SUPPLEMENTAL MATERIALS Management of Shift Work Disorder

All Literature Search Terms

(("sleep disorders, circadian rhythm"[MeSH Terms] AND "shift"[All Fields]) OR "shift work type" OR "shiftwork" OR "shiftwork disorder" OR "shiftwork sleep disorder" OR "shift work disorder" OR "shift work tolerance" AND "english"[All Fields]] AND ("1900/01/01"[PDAT]: "2020/10/01"[PDAT]) NOT "Editorial"[Publication Type] NOT "Letter"[Publication Type] NOT "Comment"[Publication Type] NOT "Biography"[Publication Type] NOT "Review"[Publication Type]

("shiftwork" or "shiftwork disorder" or "shift work" or "shift work disorder" or "circadian rhythm disorder" or "CRSWD") AND (("bright light therapy" or "light therapy")) *Filters: Humans*

("shift work" OR "shiftwork" OR "shiftwork disorder" OR "shift work sleep disorder" OR "circadian rhythm disorder" or "CRSWD" OR "daytime sleep") AND ("cognitive behav* therap*" or "cognitive therap*" or "behav* therap*" or "CBT" or "CBT-I" or "ICBT") Filters: Humans

("shift work" OR "shiftwork" OR "shiftwork disorder" OR "shift work sleep disorder" OR "circadian rhythm disorder" or "CRSWD" OR "daytime sleep") AND (("clockwise" or "clockwise shift*") OR (counterclockwise or "counterclockwise shift*")) Filters: Humans

("shift work" OR "shiftwork" OR "shiftwork disorder" OR "shift work sleep disorder" OR "circadian rhythm disorder" or "CRSWD" OR "daytime sleep") AND ("timed diet" or "timed eating" or "timed meals") Filters: Humans

Exclusion Criteria

Exclusion criteria are applied during the abstract review of all retrieved publications. Studies that meet <u>any</u> of the exclusion criteria are rejected from the systematic review.

A. Publication type

- 1. Conference abstracts
- 2. Editorials
- 3. Review
- 4. Methods

B. Study type

- 1. Animal research
- 2. Case reports
- 3. Case series

C. Language non-English

D. Diagnosis Sleep/wake symptoms NOT related to shift work will revisit for not using a diagnosis

- E. Patient population < 18 years of age
- F. Main study objective is NOT evaluating the efficacy/effectiveness of shift work treatments
- G. Does NOT include one of the following interventions of interest:
 - 1. Planned Sleep Schedules/ naps
 - 2. Timed Light and/or dark Exposure
 - 3. Timed Melatonin or other chronobiotic Administration
 - 4. Sleep Promoting Medications (e.g., Benzodiazepines, Benzodiazepine receptor agonists), or substances
 - 5. Stimulant Medications/ wake promoting medications, OTC, caffeine
 - 6. Timed Physical Activity/Exercise
 - 7. Diet and Meal Timing
 - 8. Combination Treatments
 - 9. CBT-I or Sleep hygiene
 - 10. Planned work schedule

Inclusion Criteria

Inclusion criteria are applied during the full publication review of all publications that were not rejected during the abstract review. Studies that **meet all inclusion criteria will be accepted as evidence to use in the systematic review.**

- A. Outcomes of interest (must meet at least 1)
 - a. Excessive sleepiness
 - b. total sleep time
 - c. sleep quality
 - d. circadian adaptation
 - e. quality of life
 - f. mental health
 - g. cognitive/ work performance
 - h. accident risk
- B. Publication type
 - a. RCTs:
 - i. intervention vs. attention control
 - ii. intervention vs placebo
 - iii. intervention vs standard of care
 - iv. intervention vs waitlist
 - v. intervention vs intervention
 - b. Observational studies: longitudinally/cross-sectionally examines the effect(s) of the intervention
- C. Patients: Shift work disorder diagnosis (must meet at least 1)f
 - a. Use of any of the 3 diagnostic systems, regardless of version: DSM-, ICSD, ICD-10

- b. Use of validated sleep instruments in combination with quantitative objective/subjective measure
- c. Other sleep complaints/criteria/symptoms that would require adjudication
- D. Interventions (must include at least 1)
 - a. Planned Sleep Schedules/ naps
 - b. Timed Light Exposure /dark
 - c. Timed Melatonin or other chronobiotic Administration
 - d. Sleep Promoting Medications (e.g., Benzodiazepines, Benzodiazepine receptor agonists) or substances
 - e. Stimulant or wake-promoting medications, or other alerting agents, prescription or OTC
 - f. Timed Physical Activity/Exercise
 - g. Diet and Meal Timing
 - h. Combination Treatments
 - i. CBT-I or Sleep hygiene
 - i. Planned work schedule

Abbreviations:

AASM -- American Academy of Sleep Medicine

ANAM- Automated neuropsychological assessment metrics

BDI – Beck depression inventory

CES-D – Center for Epidemiologic Studies Depression scale

CMT - Clinically Meaningful Threshold

CGI – Clinical Global Impressions Scale

CGI-I – Clinical Global Impressions-Improvement Scale

COI – conflict of interest

CPG – Clinical practice guideline

DLMO – Dim light melatonin onset

DSST – Digit symbol substitution test

EEG - Electroencephalogram

ESS – Epworth Sleepiness Scale

FDA – U.S. Food and Drug Administration

GAF – Global Assessment of Functioning

GRADE – Grading of Recommendations, Assessment, Development and Evaluation

GSDS – General Sleep Disturbance Scale

ISI – insomnia severity index

KSS – Karolinska sleepiness scale

MADRS – Montgomery-Asberg depression rating scale

MAT- Memory and attention test

MSLT - Multiple sleep latency test

MWT – Maintenance of wakefulness test

PICO – Patient, intervention, comparator, outcome

POMS-A – Profile of moods-adolescent

PSG – Polysomnography

PSQI – Pittsburgh sleep quality index

PVT – Psychomotor vigilance test

RAND-PCS – physical component of the RAND-36

RAT - Remote associate's test

RCT - Randomized controlled trial

SCI-90 – symptom check list 90

SD – Standard deviation

SF-36 - Short form 36 health questionnaire

SOL – Sleep onset latency

SMD – Standardized mean-difference

SR – Systematic review

SSI – Standard shiftwork index

SSS – Stanford sleepiness scale

TIB – Time in bed

TF – Task force

TST – Total sleep time

WASO – Wake after sleep onset

WHO-5 – world health organization- five well-being index

Table 0: Language Description

| Language | Description |
|---|---|
| Clinically meaningful | The point estimate and the entire 95% CI were all above the CMT |
| May be clinically meaningful | The point estimate was above the CMT; however, the 95% CI crossed the CMT |
| While not clinically meaningful | The point estimate was below the CMT; however, the 95% CI crossed the CMT |
| Little to no difference | The point estimate and the 95% CI fell in the no effect zone (between the CMTs) |
| Failed to show, or exclude either benefits or harms | The 95% CI crossed both CMTs |
| May [improve/worsen/increase, decrease] | The TF did not set a CMT, so clinical meaningfulness could not be noted |

Table S1. Outcome tools for cognitive performance

| | Additional Cogn | itive Perfo | ormance Tests | | | | | |
|-----------|---|--------------------------------|---|--|--|--|--|--|
| ANAM | | Mackworth clock vigilance task | | | | | | |
| 0 | mean reaction time | MAT | | | | | | |
| Choice | reaction time task | Mistak | es/near misses/accidents during the night shift | | | | | |
| Coding | task | Power | of attention test | | | | | |
| 0 | Number of correct substitutions | Quality | of episodic secondary memory | | | | | |
| Conner | 's continuous performance test | PVT | | | | | | |
| 0 | Attentiveness | 0 | number of lapses/errors | | | | | |
| 0 | No. of commission errors | 0 | reaction time | | | | | |
| 0 | No. of omission errors | 0 | speed | | | | | |
| 0 | Reaction time | RAT | | | | | | |
| Risk tak | ring | Runnin | g memory continuous performance task | | | | | |
| Delayed | d word recall | SALT | | | | | | |
| Flight si | imulator | 0 | Correct Responses (%) | | | | | |
| 0 | Deviation from altitude flight | 0 | Correction time (s) | | | | | |
| 0 | Deviation from the velocity flight envelope | 0 | Empty items (%) | | | | | |
| Difficult | ty in concentrating at work | 0 | Nonfaulty items (%) | | | | | |
| Divided | attention test | 0 | Time to respond | | | | | |

| DSST | Serial simple reaction time test | | | | | | |
|---|--|--|--|--|--|--|--|
| Dual task | Simple reaction time | | | | | | |
| control losses | Switching task | | | | | | |
| Four-choice serial reaction time | Mannequin | | | | | | |
| Free recall memory assessments | mannequin (throughput) | | | | | | |
| GO/NOGO | Math | | | | | | |
| Grammatical reasoning test | Math (throughput) | | | | | | |
| response time | Torrance test of creative thinking | | | | | | |
| Head steadiness | Two-Letter Memory and Search Test | | | | | | |
| percent of time off target | reaction time | | | | | | |
| Karolinska sleep diary | Visuo-spatial discrimination | | | | | | |
| reduced performance | Wilkinson four choice test | | | | | | |
| Letter cancellation task | reaction time (throughput) | | | | | | |
| trials without false alarms | | | | | | | |

PICO 1: Adults with shiftwork disorder Symptoms of excessive sleepiness

Armodafinil

Summary of Findings (GRADE)

Table S2. Armodafinil in adults with shiftwork disorder

| Outcomes [Tool] | Certainty of the evidence (GRADE) | Absolute Difference Armodafinil vs Control | No of Participants (studies) |
|---|-----------------------------------|--|---------------------------------|
| Excessive sleepiness or alertness [MSLT] ^a | ⊕⊕⊕⊕ ні G н | The mean difference in the armodafinil group was 4.5 minutes higher (1.83 higher to 7.17 higher) compared to control | 280 (3 RCTs) |
| Excessive sleepiness or alertness [KSS] ^b | ⊕⊕⊕⊜ MODERATE ^c | The mean difference in the armodafinil group was 0.99 points lower (1.32 lower to 0.65 lower) compared to control | 612 (3 RCTs) |
| Excessive sleepiness or alertness [CGI-C] ^a | ⊕⊕⊕⊕ ні с н | 9 · · · · · · · · · · · · · · · · · · · | 510 (2 RCTs) |
| Accident risk [Standard deviation of lateral position] ^b | ⊕⊕⊜⊖ LOW ^{d,e} | The mean difference in the armodafinil group was 0.5 meters lower (1.02 lower to 0.02 higher) compared to control | 40 (1 RCT) |
| Accident risk [off-road deviations] ^b | ⊕⊕⊜⊝ LOW ^{c,d} | The mean difference in the armodafinil group was 5.19 deviations fewer (14.29 fewer to 3.91 more) compared to control | 40 (1 RCT) |
| Accident risk [Sleep diary (commute home), mistakes made, near misses] ^b | ⊕⊕⊕⊜ MODERATE ^{d,f} | The risk ratio in the armodafinil group was 0.62 (0.40 to 0.96) with an absolute risk of 205 fewer per 1,000 (324 fewer to 22 fewer) compared to control | 110 (1 RCT) |
| Cognitive performance ^e [Multiple tests] ^g | ⊕⊕⊕⊜ MODERATE ^d | Armodafinil improves cognitive performance in the following outcome tools: DSST, RAT, free recall memory assessments, divided attention test, power of attention test quality of episodic secondary memory, delayed word recall, simple reaction time, and mistakes/near misses/accidents during the night shift. Studies included: Drake 2014 (n=40), Howard 2014 (n=24), and Czeisler 2009 (n=215) | (3 RCTs) |

| Serious adverse events ^{b,g} | ⊕⊕⊕⊖ MODERATE ^c | The risk ratio in the armodafinil group was 0.60 (0.08 to 4.54) with an absolute risk of 3 fewer per 1,000 (6 fewer to 23 more) compared to control | 616 (2 RCTs) |
|---|-------------------------------|--|-----------------|
| Adverse events leading to withdrawal ^{b,g} | ⊕⊕⊕⊖ MODERATE ^c | The risk ratio in the armodafinil group was 2.65 (0.94 to 7.49) with an absolute risk of 27 more per 1,000 (1 fewer to 105 more) compared to control | 616 (2 RCTs) |

