OR 'owls':de,ab,ti OR 'lark':de,ab,ti OR 'larks':de,ab,ti OR 'morningness':de,ab,ti OR 'eveningness':de,ab,ti OR 'morning types':de,ab,ti OR 'morning type':de,ab,ti OR 'evening types':de,ab,ti OR 'evening type':de,ab,ti) AND ('sleep':de,ab,ti OR 'sleep'/exp OR 'sleep disorder'/de OR 'circadian':de,ab,ti OR 'circadian rhythm'/exp)) AND ((random* OR factorial* OR crossover* OR cross NEXT/1 over* OR cross-over* OR placebo* OR doubl* NEXT/1 blind* OR singl* NEXT/1 blind* OR assign* OR allocat* OR volunteer* OR 'crossover procedure'/de OR 'double blind procedure'/de OR 'randomized controlled trial'/de OR 'single blind procedure'/de) OR ('clinical trial'/exp OR 'counterbalance':de,ab,ti OR 'counterbalanced':de,ab,ti OR 'crossover':de,ab,ti OR 'trial':de,ab,ti)) AND ((AND [english]/lim AND [2006-2012]/py AND [embase]/lim NOT [medline]/lim NOT ('editorial':it OR 'conference review':it OR 'conference paper':it OR 'note':it OR 'conference abstract':it OR 'letter':it OR 'review':it) NOT ([animals]/lim NOT [humans]/lim))

Terms for the literature search # 2 in PsychInfo database

((TI "circadian rhythm sleep disorders" or TI "circadian rhythm sleep disorder" or AB "circadian rhythm sleep disorders" or AB "circadian rhythm sleep disorder" or TI "chronobiology disorders" or AB "chronobiology disorders" OR TI "chronobiology disorder" or AB "chronobiology disorder" or TI "hypernychthemeral" or AB "hypernychthemeral" or TI "circadian misalignment" or AB "circadian misalignment" or TI "circadian dysregulation" or AB "circadian dysregulation")) OR ((TI "advanced" or AB "advanced" or TI "delayed" or AB "delayed") and (TI "sleep phase" or AB "sleep phase")) OR ((TI "irregular" or AB "irregular" or TI "non 24 hour" or AB "non 24 hour") AND (TI "sleep wake" or AB "sleep wake" or TI "sleep-wake" or AB "sleep-wake")) OR ((TI "idiopathic" or AB "idiopathic") and (TI "chronic" or AB "chronic") and (TI "sleep-onset" or AB "sleep-onset" or TI "sleep onset" or AB "sleep onset") and (DE "Insomnia" or TI "insomnia" or AB "insomnia")) OR ((TI "nonentrained" or AB "nonentrained" OR TI "non-entrained" OR AB "non-entrained") AND (TI "sleep" or AB "sleep" or DE "Sleep" or DE "Sleep Disorders" or TI "circadian" or AB "circadian" or DE "Human Biological Rhythms" or DE "Sleep Wake Cycle")) OR ((TI "DSPS" or AB "DSPS" or TI "ASPS" or AB "ASPS" or TI "early morning awakening" or AB "early morning awakening" or TI "phase advance*" or AB "phase advance*" or TI "phase delay*" or AB "phase delay*" or TI "phase shift*" or AB "phase shift*") and (TI "sleep" or AB "sleep" or DE "Sleep" or DE "Sleep Disorders" or TI "circadian" or AB "circadian" or DE "Human Biological Rhythms" or DE "Sleep Wake Cycle")) OR (((TI "free running" or AB "free running") and (TI "disorder" or AB "disorder" or TI "rhythm" or AB "rhythm")) and (TI "sleep" or AB "sleep" or DE "Sleep" or DE "Sleep Disorders" or TI "circadian" or AB "circadian" or DE "Human Biological Rhythms" or DE "Sleep Wake Cycle"))) OR ((TI "dark therapy" or AB "dark therapy" or TI "light therapy" or AB "light therapy" or TI "amber lenses" or AB "amber lenses" or TI "blue blocker" or AB