- a. Higher values favor the intervention
- b. Lower values favor the intervention
- c. Imprecision due to 95% CI crossing the CMT
- d. Imprecision due to small sample size (<200 participants)
- e. Imprecision due to 95% CI crossing the null
- f. Risk of bias due to selective reporting of the outcome
- g. CMT was not established by the TF

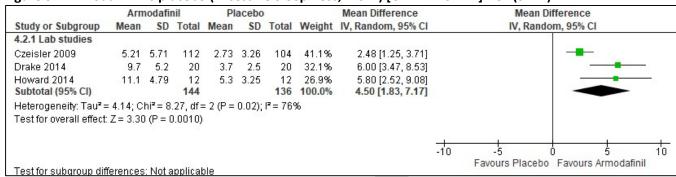
Study Characteristics

Table S3. Armodafinil in adults with shiftwork disorder

| Study Citation | Study Design | Number of Participants (% Female) | Age: mean (SD) or range | Population | Intervention (dose) | Comparator | Time of Intervention Delivery | Duration of Follow-up |
|-------------------|-------------------|---|--|------------|----------------------|------------|---|-----------------------|
| Black 2010 | non-RCT | 113 (42) | 42.7 (9.89) | SWD | Armodafinil (250 mg) | Baseline | 30-60 min before night shift, no later than 23:00 | 12 months |
| Czeisler 2009 | RCT | 245 (47) | Armodafinil: 38.9 (10.8) Placebo: 40.3 (10.8) | SWD | Armodafinil (150 mg) | Placebo | Before each night shift and no later than 23:00 | 12 weeks |
| Drake 2014 | RCT | 20 (85) | 42.7 (8.7) | SWD | Armodafinil (150 mg) | Placebo | 23:45 | 1 night |
| Erman 2011 | RCT | 383 (46) | Armodafinil: 36.7 (10.7) Placebo: 36.1 (10.8) | SWD | Armodafinil (150 mg) | Placebo | 30-60 min before night shift, no later than 23:00 | 6 weeks |
| Erman 2012 | RCT | 383 (46) | 18 to 65 | SWD | Armodafinil (150 mg) | Placebo | administered 30 to 60 minutes before the start of the night shift and no later than 11 PM | 6 weeks |
| Howard 2014 | RCT, crossover | 12 (54) | 33.75 (8.57) | SWD | Armodafinil (150 mg) | Placebo | Beginning of night shift | 1 night |
| Schwartz 2010 | non-RCT | 108 (36) | 39.6 ± 10.9 | SWD | Armodafinil (150 mg) | Baseline | 1 h before the start of the night shift but no later than 23:00 | 12 months |

Critical Outcomes

Figure S1. Armodafinil vs placebo (Excessive Sleepiness, MSLT) [CMT = 1.0 min] RCT (SWD)



^{*}Czeisler 2009: data from final visit, data extracted from Figure 2A, SEM converted to SD Drake 2014: SEM converted to SD

Figure S2. Armodafinil vs placebo (Excessive Sleepiness, KSS) [CMT = 1.0 pt] RCT (SWD)

| | Arm | nodafii | nil | PI | acebo | | | Mean Difference | Mean Difference |
|-----------------------------------|----------|--------------------|--------|-----------|----------|-------------|--------|----------------------|-------------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| 4.1.1 Lab studies | | | | | | | | | |
| Czeisler 2009 | 5.49 | 1.22 | 104 | 6.37 | 2.65 | 112 | 37.8% | -0.88 [-1.42, -0.34] | - |
| Drake 2014 | 3.28 | 1.6 | 20 | 4.64 | 2.05 | 20 | 8.6% | -1.36 [-2.50, -0.22] | |
| Subtotal (95% CI) | | | 124 | | | 132 | 46.5% | -0.97 [-1.46, -0.48] | • |
| Heterogeneity: Tau ² = | 0.00; Ch | $i^2 = 0.6$ | 5, df= | 1 (P = 0) | (.46); P | = 0% | | | |
| Test for overall effect: | Z = 3.87 | (P = 0. | 0001) | | | | | | |
| 4.1.2 Field studies | | | | | | | | | |
| Erman 2011 (JOEM) | -2.8 | 2.12 | 176 | -1.8 | 2.28 | 180 | 53.5% | -1.00 [-1.46, -0.54] | - |
| Subtotal (95% CI) | | | 176 | | | 180 | 53.5% | -1.00 [-1.46, -0.54] | • |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z = 4.29 | (P < 0. | 0001) | | | | | | |
| Total (95% CI) | | | 300 | | | 312 | 100.0% | -0.99 [-1.32, -0.65] | • |
| Heterogeneity: Tau ² = | 0.00; Ch | $j^2 = 0.6$ | 6, df= | 2(P = 0) | 1.75); P | = 0% | | +, | 1 1 |
| Test for overall effect: | Z = 5.77 | (P < 0. | 00001) | 188 | 8568 | | | - 4 | Favours Armodafinil Favours Placebo |
| Test for subgroup diffe | erences: | Chi ² = | 0.01.0 | f=1 (P | = 0.93 | $0.1^2 = 0$ | % | | Favours Armodalinii Favours Placebo |

^{*} Czeisler 2009: data from final visit, data extracted from Figure 3A, SEM converted to SD Drake 2014: data pooled across all timepoints excluding baseline Erman 2011 (JOEM): data from final visit, change from baseline data analyzed, SEM converted to SD

Armodafinil Placebo Risk Ratio Risk Ratio Study or Subgroup Events Total Events Total Weight M-H, Fixed, 95% CI M-H, Fixed, 95% CI 4.7.1 Field Study Erman 2011 (JOEM) 121 158 95 167 64.0% 1.35 [1.15, 1.58] Subtotal (99% CI) 158 167 64.0% 1.35 [1.09, 1.66] Total events 121 95 Heterogeneity: Not applicable Test for overall effect: Z = 3.70 (P = 0.0002) 4.7.2 Lab study Czeisler 2009 75 96 36.0% 1.39 [1.13, 1.72] Subtotal (99% CI) 96 36.0% 89 1.39 [1.05, 1.84] Total events 75 50 Heterogeneity: Not applicable Test for overall effect: Z = 3.05 (P = 0.002) Total (99% CI) 254 256 100.0% 1.36 [1.15, 1.61] Total events 196 145 Heterogeneity: $Chi^2 = 0.06$, df = 1 (P = 0.81); $I^2 = 0\%$ 0.2 0.5 Test for overall effect: Z = 4.79 (P < 0.00001) Favours Placebo Favours Armodafinil Test for subgroup differences: Chi² = 0.06, df = 1 (P = 0.81), l² = 0%

Figure S3. Armodafinil vs placebo (Excessive Sleepiness, CGI-C) [CMT = Not Established] RCT (SWD)

Erman 2011 (JOEM): total events was calculated from percent improvement provided by the authors

Table S4. Armodafinil vs placebo (Excessive Sleepiness, CGI-C) [CMT = 1.0 pt or 50% responders] Non-randomized study (SWD)

| Study | Study Design | Associated Disorder(s) | Outcome Tool | Study duration | Total no. of subjects | No. of subjects improved | Dosage | % of subjects with improved sleepiness |
|------------------|----------------------------------|---------------------------|--|-------------------|-----------------------|--------------------------------|-----------------|--|
| Black 2010 | Open-label extension study | Shiftwork Disorder | Excessive Sleepiness or Alertness (CGI-C) | 12 months | 105 | 92 | 250 mg | 88% |
| Schwartz 2010 | Open-label study | Shiftwork Disorder | Excessive Sleepiness or Alertness (CGI-C) | 12 months | 99 | 98 | 100 - 250 mg | 98% |

Figure S4. Armodafinil vs placebo (Accident Risk, standard deviation of lateral position (SDLP)) [CMT = any improvement] RCT (SWD)

| | Armodafinil | | | Placebo | | | Mean Difference | | Mean Difference | | |
|-------------------|-------------|------|-------|---------|------|-------|---------------------|----|--|---|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 95% CI | | |
| 4.11.1 Lab Study | | | | | | | | | | | |
| Drake 2014 | 1.25 | 0.81 | 20 | 1.75 | 0.88 | 20 | -0.50 [-1.02, 0.02] | | - | | |
| | | | | | | | | + | | | |
| | | | | | | | | -2 | -1 U 1 Favours Armodafinil Favours Placebo | 2 | |

^{*}Drake 2014: data received from authors, data averaged across the time points

^{*} Czeisler 2009: data from 12-weeks

Figure S5. Armodafinil vs placebo (Accident Risk, number of off-road deviation) [CMT = any improvement] RCT (SWD)

| | Armodafinil | | il | Placebo | | | Mean Difference | Mean Difference | | | | |
|-------------------|-------------|-------|-------|---------|-------|-------|----------------------|-----------------|-------------|----------|--------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, F | ixed, 9 | 5% CI | |
| 4.12.1 Lab Study | | | | | | | | | | | | |
| Drake 2014 | 4.8 | 13.54 | 20 | 9.99 | 15.74 | 20 | -5.19 [-14.29, 3.91] | | - | | 70 | |
| | | | | | | | | | 10 | | 1 | |
| | | | | | | | | -20 | -10 | Ó | 10 | 20 |
| | | | | | | | | Fav | ours Armoda | finil Fa | avours Place | bo |

^{*}Drake 2014: data received from authors, data averaged across the time points

Figure S6. Armodafinil vs placebo (Accident Risk, sleep diary during the commute home (number of mistakes, near misses, or accidents)) [CMT = any improvement] RCT (SWD)

| | Armod | anil | Placebo | | Risk Ratio | Ris | sk Ratio | | |
|-------------------|---------------|-------|---------------|-------|--------------------|--|---------------------|----|--|
| Study or Subgroup | Events | Total | Events | Total | M-H, Fixed, 95% CI | M-H, Fixed, 95% CI | | | |
| 4.9.1 Lab studies | | | | | | | | | |
| Czeisler 2009 | 20 | 60 | 27 | 50 | 0.62 [0.40, 0.96] | - | - | | |
| | | | | | | 0.02 0.1 | 1 10 | 50 | |
| | | | | | | The grown of the same and the s | nil Favours Placebo | 30 | |

^{*}Czeisler 2009: commute home data used, change from baseline data converted to number of mistakes, near misses, or accidents

Figure S7. Armodafinil vs placebo (Sleep diary of mistakes, near misses, or accidents during the night shift) [CMT = Not Established] RCT (SWD)

| | Armoda | afinil | Placebo | | Risk Ratio | Risk | Ratio |
|-------------------|--------|--------|---------------|-------|--------------------|---------------------|--|
| Study or Subgroup | Events | Total | Events | Total | M-H, Fixed, 95% CI | M-H, Fixe | ed, 95% CI |
| 4.24.1 Lab Study | | | | | | | |
| Czeisler 2009 | 30 | 84 | 37 | 66 | 0.64 [0.45, 0.91] | + | |
| | | | | | | 0.02 0.1 | 10 50 |
| | | | | | | Favours Armodafinil | The second section of the second section is a second section of the second section sec |

^{*}Czeisler 2009: during night shift data used, change from baseline data converted to number of mistakes, near misses, or accidents

Figure S8. Armodafinil vs placebo (Cognitive Performance, DSST number correct) [CMT = Not Established] RCT (SWD)

| | Arm | odafi | nil | PI | acebo | | Mean Difference | | Mean Di | fference | |
|-------------------|-------|-------|-------|-------|-------|-------|-------------------|-----|-----------------|---------------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed | , 95% CI | |
| 4.13.1 Lab Study | | | | | | | | | P | | |
| Drake 2014 | 60.24 | 2.6 | 20 | 56.97 | 2.66 | 20 | 3.27 [1.64, 4.90] | | | - | |
| | | | | | | | | -1 | Ţ. | | |
| | | | | | | | | -10 | -5 (| 5 | 10 |
| | | | | | | | | | Favours Placebo | Favours Armodafinil | |

^{*}Drake 2014: data averaged across 0100-0830 timepoints

Figure S9. Armodafinil vs placebo (Cognitive Performance, RAT) [CMT = Not Established] RCT (SWD)

| | Arm | odafi | nil | Pla | cebo |) | Mean Difference | | Mean Diffe | rence | |
|-------------------|-------|-------|-------|------|------|-------|--------------------|-----|--------------------|--------------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 9 | 5% CI | |
| 4.14.1 Lab Study | | | | | | | | | 0 | | |
| Drake 2014 | 11.25 | 6 | 20 | 8.75 | 4.9 | 20 | 2.50 [-0.90, 5.90] | | - | - | |
| | | | | | | | | _ | | - | 4 |
| | | | | | | | | -10 | -5 0 | 5 | 10 |
| | | | | | | | | | Favours Placebo Fa | avours Armodafinil | 1 |

Figure S10. Armodafinil vs placebo (Cognitive Performance, free recall memory assessments) [CMT = Not Established] RCT (SWD)

| | Arm | odafii | nil | PI | acebo | | Mean Difference | | Mean [| ifference | |
|-------------------|-------|--------|-------|-------|-------|-------|--------------------|-----|-----------------|-----------|------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixe | d, 95% CI | |
| 4.15.1 Lab Study | | | | | | | | | | 20 | |
| Howard 2014 | 12.08 | 2.75 | 12 | 10.33 | 3.68 | 12 | 1.75 [-0.85, 4.35] | | 75 | 1 | |
| | | | | | | | | - | - | | 1 |
| | | | | | | | | -10 | -5 | 0 : | 5 10 |
| | | | | | | | | | Favours Placebo | Favours A | rmodafinil |

Figure S11. Armodafinil vs placebo (Cognitive Performance, Divided attention test -peripheral reaction time) [CMT = Not Established] RCT (SWD)

| | Arm | odafi | nil | Pla | acebo |) | Mean Difference | Mean Difference |
|-------------------|------|-------|-------|------|-------|-------|---------------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 4.16.1 Lab Study | | | | | | | | |
| Howard 2014 | 526 | 86 | 12 | 665 | 193 | 12 | -139.00 [-258.55, -19.45] | |
| | | | | | | | | |
| | | | | | | | | -500 -250 0 250 50 Favours Armodafinil Favours Placebo |

Figure S12. Armodafinil vs placebo (Cognitive Performance, Divided attention test -central reaction time) [CMT = Not Established] RCT (SWD)

| | Arm | odafii | nil | Pla | acebo |) | Mean Difference | | Mean | Difference | е | |
|-------------------|------|--------|-------|------|-------|-------|-------------------------|--------------|-----------------------|----------------|-----------------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fix | ed, 95% C | I | |
| 4.17.1 Lab Study | | | | | | | | | | 10 | | |
| Howard 2014 | 472 | 95 | 12 | 544 | 136 | 12 | -72.00 [-165.86, 21.86] | _ | - | | | |
| | | | | | | | | | - | | - | -1- |
| | | | | | | | | -200 Favo | -100 urs Armodafin | 0 il Favour | 100 s Placeb | 200 |

Figure S13. Armodafinil vs placebo (Cognitive Performance, Power of attention test) [CMT = Not Established] RCT (SWD)

| | Armo | odafinil | | Pla | acebo | | Mean Difference | Mean Difference |
|-------------------|----------|----------|-------|----------|--------|-------|---------------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 4.19.1 Lab Study | | | | | | | | |
| Czeisler 2009 | 1,340.72 | 234.1 | 111 | 1,520.05 | 609.03 | 104 | -179.33 [-304.22, -54.44] | - t |
| | | | | | | | | -500 -250 0 250 500 |
| | | | | | | | | -500 -250 Ó 250 Favours Armodafinil Favours Place |

^{*}Czeisler 2009: data from final visit, data extracted from Figure 3G, SEM converted to SD.

Figure S14. Armodafinil vs placebo (Cognitive Performance, quality of episodic secondary memory) [CMT = Not Established] RCT (SWD)

| | Arm | nodafini | 1 | PI | acebo | | Mean Difference | | Mean Di | fference | |
|-------------------|--------|----------|-------|--------|-------|-------|---------------------|-----|-----------------|---------------|--------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed | I, 95% CI | |
| 4.20.1 Lab Study | | | | | | | | | | | |
| Czeisler 2009 | 156.58 | 54.43 | 110 | 132.34 | 66.93 | 101 | 24.24 [7.69, 40.79] | | | | |
| | | | | | | | | _ | | | |
| | | | | | | | | -50 | -25 (| 25 | 50 |
| | | | | | | | | | Favours Placebo | Favours Armod | afinil |

^{*}Czeisler 2009: data from final visit, data extracted from Figure 3C, SEM converted to SD.

Figure S15. Armodafinil vs placebo (Cognitive Performance, delayed word recall (% correct)) [CMT = Not Established] RCT (SWD)

| | Ап | modafin | il | P | lacebo | | Mean Difference | Mean Difference |
|-------------------|-------|---------|-------|-------|--------|-------|-------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 4.22.1 Lab Study | | | | | | | | 7 |
| Czeisler 2009 | 19.58 | 12.17 | 110 | 15.21 | 12.26 | 101 | 4.37 [1.07, 7.67] | - |
| | | | | | | | | |
| | | | | | | | | -10 -5 0 5 10 Favours Placebo Favours Armodafinil |

^{*}Czeisler 2009: data from final visit, data extracted from Figure 3E, SEM converted to SD.

Figure S16. Armodafinil vs placebo (Cognitive Performance, simple reaction time) [CMT = Not Established] RCT (SWD)

| Arm | nodafini | 1 | P | lacebo | | Mean Difference | M | lean Difference | e | |
|--------|----------|---------|---------------------------|--------------------|-----------------------|-----------------------------|---|--|---|---|
| Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IN | /, Fixed, 95% C | I | |
| | | | | | | | | 9 | | |
| 337.81 | 67.52 | 112 | 391 | 189.89 | 104 | -53.19 [-91.77, -14.61] | - | 100 | | |
| | | | | | | | | | 1 | |
| | | | | | | | -100 -50 | Ó definil Course | 50 | 100 |
| | Mean | Mean SD | 40°44' (000) 000 4000 000 | Mean SD Total Mean | Mean SD Total Mean SD | Mean SD Total Mean SD Total | Mean SD Total Mean SD Total IV, Fixed, 95% CI | Mean SD Total IV, Fixed, 95% CI IV 337.81 67.52 112 391 189.89 104 -53.19 [-91.77, -14.61] -50 -50 | Mean SD Total IV, Fixed, 95% CI IV, Fixed, 95% CI 337.81 67.52 112 391 189.89 104 -53.19 [-91.77, -14.61] -50 0 | Mean SD Total Mean SD Total IV, Fixed, 95% CI IV, Fixed, 95% CI 337.81 67.52 112 391 189.89 104 -53.19 [-91.77, -14.61] — — |

^{*}Czeisler 2009: data from final visit, data extracted from Figure 3I, SEM converted to SD.

Important Outcomes

Figure S17. Armodafinil vs placebo (Total Sleep Time, PSG) [CMT =15 min] RCT (SWD)

| | Arm | odafii | nil | Pla | acebo | | Mean Difference | | Mean | Difference | | |
|-------------------|-------|--------|-------|-------|-------|-------|-----------------------|-----|----------------|-------------|-------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fix | ced, 95% CI | | |
| 4.37.1 Lab Study | | | | | | | | | | 33 | | |
| Czeisler 2009 | 321.6 | 99.3 | 102 | 338.2 | 74.9 | 91 | -16.60 [-41.26, 8.06] | | - | 10 | | |
| | | | | | | | | + | 1 | | | - |
| | | | | | | | | -50 | -25 | Ò | 25 | 50 |
| | | | | | | | | | Favours Placel | oo Favours | Armodafinil | |

^{*}Czeisler 2009: Daytime sleep measured.

Figure S18. Armodafinil vs placebo (Mental health, Global Assessment of Functioning (GAF)) [CMT = Not Established] RCT (SWD)

| | Arn | nodafir | nil | Pla | acebo | | Mean Difference | | Mean D | ifference | | |
|--------------------|------|---------|-------|------|-------|-------|-------------------|-----|------------------------|----------------|-------------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixe | d, 95% CI | | |
| 4.29.1 Field Study | | | | | | | | | | | | |
| Erman 2011 (JOEM) | 72.6 | 8.75 | 177 | 67.9 | 7.65 | 182 | 4.70 [3.00, 6.40] | | | - | | |
| | | | | | | | | | | | 4 | _ |
| | | | | | | | | -20 | -10 Favours Placebo | Ó Favours A | 10 Armodafinil | 20 |

^{*}Erman 2012: SEM converted to SD.

Figure S19. Armodafinil vs placebo (Quality of Life, modified Sheehan Disability Scale) [CMT = Not Established] RCT (SWD)

| | Arm | odafii | nil | PI | acebo | | Mean Difference | | Mean | Difference | | |
|---|------|--------|-------|------|-------|-------|----------------------|-----|-----------------|------------|---------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixe | ed, 95% CI | | |
| 4.27.1 Field Study | | | | | | | | | • | 9.0 | | |
| Erman 2012 (Prim Care Companion CNS Disord) | 10.8 | 7.05 | 193 | 14.3 | 7.08 | 190 | -3.50 [-4.92, -2.08] | | - | | | |
| | | | | | | | | -10 | -5 | ļ | + | 10 |
| | | | | | | | | Fa | vours Armodafin | il Favours | Placebo | 10 |

^{*}Erman 2012: SEM converted to SD.

Figure S20. Armodafinil vs placebo (Quality of Life, FOSQ-10) [CMT = Not Established] RCT (SWD)

| 1 791500 | 4000000 | 581 | 100000 | IV, Fixed, 95% CI | | IV, | Fixed, 95% | CI | |
|----------|---------|-----|--------|--------------------|----|-----|----------------------|---------------------------------|--|
| 193 | 2.7 | 4 | 190 | 0.70 (-0.12 1.52) | | | | | |
| 193 | 2.7 | 4 | 190 | 0.70 (-0.12, 1.52) | | | 1 | | |
| | | | | 0.10[0.12, 1.02] | | | | | |
| | | | | | -4 | -2 | <u> </u> | 1 | |
| | | | | | | -4 | -4 -2 Favours Pla | -4 -2 0 Favours Placebo Favo | -4 -2 0 2 Favours Placebo Favours Armoo |

^{*}Erman 2012: SEM converted to SD.

Figure S21. Armodafinil vs placebo (WASO, PSG) [CMT = 20 min] RCT (SWD)

| | Arm | nodafir | nil | PI | acebo | | Mean Difference | | M | Mean Difference | | |
|-------------------|------|---------|-------|-------|-------|-------|----------------------|-----|-------------|-----------------|---------------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IN | , Fixed, | 95% CI | |
| 4.31.1 Lab Study | | | | | | | | | | 1 | | |
| Czeisler 2009 | 143 | 92.4 | 102 | 129.5 | 71.7 | 91 | 13.50 [-9.71, 36.71] | | | 8 1 | + | 722 |
| | | | | | | | | | | | | - 1 |
| | | | | | | | | -50 | -25 | Ó | 25 | 50 |
| | | | | | | | | F | avours Armo | dafinil | Favours Place | bo |

^{*}Czeisler 2009: Daytime sleep measured.

Figure S22. Armodafinil vs placebo (Sleep Latency, PSG) [CMT = 20 min] RCT (SWD)

| | Arm | odafii | nil | PI | acebo | | Mean Difference | N | lean Difference |
|-------------------|------|--------|-------|------|-------|-------|--------------------|---|--------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV. | V, Fixed, 95% CI |
| 4.32.1 Lab Study | | | | | | | | | 21 |
| Czeisler 2009 | 13.7 | 14.4 | 102 | 10.6 | 10.5 | 91 | 3.10 [-0.43, 6.63] | | + |
| | | | | | | | | 1 1 1 - 5 | 1 |
| | | | | | | | | -10 -5 Favours Armo | 0 5 dafinil Favours Placebo |

^{*}Czeisler 2009: Daytime sleep measured.