"blue blocker" or TI "blue-blocker" or AB "blue-blocker" or TI "blue blockers" or AB "blue blockers" or TI "blue-blockers" or AB "blue-blockers" or TI "Blue light" or AB "Blue light" or TI "bright light" or AB "bright light" or TI "eyewear" or AB "eyewear" or DE "Optical Aids" or TI "Phototherapy" or AB "Phototherapy" or DE "Phototherapy") and (TI "sleep" or AB "sleep" or DE "Sleep" or DE "Sleep Disorders" or TI "circadian" or AB "circadian" or DE "Human Biological Rhythms" or DE "Sleep Wake Cycle")) OR ((TI "chronotherapy" or AB "chronotherapy" or TI "chronotype" or AB "chronotypes" or TI "chronotypes" or AB "chronotypes" or TI "chronotherapy" or AB "chronotherapy") AND (TI "sleep" or AB "sleep" or DE "Sleep" or DE "Sleep Disorders" or TI "circadian" or AB "circadian" or DE "Human Biological Rhythms" or DE "Sleep Wake Cycle")) OR ((TI "melatonin receptor agonists" or AB "melatonin receptor agonists" or TI "melatonin receptor agonist" or AB "melatonin receptor agonist" or TI "melatonin agonist" or AB "melatonin agonist" or TI "melatonin agonists" or AB "melatonin agonists" OR TI "melatonin receptor antagonists" or AB "melatonin receptor antagonists" or TI "melatonin receptor antagonist" or AB "melatonin receptor antagonist" or TI "melatonin antagonist" or AB "melatonin antagonist" or TI "melatonin antagonists" or AB "melatonin antagonists" or TI "melatonin receptor inhibitor" or AB "melatonin receptor inhibitor" or TI "melatonin receptor inhibitors" or AB "melatonin receptor inhibitors" or TI "melatonin inhibitor" or AB "melatonin inhibitor" or TI "melatonin inhibitors" or AB "melatonin inhibitors") AND (TI "sleep" or AB "sleep" or DE "Sleep" or DE "Sleep Disorders" or TI "circadian" or AB "circadian" or DE "Human Biological Rhythms" or DE "Sleep Wake Cycle")) OR ((TI "melatonin" OR AB "melatonin" or DE "melatonin" OR TI "ramelteon" OR AB "ramelteon" OR TI "tasimelteon" OR AB "tasimelteon" OR TI "agomelatine" OR AB "agomelatine") AND (TI "sleep" or AB "sleep" or DE "Sleep" or DE "Sleep Disorders" or TI "circadian" or AB "circadian" or DE "Human Biological Rhythms" or DE "Sleep Wake Cycle")) OR ((TI "dim light melatonin onset" or AB "dim light melatonin onset" or TI "DLMO" or AB "DLMO") and (TI "sleep" or AB "sleep" or DE "Sleep" or DE "Sleep Disorders" or TI "circadian" or AB "circadian" or DE "Human Biological Rhythms" or DE "Sleep Wake Cycle")) OR ((TI "Blindness" or AB "blindness" or TI "blind person" or AB "blind person" or TI "blind people" or AB "blind people" or TI "blind subject" or AB "blind subject" or TI "blind subjects" or AB "blind subjects" or TI "blind patient" or AB "blind patient" or TI "blind patients" or AB "blind patients" or TI "enucleated" or AB "enucleated" or TI "nonsighted" or AB "nonsighted" or (TI "visual" and TI "impair*") or (AB "visual" and TI "impair*") or TI "visually impaired" or AB "visually impaired" or DE "Vision Disorders" or DE "Balint's Syndrome" or DE "Blind" or DE "Eye Disorders" or DE "Hemianopia") and (TI "sleep" or AB "sleep" or DE "Sleep" or DE "Sleep Disorders" or TI "circadian" or AB "circadian" or DE "Human Biological Rhythms" or DE "Sleep Wake Cycle")) OR ((DE "Dementia" OR DE "AIDS Dementia Complex" OR DE "Dementia with Lewy Bodies" OR DE "Presenile Dementia" OR DE "Semantic Dementia" OR DE "Senile Dementia" OR DE "Vascular Dementia" or DE "Alzheimer's Disease" OR TI "dementia" or AB "dementia" or TI "Alzheimer*" or AB "Alzheimer*") AND (TI "sleep" or AB "sleep" or DE "Sleep" or DE "Sleep Disorders" or TI "circadian" or AB "circadian" or DE

"Human Biological Rhythms" or DE "Sleep Wake Cycle")) OR ((TI "owl" or AB "owl" OR TI "owls" or AB "owls" or TI "lark" or AB "lark" OR TI "larks" or AB "larks" or TI "morningness" or AB "morningness" or TI "eveningness" or AB "eveningness" or TI "morning types" or AB "morning types" or TI "morning type" or AB "morning type" or TI "evening types" or AB "evening types" or TI "evening type" or AB "evening type" or TM "Horne and Ostberg Morningness-Eveningness Questionnaire") and (TI "sleep" or AB "sleep" or DE "Sleep" or DE "Sleep Disorders" or TI "circadian" or AB "circadian" or DE "Human Biological Rhythms" or DE "Sleep Wake Cycle")) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR "drug therapy"[Subheading] OR randomly[tiab] OR trial[tiab] OR groups[tiab]) NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms])) AND ((English[la] AND ("2006/10/01"[PDAT] : "3000/12/31"[PDAT]) NOT (Comment [pt] OR Editorial [pt] OR News [pt] OR Newspaper Article [pt] OR Letter [pt] OR Case Reports [pt] OR Review [pt]))

Terms for the literature search for harms/adverse effects of light treatment (Pub Med database))

(harm* OR "side effect*" OR "adverse effect*") and (Light* OR "light therapy*" OR "light exposure*" OR "Light treatment*") and "sleep"

Terms for the literature search for harms/adverse effects of treatment with hypnotics (Pub Med database)

(harm* OR "side effect*" OR "adverse effect*") and (hypnotic*)

Terms for the literature search for harms/adverse effects of melatonin treatment (Pub Med database)

(harm* OR "side effect*" OR "adverse effect*") and (melatonin*)

Limits used for the searches of harms/adverse effects of treatments:

Article types – meta-analysis, systematic review
Species – humans
Languages – English

APPENDIX TABLES

Appendix Table 1.

Light Treatment Compared to Placebo for ASWPD in Adults

Bibliography: Palmer et al., 2003[A]; Campbell et al., 1993[B]

Outcomes	# of Participants (studies)	Quality of the evidence (GRADE)	Absolute effects Light treatment vs. placebo (95% CI)
aMT6s acrophase	43 (1 study[A])	⊕⊕⊖⊖ LOW[1] due to imprecision	The mean urinary aMT6s acrophase in the intervention group was **15.00 min lower** (92.84 lower to 62.84 higher)
TST (actigraphy)	46 (1 study[A])	⊕⊕⊕⊖ MODERATE[2] due to imprecision	The mean TST(actigraphy) in the intervention group was **34.62 min lower** (68.28 lower to 0.96 lower)
TST (subjective)	47 (1 study[A])	⊕⊕⊕⊖ MODERATE[3] due to imprecision	The mean TST (subjective) in the intervention group was **17.93 min lower** (51.13 lower to 15.27 higher)
ISL (actigraphy)	46 (1 study[A])	⊕⊕⊕⊕ HIGH	The mean ISL (actigraphy) in the intervention group was **1.85 higher** (1.45 lower to 5.15 higher)
ISL (subjective)	47 (1 study[A])	⊕⊕⊕⊖ MODERATE[3] due to imprecision	The mean ISL (subjective) in the intervention group was **41.02 min higher** (11.28 lower to 93.32 higher)
SOT (actigraphy)	46 (1 study[A])	⊕⊕⊕⊖ MODERATE[3] due to imprecision	The mean SOT (actigraphy) in the intervention group was **24.00 min higher** (5.03 lower to 53.03 higher)
SOT (subjective)	45 (1 study[A])	⊕⊕⊕⊖ MODERATE[3] due to imprecision	The mean SOT (subjective) in the intervention group was **19.00 min higher** (12.09 lower to 50.09 higher)
SOffT (actigraphy)	46 (1 study[A])	⊕⊕⊖⊖ LOW[1] due to imprecision	The mean SOffT (actigraphy) in the intervention group was **5.00 min lower** (34.19 lower to 24.19 higher)
SOffT (subjective)	47 (1 study[A])	⊕⊕⊕⊖ MODERATE[3] due to imprecision	The mean SOffT (subjective) in the intervention group was **15.00 min lower** (44.71 lower to 14.71 higher)
CBT$_{Min}$	14 (1 study[B])	⊕⊖⊖⊖ VERY LOW[2] due to imprecision	The mean CBT$_{Min}$ in the intervention group was **141.00 min higher** (26.10 higher to 255.90 higher)

TST (PSG)	16 (1 study[B])	⊕⊖⊖⊖ **VERY LOW**[2] due to imprecision	The mean TST (PSG) in the intervention group was **51.30 min higher** (2.69 higher to 99.91 higher)
ISL (PSG)	16 (1 study[B])	⊕⊖⊖⊖ **VERY LOW**[3] due to imprecision	The mean ISL (PSG) in the intervention group was **11.70 min lower** (25.82 lower to 2.42 higher)
SOT (PSG)	16 (1 study[B])	⊕⊖⊖⊖ **VERY LOW**[1] due to imprecision	The mean SOT (PSG) in the intervention group was **15.00 min lower** (64.16 lower to 34.16 higher)
SOffT (PSG)	16 (1 study[B])	⊕⊖⊖⊖ **VERY LOW**[3] due to imprecision	The mean SOffT (PSG) in the intervention group was **29.00 min lower** (82.31 lower to 24.31 higher)