Figure S23. Armodafinil vs placebo (Sleep Efficiency, PSG) [CMT = 10%] RCT (SWD)

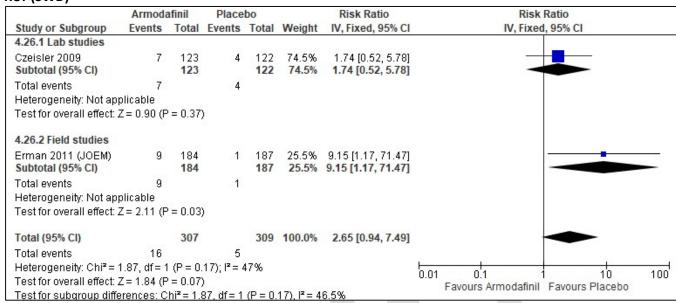
| | Arm | odafii | nil | PI | acebo | | Mean Difference | | Mean Differ | rence | |
|-------------------|------|--------|-------|------|-------|-------|---------------------|-----|--------------------|--------------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 95 | 5% CI | |
| 4.33.1 Lab Study | | | | | | | | | | | |
| Czeisler 2009 | 67.8 | 20.3 | 102 | 71.2 | 15.5 | 91 | -3.40 [-8.47, 1.67] | | | | |
| | | | | | | | | | | T. | |
| | | | | | | | | -20 | -10 Ó | 10 | 20 |
| | | | | | | | | | Favours Placebo Fa | avours Armodafinil | |

^{*}Czeisler 2009: Daytime sleep measured.

Figure S24. Armodafinil vs placebo (Serious Adverse Events) [CMT = Not Established] RCTs (SWD)

| | Armoda | afinil | Place | bo | | Risk Ratio | Risk Ratio |
|------------------------------------|--------------|-------------------|-----------------|------------|----------------|--|--------------------------------------|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Fixed, 95% CI | M-H, Fixed, 95% CI |
| 4.25.1 Lab studies | | | | | | | |
| Czeisler 2009 Subtotal (95% CI) | 1 | 123 123 | 1 | 122 122 | 40.3% 40.3% | 0.99 [0.06, 15.68] 0.99 [0.06, 15.68] | |
| Total events | 1 | | 1 | | | | |
| Heterogeneity: Not app | plicable | | | | | | |
| Test for overall effect: 2 | | = 1.00 |) | | | | |
| 4.25.2 Field studies | | | | | | | |
| Erman 2011 (JOEM) | 0 | 184 | 1 | 187 | 59.7% | 0.34 [0.01, 8.26] | |
| Subtotal (95% CI) | | 184 | | 187 | 59.7% | 0.34 [0.01, 8.26] | |
| Total events | 0 | | 1 | | | | |
| Heterogeneity: Not app | plicable | | | | | | |
| Test for overall effect: 2 | Z= 0.66 (P | = 0.51 |) | | | | |
| Total (95% CI) | | 307 | | 309 | 100.0% | 0.60 [0.08, 4.54] | |
| Total events | 1 | | 2 | | | | |
| Heterogeneity: Chi² = (| 0.25, df = 1 | (P = 0. | .62); $I^2 = I$ | 0% | | | 0.01 0.1 1 10 10 |
| Test for overall effect: 2 | Z = 0.49 (P | = 0.62 |) | | | | Favours Armodafinil Favours placebo |
| Test for subgroup diffe | erences: C | $hi^2 = 0.1$ | 25, df = 1 | (P = 0. | 62), $I^2 = 0$ | 1% | 1 avours Armodallill Pavours placebo |

Figure S25. Armodafinil vs placebo (Adverse Events leading to withdrawal) [CMT = Not Established] RCT (SWD)



Modafinil

Summary of Findings (GRADE)

Table S5. Modafinil in adults with shiftwork disorder

References: Czeisler 2005, Dagan 2006, Walsh 2004, Gill 2006, Brun 1998 **Outcomes** Certainty of the **Absolute Difference** No of Participants [Tool] evidence (studies) (GRADE) **Modafinil vs Control** The mean difference in the modafinil group was **Excessive sleepiness or** 182 $\Theta\ThetaOO$ alertness 1.4 minutes higher (0.42 higher to 2.38 higher) compared to (1 RCT) LOW^{b,c} [MSLT]a control Excessive sleepiness or $\Theta\ThetaOO$ The mean difference in the modafinil group was 183 alertness 1.1 points lower (1.69 lower to 0.51 lower) compared to (1 RCT) LOWb,c [KSS]d The risk ratio in the modafinil group was 2.08 (1.57 to 2.78) **Excessive sleepiness or** 193 $\Theta\Theta\Theta()$ alertness with an absolute risk of 387 more per 1,000 (204 more to MODERATE^b (1 RCT) [CGI-C]a,e 637 more) compared to control The mean difference in the modafinil group was Excessive sleepiness or $\Theta\ThetaOO$ 48 alertness LOW^{b,f} 0.7 points lower (0.86 lower to 0.54 lower) compared to (1 RCT) [SSS]d control **Excessive sleepiness or** $\Theta \bigcirc \bigcirc \bigcirc$ The mean difference in the modafinil group was 32 alertness VERY LOWb,f,g 5.2 minutes higher (0.67 lower to 11.07 higher) compared (1 RCT) [MWT]a **Excessive sleepiness or** $\Theta \Phi \Phi \Theta$ The mean difference in the modafinil group was 50 alertness 23.64 mm lower (40.4 lower to 6.88 lower) compared to (1 RCT) **MODERATE**^b control [VAS: Difficulty attending lecture]d

| Accident risk [Electronic diary] ^d | ⊕⊕⊕⊕ HIGH | , and the same of | 204 (1 RCT) |
|--|------------------------------|---|----------------|
| Accident risk [VAS: Difficulty driving home]d | ⊕⊕⊖⊖ LOW ^{b,g} | The mean difference in the modafinil group was 10.29 mm lower (25.52 lower to 4.94 higher) compared to control | 50 (1 RCT) |
| Cognitive performance [PVT lapses] ^d | ⊕⊕⊜⊝ LOW ^{b,c} | The mean difference in the modafinil group was 6.38 lapses fewer (11.65 fewer to 1.11 fewer) compared to control | 135 (1 RCT) |
| Cognitive performance [PVT lapses]d | ⊕⊕⊜⊝ LOW ^{b,f} | The mean difference in the modafinil group was 12.12 lapses fewer (22.44 fewer to 1.80 fewer) compared to control | 32 (1 RCT) |
| Cognitive performances [multiple tests] | ⊕⊕⊖⊖ LOW ^{b,f,g} | Modafinil improves cognitive performance in the following outcome tools: Number of correct substitutions during coding task, grammatical reasoning test response time, deviation from altitude flight, and deviation from the velocity flight envelope. Studies included: Gill 2006 (n=50), Brun 1998 (n=16), and Dagan 2006 (n=48) | (3 RCTs) |

- a. Higher values favor the intervention
- b. Imprecision due to small sample size (<200 participants)
- c. Imprecision due to 95% CI crossing the CMT
- d. Lower values favor the intervention
- e. CMT was not established by the TF
- f. Indirectness is due to the fact that participants included in the studies are healthy individuals. The effect in adults with SWD may be different.
- g. Imprecision due to 95% CI crossing the null

Study Characteristics

Table S6. Modafinil in adults with shiftwork disorder

| Study Citation | Study Design | Number of Participants (% Female) | Age (range) | Population | Intervention (dose/intensity) | Comparator | Time of Intervention Delivery | Duration of Follow- up |
|-------------------|-------------------|---|-------------|---|----------------------------------|------------|-------------------------------------|------------------------------|
| Brun 1998 | RCT, crossover | 8 (0) | 27–54 | Healthy participants | Modafinil (300 mg) | Placebo | 22:00 and 08:00 | 2 nights |
| Czeisler 2005 | RCT | 204 (39) | 18-60 | SWD | Modafinil (200 mg) | Placebo | 30-60 min before night shift | 3 months |
| Dagan 2006 | RCT, crossover | 24 (0) | 25 –31 | Healthy participants | Modafinil (200 mg) | Placebo | 23:00 | 1 night |
| Gill 2006 | RCT, crossover | 25 (20) | 27–54 | Shift workers without SWD diagnosis | Modafinil (200 mg) | Placebo | between 6:30 AM and 7:30 AM | 1 day |
| Walsh 2004 | RCT | 32 (47) | 18-55 | Healthy participants | Modafinil (200 mg) | Placebo | 22:00 | 4 nights |

Critical Outcomes

Figure S26. Modafinil vs Placebo (Excessive Sleepiness, MSLT) [CMT= 1min] RCT (SWD)

| | Mo | dafini | I | Pla | acebo | | Mean Difference | | Mea | n Differenc | e | |
|-------------------|------|--------|-------|------|-------|-------|-------------------|--------------|---------------------|---------------|------------|------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, F | ixed, 95% C | 1 | |
| 4.3.1 Lab Study | | | | | | | | | | 100 | | |
| Czeisler 2005 | 1.7 | 3.71 | 86 | 0.3 | 2.94 | 96 | 1.40 [0.42, 2.38] | | | 100 | + | |
| | | | | | | | | _ | | | 1 | |
| | | | | | | | | -4 | -2 Favours Place | U bo Favou | rs Modafin | il 4 |

^{*}Czeisler 2005:. SEM converted to SD, change from baseline data used

Figure S27. Modafinil vs Placebo (Excessive Sleepiness, KSS) [CMT= 1pt] RCT (SWD)

| | Mo | dafini | I | PI | acebo | | Mean Difference | Mean Difference |
|-----------------------|----------|--------|-------|------|-------|-------|----------------------|-----------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 4.4.1 Shiftwork disor | der, Lai | study | 1 | | | | | |
| Czeisler 2005 | -1.5 | 1.96 | 86 | -0.4 | 2.08 | 97 | -1.10 [-1.69, -0.51] | |
| | | | | | | | | |
| | | | | | | | | -4 -2 0 2 4 |
| | | | | | | | | Favours Modafinil Favours Placebo |

^{*}Czeisler 2005: change score from baseline to final used. SEM converted to SD

Figure S28. Modafinil vs Placebo (Excessive Sleepiness, CGI-C) [CMT = Not Established] RCT (SWD)

| Fuente | | | | | Risk Ratio | | | | |
|--------|-------|--------|----------|--------------------|--------------------------------|---|--|--|--|
| Events | Total | Events | Total | M-H, Fixed, 95% CI | M-H, Fixe | ed, 95% CI | | | |
| | | | | | | | | | |
| 66 | 89 | 37 | 104 | 2.08 [1.57, 2.78] | | - | | | |
| | | | | - | 02 05 | 1 1 | | | |
| _ | 66 | 66 89 | 66 89 37 | 66 89 37 104 | 66 89 37 104 2.08 [1.57, 2.78] | 66 89 37 104 2.08 [1.57, 2.78] 0.2 0.5 Favours Placebo | | | |

^{*}Czeisler 2005: Treated as a dichotomous result, participants counted as improved if they were at least minimally improved on the CGI-C test at the final visit (data in supplementary appendix table 2)

Figure S29. Modafinil vs Placebo (Excessive Sleepiness, SSS) [CMT= 1pt] RCT (Healthy participants)

| | Mo | odafini | I | PI | acebo | | Mean Difference | Mean Differer | ice |
|-------------------|------|---------|-------|------|-------|-------|----------------------|------------------------|-------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% | CI |
| 5.1.1 Lab Study | | | | | | | | | |
| Dagan 2006 | 2.65 | 0.24 | 24 | 3.35 | 0.33 | 24 | -0.70 [-0.86, -0.54] | + | |
| | | | | | | | | | |
| | | | | | | | | -4 -2 0 | 2 4 |
| | | | | | | | | Favours Modafinil Favo | urs Placebo |

^{*}Dagan 2006:data extracted from the Figure 2C

Figure S30. Modafinil vs Placebo (Excessive Sleepiness, MWT) [CMT= 2 min] RCT (Healthy participants)

| | Mo | dafin | il | PI | acebo | | Mean Difference | | Difference | | |
|-------------------|------|-------|-------|------|-------|-------|---------------------|-----|-----------------|--------------|--------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixe | ed, 95% CI | |
| 5.3.1 Lab Study | | | | | | | | | | 33 | |
| Walsh 2004 | 25.1 | 5.4 | 16 | 19.9 | 10.7 | 16 | 5.20 [-0.67, 11.07] | | | +- | |
| | | | | | | | | | | 1 | |
| | | | | | | | | -20 | -10 | 0 10 | 20 |
| | | | | | | | | | Favours Placebo | Favours Moda | afinil |