[1] CI of the absolute effect crosses the clinical significance threshold (defined by the TF) on both sides of the "no effect" line

[2] CI of the absolute effect crosses the clinical significance threshold defined by the TF

[3] CI of the absolute effect crosses the clinical significance threshold (defined by the TF) and the "no effect" line

aMT6 – 6-sulfatoxymelatonin (urinary metabolite of melatonin)
TST – Total Sleep Time
ISL – Initial Sleep Latency
SOT – Sleep Onset Time
SOffT – Sleep Offset Time
CBT_{Min} – Core Body Temperature Minimum
CI - Confidence Interval
Min-Minutes
PSG-Polysomnography
TF-Task Force

Appendix Table 2.

Melatonin Treatment Compared to Placebo for DSWPD in Adults with and without Depression

Bibliography: Kayumov et al., 2001 [A]; Mundey et al., 2005[B]; Rahman et al., 2010 [C]

Outcomes	# of Participants (studies)	Quality of the evidence (GRADE)	Absolute effects Melatonin treatment vs. control (95% CI)
TST (PSG) (subgroup with comorbid depression)	28* (2 studies [A,C])	⊕⊕⊖⊖ **LOW**[1,2] due to inconsistency, imprecision	The mean TST (PSG) in the intervention groups was **41.44 min higher** (13.19 higher to 69.70 higher)
ISL (PSG) (subgroup with comorbid depression)	28* (2 studies [A,C])	⊕⊕⊕⊕ **HIGH**	The mean ISL (PSG) in the intervention groups was **43.52 min lower** (52.60 lower to 34.45 lower)
DLMO (min)	11 (1 study[B])	⊕⊕⊖⊖ **LOW**[4] due to imprecision	The mean DLMO in the intervention group was **55.00 min lower** (196.12 lower to 86.12 higher)
TST (actigraphy)	11 (1 study[B])	⊕⊕⊕⊖ **MODERATE**[3] due to imprecision	The mean TST (actigraphy) in the intervention group was **15.80 min higher** (13.53 lower to 45.13 higher)
ISL (actigraphy)	11 (1 study[B])	⊕⊕⊕⊖ **MODERATE**[3] due to imprecision	The mean ISL (actigraphy) in the intervention group was **2.40 min lower** (18.08 lower to 13.28 higher)
SOT (actigraphy)	11 (1 study[B])	⊕⊕⊖⊖ **LOW**[4] due to imprecision	The mean SOT (actigraphy) in the intervention group was **3.00 min higher** (130.58 lower to 136.58 higher)
SOffT (actigraphy)	11 (1 study[B])	⊕⊕⊖⊖ **LOW**[4] due to imprecision	The mean SOffT (actigraphy) in the intervention group was **25.80 min higher** (102.28 lower to 153.88 higher)
ISL(PSG) (subgroup with no depression)	12* (1 study[C])	⊕⊕⊕⊕ **HIGH**	The mean ISL (PSG) (no depression) in the intervention groups was **37.70 min lower** (43.65 lower to 31.75 lower)
TST (PSG) (subgroup with no depression)	12* (1 study[C])	⊕⊕⊕⊕ **HIGH**	The mean TST (PSG) (no depression) in the intervention groups was **56.00 min higher** (48.51 higher to 63.49 higher)

* In studies with crossover design, where more than one measurements were taken on the same patients, all calculations were made based on the number of measurements
[1] High level of heterogeneity
[2] CI of the absolute effect crosses the clinical significance threshold defined by the TF
[3] CI of the absolute effect crosses the clinical significance threshold (defined by the TF) and the "no effect" line
[4] CI of the absolute effect crosses the clinical significance threshold (defined by the TF) on both sides of the "no effect" line

TST – Total Sleep Time

ISL – Initial Sleep Latency
DLMO – Dim Light Melatonin Onset
SOT – Sleep Onset Time
SOffT – Sleep Offset Time
CI - Confidence Interval
PSG-Polysomnography
TF-Task Force
Min-Minutes

Appendix Table 3.