*Walsh 2004: nightshift 4 data

Figure S31. Modafinil vs Placebo (Excessive Sleepiness, VAS: difficulty attending lecture after taking pill) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)

| | Mc | dafini | 1 | D | lacebo | 1 | Mean Difference | Mean Difference |
|--------------------|-------|--------|----|-------|--------|-------|------------------------|-----------------------------------|
| Study or Subgroup | Mean | | | Mean | | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 5.10.1 Field Study | | | | | | | | |
| Gill 2006 | 35.78 | 34.2 | 25 | 59.42 | 25.65 | 25 | -23.64 [-40.40, -6.88] | |
| | | | | | | | | |
| | | | | | | | | -50 -25 0 25 50 |
| | | | | | | | | Favours Modafinil Favours Placebo |

^{*}Gill 2006: VAS scale, lower is better. Data was extracted from Figure 2A; SEM converted to SD

Figure S32. Modafinil vs Placebo (Accident Risk, E-diary- patients reporting accidents or near accidents) [CMT= any decrease] RCT (SWD)

| | Modaf | inil | Place | bo | Risk Ratio | Risk Ratio |
|--------------------|--------|-------|--------|-------|--------------------|-----------------------------------|
| Study or Subgroup | Events | Total | Events | Total | M-H, Fixed, 95% CI | M-H, Fixed, 95% CI |
| 4.10.1 Lab studies | | | | | | |
| Czeisler 2005 | 28 | 96 | 58 | 108 | 0.54 [0.38, 0.78] | |
| | | | | | | |
| | | | | | | 0.2 0.5 1 2 5 |
| | | | | | | Favours Modafinil Favours Placebo |

^{*}Czeisler 2005: Patients reporting accidents or near accidents during the commute home

Figure S33. Modafinil vs Placebo (Accident Risk, VAS: difficulty driving home) [CMT= any improvement] RCT (Shift workers without SWD diagnosis)

| | M | odafinil | | PI | acebo | | Mean Difference | | Mean Di | fference | |
|--------------------|------|----------|-------|-------|-------|-------|-----------------------|-----|-------------------|----------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed | , 95% CI | |
| 5.29.1 Field Study | | | | | | | | | | 88 | |
| Gill 2006 | 21.7 | 24.55 | 25 | 31.99 | 30.1 | 25 | -10.29 [-25.52, 4.94] | | - | | |
| | | | | | | | | 17 | 69 | į. | 11 |
| | | | | | | | | -50 | -25 (| 25 | 50 |
| | | | | | | | | | Favours Modafinil | Favours Placeb | 0 |

^{*}Gill 2006: VAS scale, lower is better. Data was extracted from Figure 2C; SEM converted to SD

Figure S34. Modafinil vs Placebo (Cognitive Performance, PVT lapses) [CMT= 1 lapse] RCT (SWD)

| | Modafinil | | | | | | Mean Difference | | | | | |
|-----------------------|-----------|----------|-------|------|-------|-------|-----------------------|-----------|--------------------|---------------|------------------|-------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, | | | |
| 5.20.1 Shiftwork Disc | order, La | ab Study | / | | | | | | | 16 | | |
| Czeisler 2005 | -2.63 | 15.44 | 66 | 3.75 | 15.78 | 69 | -6.38 [-11.65, -1.11] | | + | 100 | | |
| | | | | | | | - | 1- | | \perp | - 1- | |
| | | | | | | | | -20 Fa | -10 avours Moda | u afinil F | 10 avours Pla | 20 acebo |

^{*}Czeisler 2005: Change from baseline data. SD calculated from p value $\,$

Figure S35. Modafinil vs Placebo (Cognitive Performance, PVT lapses) [CMT= 1 lapse] RCT (Healthy participants)

| | Mo | odafini | I | Placebo | | | Mean Difference | Mean Difference |
|-----------------------|-------|---------|-------|---------|------|-------|------------------------|-----------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 5.21.2 Healthy, Lab 9 | Study | | | | | | | |
| Walsh 2004 | 6.63 | 9.86 | 16 | 18.75 | 18.6 | 16 | -12.12 [-22.44, -1.80] | |
| | | | | | | | | |
| | | | | | | | | -50 -25 0 25 5 |
| | | | | | | | | Favours Modafinil Favours Placebo |

^{*}Walsh 2004: data from nightshift 4, data extracted from Figure 3, SEM converted to SD

Figure S36. Modafinil vs Placebo (Cognitive Performance, number of correct substitutions during coding task) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)

| | | | | | - | | | - 6 7 |
|--------------------|-------|--------|-------|---------|------|-------|--------------------|-----------------------------------|
| | Mo | dafini | I | Placebo | | | Mean Difference | Mean Difference |
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 5.28.1 Field Study | | | | | | | | * |
| Gill 2006 | 42.62 | 10.5 | 25 | 41.78 | 12.6 | 25 | 0.84 [-5.59, 7.27] | · · |
| | | | | | | | | |
| | | | | | | | | -20 -10 0 10 20 |
| | | | | | | | | Favours Placebo Favours Modafinil |

^{*}Gill 2006: Data was extracted from Figure 3; SEM converted to SD.

Figure S37. Modafinil vs Placebo (Cognitive Performance, grammatical reasoning test response time (%of scores of baseline conditions)) [CMT = Not Established] RCT (Healthy participants)

| | Modafinil | | | | | | Mean Difference | Mean Difference | | | | | | | | | |
|-------------------|---|------|---|-------|------|----------------------|------------------------|--|--|----|-------|-------------------|-------------------|--|--|--|--|
| Study or Subgroup | , | | | | | bgroup Mean SD Total | | | | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | | | | |
| Brun 1998 | 98.65 | 10.6 | 8 | 112.4 | 16.1 | 8 | -13.75 [-27.11, -0.39] | -20 -10 0 10 20 Favours Modafinil Favours Placebo | | | | | | | | | |

^{*}Brun 1998: data averaged across the night for both the first 3 minutes and the next 3 minutes of each testing session, data extracted from Figure 2, SEM converted to SD

Figure S38. Modafinil vs Placebo (Cognitive Performance, deviation from altitude flight) [CMT = Not Established] RCT (Healthy participants)

| | Mo | dafini | I | PI | acebo | | Mean Difference | | Mean Di | fference | |
|-------------------|-------|--------|-------|-------|-------|-------|-------------------------|------|--|-------------------------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed | i, 95% CI | |
| Dagan 2006 | 559.2 | 43.5 | 24 | 623.7 | 53.5 | 24 | -64.50 [-92.09, -36.91] | | - | | |
| | | | | | | | | -100 | The second secon | 0 50 Favours Placebo | 100 |

^{*}Dagan 2006: data extracted from the figure 2b

Figure S39. Modafinil vs Placebo (Cognitive Performance, deviation from the velocity flight envelope (5am+7am)) [CMT = Not Established] RCT (Healthy participants)

| | M | odafinil | | P | lacebo | | Mean Difference | Mean D | ifference | |
|-------------------|-------|----------|-------|-------|--------|-------|-----------------------|----------|-------------------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixe | d, 95% CI | |
| Dagan 2006 | 32.22 | 2.645 | 24 | 42.05 | 4.185 | 24 | -9.83 [-11.81, -7.85] | + | | |
| | | | | | | | | -20 -10 | 0 10 Favours Placebo | 20 |

Important Outcomes

Figure S40. Modafinil vs Placebo (Total Sleep Time, PSG) [CMT= 15 min] RCT (SWD)

| | Mo | dafini | I | Pla | acebo | | Mean Difference | | N | lean Differ | ence | |
|-----------------------|-----------|--------|-------|------|-------|-------|-----------------------|-----|-------------------|---------------|-----------------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Random, 95% CI | | IV, | Random, 9 | 95% CI | |
| 5.32.1 Shiftwork Disc | order, La | ab Stu | dy | | | | | | | 187 | | |
| Czeisler 2005 | 1.4 | 88.8 | 72 | 4.6 | 81.2 | 78 | -3.20 [-30.50, 24.10] | | 82 | - 1 | F0 | |
| | | | | | | | | | | 20 5 | | |
| | | | | | | | | -50 | -25 Favours Pl | 0 acebo Fa | 25 vours Modafinil | 50 |

^{*}Czeisler 2005: change from baseline data

Figure S41. Modafinil vs Placebo (Total Sleep Time, PSG) [CMT= 15 min] RCT (Healthy participants)

| | Mo | dafini | I | PI | acebo | | Mean Difference | Mean Difference |
|---------------------|---------|--------|-------|-------|-------|-------|-----------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 5.33.2 Healthy, Lab | Studies | | | | | | | |
| Walsh 2004 | 339.8 | 69.2 | 16 | 306.9 | 71.8 | 16 | 32.90 [-15.96, 81.76] | i] |
| | | | | | | | | 1 1 1 |
| | | | | | | | | -200 -100 0 100 2 Favours Placebo Favours Modafinil |

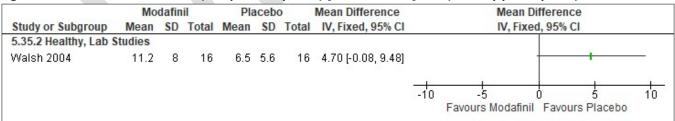
^{*}Walsh 2004: day sleep on day 4, after 8-hour night shift

Figure S42. Modafinil vs Placebo (Sleep Latency, PSG) [CMT= 20 min] RCT (SWD)

| | Mo | dafini | I | PI | acebo | | Mean Difference | | Mean Difference | | | | | | |
|-----------------------|-----------|--------|-------|------|-------|-------|--------------------|-----|-----------------|-------------------|-------------|------|--|--|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, F | IV, Fixed, 95% CI | | | | | |
| 5.34.1 Shiftwork Disc | order, La | ab Stu | dy | | | | | | | 120 | | | | | |
| Czeisler 2005 | 2.9 | 17.9 | 72 | 1.3 | 12.4 | 78 | 1.60 [-3.37, 6.57] | | 10 | 185 | + | 30 | | | |
| | | | | | | | | - | - 1 | 70 0 | - 1 | | | | |
| | | | | | | | | -10 | -5 | 0 | 5 | 10 | | | |
| | | | | | | | | | Favours Modat | finil F | avours Plac | cebo | | | |

^{*}Czeisler 2005: change from baseline data

Figure S43. Modafinil vs Placebo (Sleep Latency, PSG) [CMT= 20 min] RCT (Healthy participants)



^{*}Walsh 2004: data from day sleep on day 4

^{*}Dagan 2006: data extracted from the figures 2e and 2g, data for 5 am and 7 am pooled

Figure S44. Modafinil vs Placebo (Sleep Efficiency, PSG) [CMT= 10%] RCT (SWD)

| Mo | odafini | il | Pla | cebo |) | Mean Difference | Mean Difference |
|------|---------|---------|---------------------|--------------------|-----------------------|-----------------------------|---|
| Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| | | | | | | | 1 |
| 1.4 | 16.7 | 72 | 1.2 | 17 | 78 | 0.20 [-5.20, 5.60] | A |
| | | | | | | | 1. 1. 1. 1. |
| | | | | | | | -20 -10 0 10 20 Favours Placebo Favours Modafinil |
| | Mean | Mean SD | 90/24/19 (NYS) #350 | Mean SD Total Mean | Mean SD Total Mean SD | Mean SD Total Mean SD Total | |

Figure S45. Modafinil vs Placebo (Sleep Efficiency, PSG) [CMT= 10%] RCT (Healthy)

| ean SD ies | Total | Mean | SD | Total | IV. Fixed, 95% CI | | IV/ Fin | | VEN. 01 | |
|---------------|----------|-------------|------------------|-----------------------|--------------------------|--|---------|--------------|-----------|--|
| ies | | | | Total | IV, FIXEU, 95% CI | | IV, FIX | xea, s | 95% CI | |
| | | | | | | | | | | |
| 33.7 12.4 | 16 | 79.2 | 14.9 | 16 | 4.50 [-5.00, 14.00] | | 200 | + | + | |
| | | | | | 85 | 1 | | \downarrow | | |
| 3 | 3.7 12.4 | 3.7 12.4 16 | 3.7 12.4 16 79.2 | 3.7 12.4 16 79.2 14.9 | 3.7 12.4 16 79.2 14.9 16 | 3.7 12.4 16 79.2 14.9 16 4.50 [-5.00, 14.00] | -20 | -20 -10 | -20 -10 0 | |

^{*}Walsh 2004: data from day sleep on day 4

Figure S46. Modafinil vs Placebo (Sleep Efficiency, sleep diary) [CMT= 10%] RCT (SWD)

| | Mo | dafini | I | Pla | acebo | | Mean Difference | Mean Difference |
|-------------------|------|--------|-------|------|-------|-------|---------------------|-----------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 4.36.1 Lab Study | | | | | | | | |
| Czeisler 2005 | 7.3 | 18.5 | 78 | 9.5 | 18.3 | 84 | -2.20 [-7.87, 3.47] | |
| | | | | | | | | |
| | | | | | | | | -10 -5 0 5 10 |
| | | | | | | | | Favours Placebo Favours Modafinil |

Acute bright light

Summary of Findings (GRADE)

Table S7. Acute bright light in adults with shiftwork disorder

References: Bjorvatn 1999, Kakooei 2010, Lowden 2004, Lowden 2012, Griepentrog 2018, Yoon 2002, Babkoff 2002, Costa 1995, Costa 1993, Badia 1991, Campbell 1990, Campbell 1995, Dawson 1991, Wright 1997, Ruger 2006, Weisgerber 2017, Leproult 1997, Figueiro 2016, Daurat 2000 (bio signals), Foret 1998, Huang 2013, Lammers-vanderHoist 2021, Dawson 1995, Leppamaki 2003, Horowitz 2001

| Outcomes [Tool] | Certainty of the evidence (GRADE) | Absolute Difference Acute bright light vs Control | No of Participants (studies) |
|--|---|---|---------------------------------|
| Excessive sleepiness or alertness [KSS] ^a | rom _{p'c} ⊕⊕⊜⊝ | The mean difference in the acute bright light group was 0.02 points more (0.40 fewer to 0.43 more) compared to control | 104 (2 RCTs) |
| Excessive sleepiness or alertness [KSS] ^a | ⊕○○○ VERY LOW ^{b,c,d} | The mean difference in the acute bright light group was 0.22 points fewer (0.48 fewer to 0.04 more) compared to control | 37 (2 non-RCTs) |
| Excessive sleepiness or alertness [KSS] ^a | ⊕○○○ VERY LOW ^{b,c,d,e} | The mean difference in the acute bright light group was 0.73 points fewer (1.43 fewer to 0.02 fewer) compared to control | 62 (2 RCTs) |

| Excessive sleepiness or | \oplus | The mean difference in the acute bright light group was 0.42 | |
|---|--|--|---------------------------------|
| alertness | VERY LOW ^{b,c,e} | points fewer (0.92 fewer to 0.08 more) compared to control | (1 RCT) |
| [SSS]ª | | | |
| Excessive sleepiness or | \oplus | The mean difference in the acute bright light group was 0.04 | |
| alertness | VERY LOWb,c,d | points fewer (0.53 fewer to 0.45 more) compared to control | (2 RCTs) |
| [SSS] ^a | | | |
| Excessive sleepiness or | $\Theta\ThetaOO$ | The mean difference in the acute bright light group was | 36 |
| alertness | LOW ^{b,c} | | (1 RCT) |
| [VAS (alertness)] ^{f,g} | | control | |
| Excessive sleepiness or | ФООО | The mean difference in the acute bright light group was | 27 |
| alertness | VERY LOW ^{b,c,d,h} | | (1 RCT) |
| [VAS (alertness)] ^{f,g} | VERT LOW **** | control | (1101) |
| Excessive sleepiness or | $\Phi \cap \cap \cap$ | | 22 |
| alertness | ⊕○○○ VERY LOW ^{b,c,e} | | (1 RCT) |
| [VAS (ratings of arousal)] ^{f,g} | VERY LOW ",c,c | 7.7 lower (21.04 lower to 0.24 mgner) compared to control | (I NCI) |
| | • | TI 1:00 | 24 |
| Excessive sleepiness or | ФООО | | 24 (4. DCT) |
| alertness | VERY LOW ^{b,c,d,h} | 1.00 lower (0.38 lower to 2.38 higher) compared to control | (1 RCT) |
| [VAS (Fatigue] ^{f,g} | 0.00 | | |
| Excessive sleepiness or | \oplus | | 30 |
| alertness | VERY LOW ^{b,c,e} | 0.9 more (3.14 fewer to 4.94 more) compared to control | (1 RCT) |
| [Fatigue rating scale] ^{a,f} | | | |
| Excessive sleepiness or | Θ | | 30 |
| alertness | VERY LOW ^{b,c,h} | | (1 RCT) |
| [Seven point scale] ^{a,f} | | on night one and 0.4 lower (1.63 lower to 0.83 higher) on | |
| | | night two. | |
| Excessive sleepiness or | Θ | The mean difference in the acute bright light group was | 39 |
| alertness | VERY LOWb,c,d | 2.58 minutes more (0.35 more to 4.81 more) compared to | (2 RCTs) |
| [MWT] ^g | | control | |
| Excessive sleepiness or | $\Theta\ThetaOO$ | The mean difference in the acute bright light group was 5.09 | 76 |
| alertness | LOW ^{c,d} | minutes more (2.70 more to 7.47 more) compared to | (2 RCTs) |
| [RTSW] ^g | | control | |
| Excessive sleepiness or | ФООО | Alertness was measured by EEG and reported Alpha, Beta, | |
| alertness | VERY LOW ^{c,d,e} | | (1 RCT) |
| [EEG] ^f | | bright light. | . , |
| Excessive sleepiness or | ФООО | | 16 |
| alertness | VERY LOW ^{b,c,d} | | (2 RCTs) |
| [GADS] ^{f,g} | VERT LOW | die | (=) |
| Accident risk | ФООО | The mean difference in the acute bright light group was | 38 |
| [Variability of Lane Position] ^a | VERY LOW ^{b,c,d,e} | | (1 RCT) |
| | | | <u> </u> |
| Accident risk | ⊕000 | | 38 |
| [Total number of accidents/ | VERY LOW ^{b,c,d,e} | 8.98 lower (22.39 lower to 4.43 higher) compared to control | (1 RCT) |
| incidents] ^a | | | |
| · | | | |
| Accident risk | ФООО | | 38 |
| | ⊕○○○ VERY LOW ^{b,c,d,e} | 4.09 movements fewer (9.14 fewer to 0.96 more) compared | |
| Accident risk | VERY LOW ^{b,c,d,e} | | |
| Accident risk [Steering Wheel Movements]a Sleep quality | | 4.09 movements fewer (9.14 fewer to 0.96 more) compared to control The mean difference in the acute bright light group was | |
| Accident risk [Steering Wheel Movements] ^a | VERY LOW ^{b,c,d,e} | 4.09 movements fewer (9.14 fewer to 0.96 more) compared to control The mean difference in the acute bright light group was | (1 RCT) |
| Accident risk [Steering Wheel Movements] ^a Sleep quality [Sleep quality index] ^{f,g} | VERY LOW ^{b,c,d,e} UCRY LOW ^{b,c,e} | 4.09 movements fewer (9.14 fewer to 0.96 more) compared to control The mean difference in the acute bright light group was 0 (0.28 lower to 0.28 higher)) compared to control | (1 RCT) 36 (1 RCT) |
| Accident risk [Steering Wheel Movements]a Sleep quality | VERY LOW ^{b,c,d,e} OOO VERY LOW ^{b,c,e} | 4.09 movements fewer (9.14 fewer to 0.96 more) compared to control The mean difference in the acute bright light group was 0 (0.28 lower to 0.28 higher)) compared to control The mean difference in the acute bright light group was 2.50 | (1 RCT) 36 (1 RCT) 17 |
| Accident risk [Steering Wheel Movements]a Sleep quality [Sleep quality index]f,g Cognitive performance | VERY LOW ^{b,c,d,e} UCRY LOW ^{b,c,e} | 4.09 movements fewer (9.14 fewer to 0.96 more) compared to control The mean difference in the acute bright light group was 0 (0.28 lower to 0.28 higher)) compared to control The mean difference in the acute bright light group was 2.50 | (1 RCT) 36 (1 RCT) |
| Accident risk [Steering Wheel Movements]a Sleep quality [Sleep quality index]f,g Cognitive performance [PVT lapses]a | VERY LOW ^{b,c,d,e} OCT VERY LOW ^{b,c,e} VERY LOW ^{b,c,d,e} | 4.09 movements fewer (9.14 fewer to 0.96 more) compared to control The mean difference in the acute bright light group was 0 (0.28 lower to 0.28 higher)) compared to control The mean difference in the acute bright light group was 2.50 lapses fewer (6.31 fewer to 1.31 more) compared to control. | (1 RCT) 36 (1 RCT) 17 |
| Accident risk [Steering Wheel Movements]a Sleep quality [Sleep quality index]f,g Cognitive performance [PVT lapses]a Cognitive performance | VERY LOW ^{b,c,d,e} ⊕○○○ VERY LOW ^{b,c,e} VERY LOW ^{b,c,d,e} | 4.09 movements fewer (9.14 fewer to 0.96 more) compared to control The mean difference in the acute bright light group was 0 (0.28 lower to 0.28 higher)) compared to control The mean difference in the acute bright light group was 2.50 lapses fewer (6.31 fewer to 1.31 more) compared to control. The evidence is very uncertain about the effect of bright | (1 RCT) 36 (1 RCT) 17 (1 RCT) |
| Accident risk [Steering Wheel Movements]a Sleep quality [Sleep quality index]f,g Cognitive performance [PVT lapses]a | VERY LOW ^{b,c,d,e} OCT VERY LOW ^{b,c,e} VERY LOW ^{b,c,d,e} | 4.09 movements fewer (9.14 fewer to 0.96 more) compared to control The mean difference in the acute bright light group was 0 (0.28 lower to 0.28 higher)) compared to control The mean difference in the acute bright light group was 2.50 lapses fewer (6.31 fewer to 1.31 more) compared to control. The evidence is very uncertain about the effect of bright light on cognitive performance. 10 studies reported on the | (1 RCT) 36 (1 RCT) 17 |
| Accident risk [Steering Wheel Movements]a Sleep quality [Sleep quality index]f,g Cognitive performance [PVT lapses]a Cognitive performance | VERY LOW ^{b,c,d,e} ⊕○○○ VERY LOW ^{b,c,e} VERY LOW ^{b,c,d,e} | 4.09 movements fewer (9.14 fewer to 0.96 more) compared to control The mean difference in the acute bright light group was 0 (0.28 lower to 0.28 higher)) compared to control The mean difference in the acute bright light group was 2.50 lapses fewer (6.31 fewer to 1.31 more) compared to control. The evidence is very uncertain about the effect of bright | (1 RCT) 36 (1 RCT) 17 (1 RCT) |

| | | Visuo-spatial discrimination, letter cancellation task, dual task, Wilkinsons four choice, switching tasks, GO/NOGO, MAT, and SALT. The following studies were analyzed: Figueiro 2016, Griepentrog 2018, Lammers-vanderHolst 2021, Weisgerber 2017, Wright 1997, Babkoff 2002, Campbell 1990, Costa 1993, Foret 1998, Bjorvatn 1999, and Dawson 1995 | |
|--|---------------------------------|---|-------------------|
| Cognitive performance [Reduced performance] ^{a,f} | ⊕○○○ VERY LOW ^{b,c} | The mean difference in the acute bright light group was 10.40% lower (18.14 lower to 2.66 lower) compared to control. | 36 (1 non-RCT) |

- a. Lower values favor the intervention
- b. Risk of bias due to lack of blinding
- c. Imprecision due to small sample size (<200 participants)
- d. Indirectness is due to the fact that participants included in the studies are healthy individuals. The effect in adults with SWD may be different.
- e. Imprecision due to 95% CI crossing the CMT
- f. CMT was not established by the TF
- g. Higher values favor the intervention
- h. Imprecision due to the 95% CI crossing the null