Melatonin Treatment Compared to Placebo for DSWPD in Children/Adolescents with No Comorbidities

Bibliography: van Geijlswijk et al., 2010

Outcomes	# of Participants (studies)	Quality of the evidence (GRADE)	Absolute effects Melatonin treatment vs. control (95% CI)
DLMO (0.05 mg/kg melatonin)	29 (1 study)	⊕⊕⊖⊖ **LOW**[1] due to imprecision	The mean DLMO (0.05 mg/kg melatonin) in the intervention groups was **28.68 min lower** (91.15 lower to 33.78 higher)
DLMO (0.1 mg/kg melatonin)	31 (1 study)	⊕⊕⊖⊖ **LOW**[1] due to imprecision	The mean DLMO (0.1 mg/kg melatonin) in the intervention groups was **12.35 min lower** (74.68 lower to 49.98 higher)
DLMO (0.15 mg/kg melatonin)	32 (1 study)	⊕⊕⊕⊖ **MODERATE**[2] due to imprecision	The mean DLMO (0.15 mg/kg melatonin) in the intervention groups was **33.63 min lower** (85.08 lower to 17.83 higher)
ISL (actigraphy, 0.05 mg/kg melatonin)	32 (1 study)	⊕⊕⊕⊕ **HIGH**	The mean ISL (0.05 mg/kg melatonin) in the intervention groups was **38.39 min lower** (58.53 lower to 18.24 lower)
ISL (actigraphy, 0.1 mg/kg melatonin)	33 (1 study)	⊕⊕⊕⊕ **HIGH**	The mean ISL (0.1 mg/kg melatonin) in the intervention groups was **44.24 min lower** (64.44 lower to 24.04 lower)
ISL (actigraphy, 0.15 mg/kg melatonin)	34 (1 study)	⊕⊕⊕⊕ **HIGH**	The mean ISL (0.15 mg/kg melatonin) in the intervention groups was **43.80 min lower** (63.54 lower to 24.06 lower)
SOT (actigraphy, 0.05 mg/kg melatonin)	32 (1 study)	⊕⊕⊕⊖ **MODERATE**[2] due to imprecision	The mean SOT (0.05 mg/kg melatonin) in the intervention groups was **19.92 min lower** (48.48 lower to 8.65 higher)

SOT (actigraphy, 0.1 mg/kg melatonin)	33 (1 study)	⊕⊕⊕⊖ **MODERATE**[3] due to imprecision	The mean SOT (0.1 mg/kg melatonin) in the intervention groups was **33.70 min lower** (56.46 lower to 10.95 lower)
SOT (actigraphy, 0.15 mg/kg melatonin)	34 (1 study)	⊕⊕⊕⊕ **HIGH**	The mean SOT (0.15 mg/kg melatonin) in the intervention groups was **42.77 min lower** (63.78 lower to 21.77 lower)

[1] CI of the absolute effect crosses the clinical significance threshold defined by the TF on both sides of the "no effect" line

[2] CI of the absolute effect crosses the clinical significance threshold (defined by the TF) and the "no effect" line

[3] CI of the absolute effect crosses the clinical significance threshold defined by the TF

DLMO – dim light melatonin onset
ISL – Initial Sleep Latency
SOT – Sleep Onset Time
CI - Confidence Interval
Mg-Milligrams
Min-Minutes
Kg-Kilograms
TF-Task Force

Appendix Table 4.

Melatonin Treatment Compared to Placebo for DSWPD in Children/Adolescents Comorbid with Psychiatric Conditions

Bibliography: Smits et al., 2001 [A]; van der Heijden et al., 2007[B]

Outcomes	# of Participants (studies)	Quality of the evidence (GRADE)	Absolute effects **Melatonin treatment vs. placebo** (95% CI)
DLMO	132 (2 studies[A,B])	⊕⊕⊕⊕ **HIGH**	The mean DLMO in the intervention groups was **54.22 min lower** (76.78 lower to 31.67 lower)
SOT (actigraphy)	130 (2 studies[A,B])	⊕⊕⊕⊕ **HIGH**	The mean SOT (actigraphy) in the intervention groups was **36.57 min lower** (56.18 lower to 16.96 lower)
TST (actigraphy)	105 (1 study[B])	⊕⊕⊕⊖ **MODERATE**[1] due to imprecision	The mean TST (actigraphy) in the intervention group was **18.50 min higher** (1.15 lower to 38.15 higher)
ISL (actigraphy)	105 (1 study[B])	⊕⊕⊕⊖ **MODERATE**[2] due to imprecision	The mean ISL (actigraphy) in the intervention group was **18.70 min lower** (30.39 lower to 7.01 lower)
TST (subjective)	31 (1 study[A])	⊕⊕⊕⊖ **MODERATE**[1]	The mean TST (subjective) in the intervention group was **29.00 min higher** (3.86 lower to 61.86 higher)