Study Characteristics

Table S8. Acute bright light in adults with shiftwork disorder

| Study Citation | Study Design | Number of Participants (% Female) | Age (years) | Population | Intervention (dose/intensity) | Comparator | Time of Intervention Delivery | Duration of Follow-up |
|-------------------|-------------------|---|----------------|---|---|---|--|--------------------------|
| Babkoff 2002 | RCT, crossover | 12 (42) | 24.6 | Shift workers without SWD diagnosis | Bright light (3,000 lux) | Dim light (- 20-50 Iux) and placebo | light exposure from 01:30- 02:30 | 1 day |
| Badia 1991 | RCT | 19 (0) | 18 to 32 | Healthy participants | Bright light (5,000 - 10,000 lux) | Dim light (50 lux) | Continuous light during the night (23:00- 08:00) | 1 day |
| Bjorvatn 1999 | non-RCT | 7 (0) | 38.9 | Shift workers without SWD diagnosis | Bright light (10,000 lux) | Normal light (20-700 lux) | 30 min between 03:30-05:30 during the first night at the platform | 1 day |
| Campbell 1990 | RCT | 25 (60) | 22.0 ± 2.6 | Healthy participants | Bright light (10- 20 lux, 100 lux or 1000 lux) | dim ambient light (10-20 lux) | 23:00 to 07:00 on second simulated night shift | 3 nights |
| Campbell 1995 | RCT | 26 (27) | 49.1 ± 6.4 | Healthy participants | Bright light (>4,000 lux) Bright light (1,000 lux) | dim light (<100 lux) | 4-hour pulse of bright light from 24:00 to 04:00 on night shift one Exposure lasted for duration of the night shift on night shifts two and three | 3 nights |

| Costa 1993 | non-RCT, crossover | 15 (100) | 23.4 (range 21- 29) | Shift workers without SWD diagnosis | Bright Light (2350 lux) | normal light (100 lux) | 4 x 20min during the night shift (before work and every 2hrs while working) | 2 nights |
|----------------------------------|-----------------------|----------|---|---|--|---|---|----------|
| Costa 1995 | non-RCT, crossover | 15 (100) | 23.4 (range 21- 29) | Shift workers without SWD diagnosis | Bright Light (2350 lux) | normal light (100 lux) | 4 x 20min during the night shift (before work and every 2hrs while working) | 2 nights |
| Daurat 2000 (Bio Signals) | RCT, crossover | 4 | 19–25 | Healthy participants | Bright light (2,000 lux) | Dim lux (<50 lux) | 20:00 to 08:00 in Experiment A 20:00–00:00 or 04:00–08:00 in Experiment B | 1 night |
| Dawson 1991 | RCT | 13 (46) | 21.2 ± 3.1 | Healthy participants | bright light (6,000 lux) | normal ambient room illumination (150-200 lux) | 24:00-04:00 on the first night shift | 1 night |
| Figueiro 2016 | RCT, crossover | 17 (53) | 22.5 years ± 5.9 | Healthy participants | white light goggles (361 + 4 lux) | dim light (<5 lux) | 19:00-21:00, 23:00-01:00, or 03:00-05:00 (120 min for each session) | 1 night |
| Foret 1998 | RCT | 8 (0) | 19-23 | Healthy participants | bright light (700-1,000 lux) | dim light (50 lux) | 20:00 - 08:00 | 1 night |
| Griepentrog 2018 | RCT, crossover | 31 (71) | 29 (IQR 26-32) | Shift workers without SWD | Bright light (10,000 lux) | Ambient light (300 lux) | 19:00-05:00 | 4 weeks |
| Horowitz 2001 | RCT | 27 (74) | 26.99 ± 6.22 | diagnosis Healthy participants | Bright light (2,500 lux) | room light (150 lux) | 23:00-05:00 | 3 nights |
| Huang 2013 | RCT | 92 (100) | 30.2 ± 4.5 (bright light) 30.3 ± 4.7 (control) | Shift workers without SWD diagnosis | Bright light (7,000-10,000 lux) | normal illumination (100-400 lux) | 23:00-00:00 | ≥10 days |
| Kakooei 2010 | RCT | 34 (100) | 27 | Shift workers without SWD diagnosis | bright light (4,500 lux) | dim light (300 lux) | 21:15–22:00 and 3:15–4:00 | 30 days |
| Lammers-van der Holst 2021 | RCT | 29 (52) | 27.7 ± 6.3 | Healthy participants | bright light (~8,000, ~2,500 and ~1,250 lux) | 103 lux | 23:00-07:00 (alternating 30 min intervals) | 4 weeks |
| Leppamaki 2003 | non-RCT | 86 (100) | 39.2 ±7.8 | Shift workers without SWD diagnosis | bright light (5000 lux) | Baseline | 20 minutes, between 22:00 - 23:00, 24:00 - 01:00, 02:00 - 03:00, and 04:00 - 05:00 | 6 weeks |
| Leproult 1997 | non-RCT | 17 (0) | 20-30 years | Healthy participants | bright light (2,000-5,000 lux) | Baseline | 3-h period of exposure to 5000 lux was bracketed by 30 min of exposure | |

| | | | | | | | to 2000-2500 lux | |
|--------------------|-------------------|----------|------------------|---|--|---|--|----------|
| Lowden 2004 | RCT, crossover | 18 (6) | 36.2 (3.0) | Shift workers without SWD diagnosis | bright light (2,500 lux) | Normal illumination (300 lx) | all breaks (20 min) during night work | 4 weeks |
| Lowden 2012 | non-RCT | 30 (7) | 47.2 (13.7) | Shift workers without SWD diagnosis | Dynamic lighting system: white/blue strong light (745 lux), moderate yellow light (700 lux), weak yellow light (650 lux) | weak yellow light (200 lux) | 0:00-02:00 on night 1, 0:00- 01:00 on night 2 | 1 week |
| Ruger 2006 | RCT, crossover | 12 (0) | 21.8 (SD 1.9) | Healthy participants | bright light (5,000 lux) | dim light (10 lux) | 00:00-04:00 | 3 days |
| Weisgerber 2017 | RCT, crossover | 21 (29) | 22.8 ± 4 | Healthy participants | bright light (5600 lux) | dim light (35 lux) | 45 minutes after six hours of sleep deprivation | 1 night |
| Wright 1997 | RCT | 46 (0) | 18–25 y | Healthy participants | Bright Light- Placebo (2500 lux/200 mg sugar) Dim Light- Caffeine (≤100 lux/200 mg caffeine) Bright Light- Caffeine (2500 lux/200 mg caffeine) | Dim Light- Placebo (≤100 lux/200 mg sugar) | bright light from 20.00 to 08.00 hours Caffeine at 20.00 and 02.00 hours each night | 2 nights |
| Yoon 2002 | RCT, crossover | 12 (100) | 21-24 | Shift workers without SWD diagnosis | Bright light (4,000-6,000 lux) Sunglasses | room light followed by 1 hr exposure to sunlight or 10,000 lux from 08:30- 09:30 | Bright light from 01:00 to 05:00 Sunglasses on the drive home (08:30-09:30) | 4 days |

Critical Outcomes

Figure S47. Bright Light vs Control (Excessive Sleepiness, KSS) [CMT = 2 pts] RCT (Shift workers without SWD diagnosis)

| | Brig | ht Lig | ht | C | ontrol | | | Mean Difference | Mean Difference |
|---|----------|---------|---------|------------------------|--------|-------|--------|---------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 18.1.2 Field Studies |) | | | | | | | | |
| Kakooei 2010 | 3.52 | 1.45 | 34 | 3.16 | 1.29 | 34 | 40.7% | 0.36 [-0.29, 1.01] | - ■ - - |
| Lowden 2004 | 3.91 | 0.64 | 18 | 4.13 | 0.98 | 18 | 59.3% | -0.22 [-0.76, 0.32] | |
| Subtotal (95% CI) | | | 52 | | | 52 | 100.0% | 0.02 [-0.40, 0.43] | • |
| Heterogeneity: Chi ^z = Test for overall effect: | | | |); I ^z = 44 | % | | | | |
| Total (95% CI) | | | 52 | | | 52 | 100.0% | 0.02 [-0.40, 0.43] | * |
| Heterogeneity: Chi ² = | 1.80, df | = 1 (P | = 0.18) | $ \cdot ^2 = 44$ | % | | | - | |
| Test for overall effect: | Z = 0.08 | B(P=0) | 0.94) | ă. | | | | | -4 -2 U 2 4 Favours Bright Light Favours Control |
| Test for subgroup dif | ferences | : Not a | pplical | ole | | | | | ravours bright Light Favours Control |

^{*}Lowden 2004: data averaged over 3 weeks.

Figure S48. Bright Light vs Control (Excessive Sleepiness, KSS) [CMT = 2 pts] non-randomized studies (Shift workers without SWD diagnosis)

| | Brig | ht Lig | ht | C | ontrol | | | Mean Difference | Mean Difference |
|-----------------------------------|----------|---------|---------|-------------------------|--------|-------|--------|---------------------|--------------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 18.2.2 Field Studies | | | | | | | | | _ |
| Bjorvatn 1999 | 4.7 | 0.26 | 7 | 4.9 | 0.26 | 7 | 93.7% | -0.20 [-0.47, 0.07] | |
| Lowden 2012 | 4.65 | 1.14 | 7 | 5.17 | 1.28 | 16 | 6.3% | -0.52 [-1.57, 0.53] | |
| Subtotal (95% CI) | | | 14 | | | 23 | 100.0% | -0.22 [-0.48, 0.04] | • |
| Heterogeneity: Chi ² = | 0.33, df | = 1 (P | = 0.56 | $ \mathbf{r} ^2 = 09$ | 6 | | | | |
| Test for overall effect | Z = 1.64 | P = 0 | 0.10) | | | | | | |
| Total (95% CI) | | | 14 | | | 23 | 100.0% | -0.22 [-0.48, 0.04] | • |
| Heterogeneity: Chi ² = | 0.33, df | = 1 (P | = 0.56) | $ \mathbf{r} ^2 = 09$ | 6 | | | | -2 -1 1 2 |
| Test for overall effect | Z = 1.64 | (P = 0 | 0.10) | | | | | | Favours Bright Light Favours Control |
| Test for subgroup dif | ferences | : Not a | pplical | ole | | | | | Favours Bright Light Favours Control |

^{*}Bjorvatn 1999: data reported at the platform

Lowden 2012: data extracted from Figure 2, pooled average from 3 nights; SEM converted to SD.

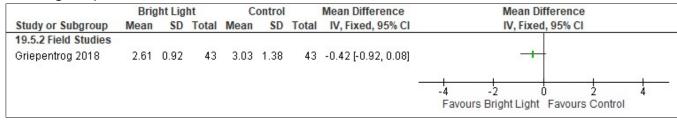
Figure S49. Bright Light vs Control (Excessive Sleepiness, KSS) [CMT = 2 pts] RCTs (Healthy participants)

| | Brig | ht Lig | ht | C | ontrol | | | Mean Difference | Mean Difference |
|-----------------------------------|-------------|---------|----------|-----------------------|--------|-------|--------|----------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 19.2.1 Lab Studies | | | | | | | | | |
| Ruger 2006 | 6.23 | 1.64 | 12 | 7.07 | 1.26 | 12 | 36.3% | -0.84 [-2.01, 0.33] | |
| Weisgerber 2017 | 7.28 | 1.66 | 19 | 7.94 | 1.05 | 19 | 63.7% | -0.66 [-1.54, 0.22] | |
| Subtotal (95% CI) | | | 31 | | | 31 | 100.0% | -0.73 [-1.43, -0.02] | • |
| Heterogeneity: Chi²= | 0.06, df | = 1 (P | = 0.81) | $ ^2 = 09$ | 6 | | | | |
| Test for overall effect | :: Z = 2.02 | 2(P=0) | 0.04) | | | | | | |
| Total (95% CI) | | | 31 | | | 31 | 100.0% | -0.73 [-1.43, -0.02] | • |
| Heterogeneity: Chi ² = | 0.06, df | = 1 (P | = 0.81) | $ \mathbf{r} = 09$ | 6 | | | | |
| Test for overall effect | Z = 2.02 | 2(P=0) | 0.04) | | | | | | Favours Bright Light Favours Dim Light |
| Test for subgroup dif | fferences | : Not a | applical | ble | | | | | ravours bright Light Pavours Diff Light |

^{*}Weisgerber 2017: SEM converted SD. KSS data from post-light and post-drive extracted from Figure 3A and averaged.