			due to imprecision	

Outcome	#	Quality	Absolute effect
ISL (subjective)	33 (1 study[A])	⊕⊕⊕⊖ **MODERATE**[1] due to imprecision	The mean ISL (subjective) in the intervention group was **15.10 min lower** (36.64 lower to 6.44 higher)
SOT (subjective)	33 (1 study[A])	⊕⊕⊕⊖ **MODERATE**[1] due to imprecision	The mean SOT (subjective) in the intervention group was **17.00 min lower** (57.74 lower to 23.74 higher)
SOffT (subjective)	32 (1 study[A])	⊕⊕⊖⊖ **LOW**[3] due to very serious imprecision	The mean SOffT (subjective) in the intervention group was **1.00 min higher** (25.30 lower to 27.30 higher)

[1] CI of the absolute effect crosses the "no effect" line and the clinical significance threshold defined by the TF
[2] CI of the absolute effect crosses the clinical significance threshold defined by the TF
[3] CI of the absolute effect crosses the clinical significance threshold (defined by the TF) on both sides of the "no effect" line

TST – Total Sleep Time
ISL – Initial Sleep Latency
DLMO – Dim Light Melatonin Onset
SOT – Sleep Onset Time
SOffT – Sleep Offset Time
CI - Confidence Interval
TF-Task Force
Min-Minutes

Appendix Table 5.

Vitamin B12 Compared to Placebo for DSWPD in Adults

Bibliography: Okawa et al., 1997

Outcomes	# of Participants (studies)	Quality of the evidence (GRADE)	Absolute effects Vit B12 vs. placebo (95% CI)
TST (subjective)	50 (1 study)	⊕⊖⊖⊖ **VERY LOW**[1] due to imprecision	The mean TST (subjective) in the intervention groups was **19.80 min higher** (8.05 higher to 31.55 higher)
SOT (subjective)	50 (1 study)	⊕⊖⊖⊖ **VERY LOW**[1] due to imprecision	The mean SOT (subjective) in the intervention groups was **19.00 min lower** (32.44 lower to 5.56 lower)

[1] CI of the absolute effect crosses the clinical significance threshold defined by the TF

TST – Total Sleep Time
SOT – Sleep Onset Time

CI - confidence interval
TF-Task Force
Min-Minutes

Appendix Table 6.

Light/Combination Treatment Compared to Controls for DSWPD in Adults

Bibliography: Cole et al., 2002[(A)]; Lack, Bramwell et al., 2007[(B)]

Outcomes	# of Participants (studies)	Quality of the evidence (GRADE)	Combination treatment vs. control (95% CI)
TST (subjective)	18 (1 study[B])	⊕⊖⊖⊖ **VERY LOW**[1,2] due to risk of bias, imprecision	The mean TST (subjective) in the intervention groups was **24.60 min higher** (49.96 lower to 99.16 higher)
SOT (subjective)	18 (1 study[B])	⊕⊕⊖⊖ **LOW**[1,3] due to risk of bias, imprecision	The mean SOT (subjective) in the intervention groups was **62.00 min lower** (126.88 lower to 2.88 higher)
SOffT (subjective)	18 (1 study[B])	⊕⊖⊖⊖ **VERY LOW**[1,2] due to risk of bias, imprecision	The mean SOffT (subjective) in the intervention groups was **37.00 min lower** (161.64 lower to 87.64 higher)
aMT6s acrophase	45 (1 study[A])	⊕⊕⊕⊖ **MODERATE**[3] due to imprecision	The mean aMT6s acrophase in the intervention groups was **40.00 min lower** (102.38 lower to 22.38 higher)
SOT (actigraphy)	54 (1 study[A])	⊕⊕⊖⊖ **LOW**[2] due to imprecision	The mean SOT (actigraphy) in the intervention groups was **0.00 min higher** (48.39 lower to 48.39 higher)
SOffT (actigraphy)	54 (1 study[A])	⊕⊕⊖⊖ **LOW**[2] due to imprecision	The mean SOffT (actigraphy) in the intervention group was **0.00 min higher** (43.13 lower to 43.13 higher)
aMT6s acrophase (group with aMT6s acrophase earlier than 6 AM)	22 (1 study[A])	⊕⊕⊖⊖ **LOW**[2] due to imprecision	The mean aMT6s (group with aMT6s acrophase earlier than 6 AM)in the intervention group was **1.00 min lower** (66.62 lower to 64.62 higher)
aMT6s acrophase (group with aMT6s acrophase later than 6 AM)	23 (1 study[A])	⊕⊕⊕⊖ **MODERATE**[4] due to imprecision	The mean aMT6s (group with aMT6s acrophase later than 6 AM) in the intervention groups was **83.00 min lower** (157.91 lower to 8.09 lower)

SOT (actigraphy) (group with aMT6s acrophase earlier than 6 AM)	22 (1 study[A])	⊕⊕⊖⊖ **LOW**[2] due to imprecision	The mean SOT (actigraphy) (group with aMT6s acrophase earlier than 6 AM). in the intervention group was **13.00 min higher** (42.09 lower to 68.09 higher)
SOT (actigraphy) (group with aMT6s acrophase later than 6 AM)	23 (1 study[A])	⊕⊕⊖⊖ **LOW**[2] due to imprecision	The mean SOT (actigraphy) (group with aMT6s acrophase later than 6 AM) in the intervention group was **26.00 min lower** (107.53 lower to 55.53 higher)
SOffT(actigraphy) (group with aMT6s acrophase earlier than 6 AM)	22 (1 study[A])	⊕⊕⊖⊖ **LOW**[2] due to imprecision	The mean SOffT (actigraphy) (group with aMT6s acrophase earlier than 6 AM) in the intervention group was **7.00 min higher** (44.99 lower to 58.99 higher)
SOffT (actigraphy) (group withaMT6s acrophase later than 6 AM)	23 (1 study[A])	⊕⊕⊖⊖ **LOW**[2] due to imprecision	The mean SOffT (actigraphy) (group with aMT6s acrophase later than 6 AM) in the intervention group was **23.00 min lower** (89.12 lower to 43.12 higher)

[1] This is a short paper with lack of detail in methods and results; a lot of information is missing
[2] Confidence interval of the absolute effect crosses the clinical significance threshold (defined by the TF) on both sides of the "no effect line"
[3] Confidence interval of the absolute effect crosses the "no effect" line
[4] Confidence interval of the absolute effect crosses the clinical significance threshold defined by the TF

TST – Total Sleep Time
SOT – Sleep Onset Time
SOffT – Sleep Offset Time
aMT6 – 6-sulfatoxymelatonin (urinary metabolite of melatonin)
CI - Confidence Interval
TF-Task Force
Min-Minutes

Appendix Table 7.

Light/Combination Treatment (multicomponent behavioral interventions + light) Compared to Controls for DSWPD in Children/Adolescents

Bibliography: Gradisar et al., 2011

Outcomes (Weekdays)	# of Participants (studies)	Quality of the evidence (GRADE)	Absolute effects Light/Combination treatment vs. control (95% CI)
TST (subjective)	40 (1 study)	⊕⊕⊕⊖ **MODERATE**[1] due to risk of bias	The mean TST (subjective) in the intervention groups was **72.00 min higher** (37.35 higher to 106.65 higher)
ISL (subjective)	40 (1 study)	⊕⊕⊕⊖ **MODERATE**[1] due to risk of bias	The mean ISL (subjective) in the intervention groups was **43.10 min lower** (63.74 lower to 22.46 lower)
SOT (subjective)	40 (1 study)	⊕⊕⊖⊖ **LOW**[1,2] due to risk of bias, imprecision	The mean SOT (subjective) in the intervention groups was **42.00 min lower** (81.26 lower to 2.74 lower)
SOffT (subjective)	40 (1 study)	⊕⊕⊖⊖ **LOW**[1,2] due to risk of bias, imprecision	The mean SOffT (subjective) in the intervention groups was **23.00 min lower** (45.13 lower to 0.87 lower)

[1] Study was not blinded, and an intention to treat analysis was NOT utilized

[2] CI of the absolute effect does not reach clinical significance threshold defined by the TF

TST – Total Sleep Time
ISL – Initial Sleep Latency
SOT – Sleep Onset Time
SOffT – Sleep Offset Time
CI - Confidence Interval
TF-Task Force
Min-Minutes

Appendix Table 8.

Melatonin Treatment Compared to Placebo for N24SWD in Blind Adults

Bibliography: Lockley et al., 2000; Sack et al., 2000; Hack et al., 2003

Outcomes	# of Participants (studies)	Quality of the evidence (GRADE)	Relative effect (95% CI)
Entrainment (Yes/No)	36 (3 studies)	⊕⊕⊖⊖ **LOW**	**OR 21.18** (3.22 to 139.17)

CI - Confidence Interval
OR-Odds Ratio

Appendix Table 9.

Light Treatment Compared to Placebo for ISWRD in Elderly With Dementia

Bibliography: Dowling et al., 2008 (A); Mishima et al., 1994 (B)

Outcomes	# of Participants (studies)	Quality of the evidence (GRADE)	Absolute effects Light treatment vs. control (95% CI)
TST (actigraphy)	35 (1 study[A])	⊕⊖⊖⊖ **VERY LOW**[1,2] due to risk of bias, imprecision	The mean TST (actigraphy) in the intervention group was **9.00 min higher** (67.14 lower to 85.14 higher)

[1] A. No intention-to-treat principle: only completed cases were analyzed. B. Selective reporting: dropouts are not described and some actigraphy variables are not reported (sleep onset, offset, sleep efficiency etc.)

[2] CI of the absolute value crosses the clinical significance threshold (defined by the TF) on both sides of the "no effect" line

Outcomes	# of Participants (studies)	Quality of the evidence (GRADE)	Absolute effects Light treatment vs. control (95% CI)
TST (subjective)	24 (1 study[B])	⊕⊖⊖⊖ **VERY LOW**[1,2] due to risk of bias, imprecision	The mean TST (subjective) in the intervention group was **30.00 min higher** (35.63 lower to 95.63 higher)

[1] A. No blinding, B. No intention-to-treat principle observed. C. Role of control group is vaguely described

[2] CI of the absolute effect crosses the clinical significance threshold (defined by the TF) on both side of the "no effect" line

TST – Total Sleep Time
CI - Confidence Interval
TF-Task Force
Min-Minutes

Appendix Table 10.

Melatonin Treatment Compared to Placebo for ISWRD in Elderly with Dementia

Bibliography: Serfaty et al., 2002

Outcomes	# of Participants (studies)	Quality of the evidence (GRADE)	Absolute effects
			Melatonin treatment vs. placebo (95% CI)
TST (actigraphy)	25 (1 study)	⊕⊕⊖⊖ **LOW**[1] due to imprecision	The mean TST (actigraphy) in elderly in the intervention group was **26.23 min higher** (84.43 lower to 136.89 higher)

[1] CI of the absolute effect crosses the clinical significance threshold (defined by the TF) on both sides of "no effect" line

TST – Total Sleep Time
CI - Confidence Interval
TF-Task Force
Min-Minute

Appendix Table 11

Melatonin Treatment Compared to Placebo for ISWRD in Children/Adolescents with Neurologic Disorders

Bibliography: Wright et al., 2011

Outcomes	# of Participants (studies)	Quality of the evidence (GRADE)	Absolute effects
			Melatonin treatment vs. placebo (95% CI)
TST (subjective) (min)	34 (1 study)	⊕⊕⊕⊖ **MODERATE**[1] due to imprecision	The mean TST (subjective) in the intervention group was **48.45 min higher** (6.29 higher to 90.61 higher)
ISL (subjective) (min)	34 (1 study)	⊕⊕⊕⊖ **MODERATE**[1] due to imprecision	The mean ISL (subjective) in the intervention group was **51.71 min lower** (89.93 lower to 13.49 lower)

[1] CI of the absolute effect crosses the clinical significance threshold defined by the TF

TST – Total Sleep Time
ISL – Initial Sleep Latency
CI - Confidence Interval
TF-Task Force
Min-Minutes

Appendix Table 12

Comparison of Combination of Light Therapy and Melatonin/Placebo for ISWRD in Elderly with Dementia

Bibliography: Dowling et al., 2008

Outcomes	No of Participants (studies)	Quality of the evidence (GRADE)	Absolute effects **Combination treatment vs. control** (95% CI)
TST (actigraphy)	32 (1 study)	⊕⊖⊖⊖ **VERY LOW**[1,2] due to risk of bias, imprecision	The mean TST (actigraphy) in the intervention group was **23.00 min lower** (101.31 lower to 55.31 higher)

[1] A. No intention-to-treat principle: only completed cases were analyzed. B. Selective reporting: dropouts are not described and some actigraphy variables are not reported (sleep onset,/offset, etc.)

[2] CI of the absolute effect crosses the clinical significance threshold (defined by the TF) on both sides of the "no effect" line

PSWS – Prescribed Sleep-Wake Scheduling
TST – Total Sleep Time
CI - Confidence Interval
TF-Task Force
Min-Minutes