Ruger 2006: data extracted from Figure 3B, averaged across the night (24:00-5:00), SEM converted to SD

Figure S50. Bright Light vs Control (Excessive Sleepiness, SSS) [CMT = 1 pt] RCT (Shift workers without SWD diagnosis)



^{*}Griepentrog 2018: Data extracted from Figure 3, SEM converted to SD

Figure S51. Bright Light vs Control (Excessive Sleepiness, SSS) [CMT = 1 pt] RCT (Healthy participants)

| | • | | , | • | | • | • | , | • • • • • • | | |
|-----------------------------------|----------|-------------|----------|------|----------|-------|--------|---------------------|--|--|--|
| | Br | ight Ligh | t | D | im Light | | | Mean Difference | Mean Difference | | |
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI | | |
| 20.3.1 Lab studies | | | | | | | | | | | |
| Leproult 1997 | 3.5 | 2.0616 | 17 | 3.8 | 2.0616 | 17 | 12.6% | -0.30 [-1.69, 1.09] | - | | |
| Wright 1997 | 4.33 | 0.6 | 10 | 4.33 | 0.6 | 10 | 87.4% | 0.00 [-0.53, 0.53] | - | | |
| Subtotal (95% CI) | | | 27 | | | 27 | 100.0% | -0.04 [-0.53, 0.45] | • | | |
| Heterogeneity: Chi ² = | 0.16, df | = 1 (P = I | 0.69); P | = 0% | | | | | | | |
| Test for overall effect: | Z = 0.15 | 5 (P = 0.8 | 8) | | | | | | | | |
| Total (95% CI) | | | 27 | | | 27 | 100.0% | -0.04 [-0.53, 0.45] | • | | |
| Heterogeneity: Chi ² = | 0.16, df | = 1 (P = 1 | 0.69); P | = 0% | | | | | - | | |
| Test for overall effect: | Z = 0.15 | 5 (P = 0.8) | 8) | | | | | | -4 -2 U 2 4 Bright light Control (dim light) | | |
| Test for subgroup diff | ferences | : Not app | licable | ! | | | | | Bright light Control (diri light) | | |

^{*}Wright 1997: SEM converted SD.

Leproult 1997: data extracted from Figure 3, averaged across all timepoints, SEM converted to SD

Figure S52. Bright Light vs Control (Excessive Sleepiness, VAS – Alertness) [CMT = Not Established] RCT (Shift workers without a SWD diagnosis)

| | Brig | ht Lig | ht | C | ontrol | | | Mean Difference | Mean Difference |
|-----------------------------------|----------|-----------|---------|-----------------------|---------|-------------|--------|----------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 7.5.1 Field Study (no | sunglas | ses) | | | | | | | |
| Yoon 2002 | 105.9 | 20.4 | 12 | 83.1 | 18.5 | 6 | 51.1% | 22.80 [4.03, 41.57] | |
| Subtotal (95% CI) | | | 12 | | | 6 | 51.1% | 22.80 [4.03, 41.57] | |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect | Z = 2.38 | B (P = 0) | 0.02) | | | | | | |
| 7.5.2 Field Study (Su | nglasse | s) | | | | | | | |
| Yoon 2002 | 116.8 | 21.6 | 12 | 83.1 | 18.5 | 6 | 48.9% | 33.70 [14.50, 52.90] | |
| Subtotal (95% CI) | | | 12 | | | 6 | 48.9% | 33.70 [14.50, 52.90] | |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect | Z = 3.44 | P = 0 | 0.0006) | | | | | | |
| Total (95% CI) | | | 24 | | | 12 | 100.0% | 28.13 [14.71, 41.55] | • |
| Heterogeneity: Chi ^z = | 0.63, df | = 1 (P | = 0.43) | $ \mathbf{r} = 09$ | 6 | | | | -50 -25 0 25 |
| Test for overall effect: | Z = 4.11 | (P < 0 | 0.0001) | | | | | | -50 -25 0 25 5 Favours Control Favours Bright Light |
| Test for subgroup dif | ferences | : Chi²: | = 0.63, | df = 1 (i | 0 = 0.4 | 3), $ z =$ | 0% | | r avours Control Pavours Bright Light |

^{*}Yoon 2002: Data from Days 2-3, percent alertness compared with average of total 12 study days as 100%). control, n=12 participants were halved as to not double count

Figure S53. Bright Light vs Control (Excessive Sleepiness, VAS (Alertness)) [CMT = Not Established] RCT (healthy participants)

| | Bri | ght Ligh | nt | Co | ntro | 1 | Mean Difference | Mean Difference |
|--------------------|-------|----------|-------|-------|------|-------|---------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 19.7.1 Lab Studies | | | | | | | | ľ. |
| Horowitz 2001 | 40.76 | 18.68 | 13 | 35.25 | 15 | 14 | 5.51 [-7.33, 18.35] | 10 to |
| | | | | | | | NO. | -20 -10 0 10 20 |
| | | | | | | | | Favours Control Favours Bright Light |

^{*}Horowitz 2001: 100 mm=alert, data extracted from Figure 3A, night one data analyzed

Figure S54. Bright Light vs Control (Excessive Sleepiness, VAS - Rating of Arousal) [CMT = Not Established] RCT (shift workers without a diagnosis of SWD)

| • • | | | | | | | | | | | |
|-------------------|-------|----------|-------|-------|--------|-------|----------------------|-----|-----------------|----------------------|----|
| | Bri | ght Ligh | nt | C | ontrol | | Mean Difference | | Mean Di | fference | |
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed | , 95% CI | |
| 7.6.1 Lab Study | | | | | | | | | 1 | | |
| Babkoff 2002 | 38.45 | 17.58 | 11 | 46.15 | 15.72 | 11 | -7.70 [-21.64, 6.24] | | | 1 Se | |
| | | | | | | | | 1 | 9 | 11 | 81 |
| | | | | | | | | -50 | -25 (| 25 | 50 |
| | | | | | | | | | Favours Control | Favours Bright Light | |

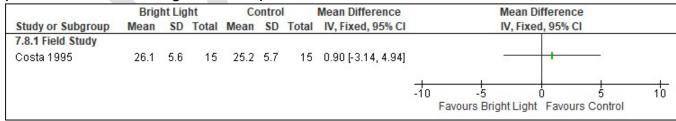
^{*}Babkoff 2002: Data extracted from graph (0230-0830); SEM converted to SD. Higher value represents higher arousal.

Figure S55. Bright Light vs Control (Excessive Sleepiness, VAS (Fatigue)) [CMT = Not Established] RCT (healthy participants)

| | Brig | ht Lig | ht | C | ontrol | | Mean Difference | Mean Difference |
|--------------------|------|--------|-------|------|--------|-------|--------------------|--------------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 19.8.1 Lab Studies | | | | | | | | |
| Ruger 2006 | 4.8 | 1.73 | 12 | 3.8 | 1.73 | 12 | 1.00 [-0.38, 2.38] | ++- |
| | | | | | | | | -4 -2 0 2 4 |
| | | | | | | | | Favours Control Favours Bright Light |

Ruger 2006: VAS fatigue=The scale consists of 18 items relating to the subjective experience of fatigue

Figure S56. Bright Light vs Control (Excessive Sleepiness, Fatigue Ratings) [CMT = Not Established] RCT (shift workers without a diagnosis of SWD)



^{*}Costa 1995: First night of bright light, overall fatigue (5 min to 35 max).

Figure S57. Bright Light vs Control (Excessive Sleepiness, seven-point scale first night) [CMT = Not Established] RCT (shift workers without a diagnosis of SWD)

| 15 5.3 1.5 15 0.50 [| |
|----------------------|---------------|
| 15 5.3 1.5 15 0.50 [| [-0.57, 1.57] |
| 15 5.3 1.5 15 0.50 [| [-0.57, 1.57] |
| | 8 80 80 |
| | |
| | |

^{*}Costa 1993: data from the end of first night

Figure S58. Bright Light vs Control (Excessive Sleepiness, seven-point scale second night) [CMT = Not Established] RCT (shift workers without a diagnosis of SWD)

| | Brig | ht Lig | ht | Din | ı Ligh | ht | Mean Difference | Mean Difference |
|--------------------|------|--------|-------|------|--------|-------|---------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 19.9.1 Field Study | | | | | | | | 1 |
| Costa 1993 | 4.9 | 1.9 | 15 | 5.3 | 1.5 | 15 | -0.40 [-1.63, 0.83] | |
| | | | | | | | _ | |
| | | | | | | | | -4 -2 0 2 |
| | | | | | | | | Favours Bright Light Favours Dim Light |

^{*}Costa 1993: data from the end of second night

Figure S59. Bright Light vs Control (Excessive Sleepiness, MWT) [CMT = +2.0 min] RCTs (Healthy participants)

| | Bright Light | | | | | | | Mean Difference | Mean Difference |
|-----------------------------------|--------------|---------|---------|---------------|------|-------|--------|--------------------|---------------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 19.1.1 Lab Studies | | | | | | | | | |
| Badia 1991 | 13.62 | 2.5 | 10 | 9.72 | 3.78 | 9 | 58.5% | 3.90 [0.98, 6.82] |] |
| Wright 1997 | 13.08 | 3.32 | 10 | 12.35 | 4.49 | 10 | 41.5% | 0.73 [-2.73, 4.19] |] - |
| Subtotal (95% CI) | | | 20 | | | 19 | 100.0% | 2.58 [0.35, 4.81] | • |
| Heterogeneity: Chi ² = | 1.89, df | = 1 (P | = 0.17 | $ 1^2 = 47 $ | % | | | | |
| Test for overall effect | Z = 2.27 | P = 0 |).02) | | | | | | |
| Total (95% CI) | | | 20 | | | 19 | 100.0% | 2.58 [0.35, 4.81] | • |
| Heterogeneity: Chi ² = | 1.89, df | = 1 (P | = 0.17) | $ 1^2 = 47 $ | % | | | | -20 -10 0 10 20 |
| Test for overall effect | Z = 2.27 | P = 0 | 0.02) | | | | | | Favours Control Favours Bright light |
| Test for subgroup dif | ferences | : Not a | pplicat | ole | | | | | 1 avours Control Pavours Bright light |

^{*}Wright 1997: Night 1 data extracted from graph and averaged across the 4 naps (acute); SEM converted to SD. Badia 1991: data extracted from figure 6, averaged across the blocks, SEM converted to SD

Figure S60. Bright Light vs Control (Excessive Sleepiness, RTSW) [CMT = +2.0 min] RCTs (Healthy participants)

| | Bright Light | | | | m Light | | | Mean Difference | Mean Difference |
|-----------------------------------|--------------|---------|----------|--------------------|---------|-------|--------|--------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 2.7.1 Lab Studies | | | | | | | | | |
| Campbell 1990 | 17.13 | 5 | 25 | 11.08 | 5.075 | 25 | 72.9% | 6.05 [3.26, 8.84] | |
| Campbell 1995 | 14.55 | 5.8 | 13 | 12.05 | 6.1 | 13 | 27.1% | 2.50 [-2.08, 7.08] | - • - |
| Subtotal (95% CI) | | | 38 | | | 38 | 100.0% | 5.09 [2.70, 7.47] | • |
| Heterogeneity: Chi ² = | 1.68, df | = 1 (P | 9 = 0.19 |); $ z = 4^\circ$ | 1% | | | | |
| Test for overall effect | Z= 4.18 | (P < | 0.0001 |) | | | | | |
| Total (95% CI) | | | 38 | | | 38 | 100.0% | 5.09 [2.70, 7.47] | • |
| Heterogeneity: Chi²= | 1.68, df | = 1 (P | = 0.19 |); $I^2 = 4^\circ$ | 1% | | | F. | 20 -10 0 10 20 |
| Test for overall effect | Z = 4.18 | (P < | 0.0001 |) | | | | 1-2 | 20 -10 0 10 20 Favours Dim Light Favours Bright Light |
| Test for subaroup dif | ferences | : Not a | applica | ble | | | | | Pavouis Dilli Light Pavouis Bright Light |

^{*} Campbell 1995: data extracted from Figure 3, night shift 2, data averaged across the night, SEM converted to SD

Figure S61. Bright Light vs Control (Excessive Sleepiness, EEG-Alpha) [CMT = Not Established] RCT (Healthy participants)

| | Bri | ght Ligh | nt | (| ontrol | | Mean Difference | Mean Difference | |
|-------------------|-------|----------|-------|-------|--------|-------|----------------------|---|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | |
| 6.6.1 Lab Studies | | | | | | | | | |
| Figueiro 2016 | 0.989 | 0.276 | 17 | 1.172 | 0.264 | 17 | -0.18 [-0.36, -0.00] | | |
| | | | | | | | | | _ |
| | | | | | | | | -1 -0.5 0 0.5 Favours Bright Light Favours Control | 1 |

^{*}Figueiro 2016: White Light- 361±4 lux, Dim Light < 5 lux. Cross-over study (acceptable washout period). SEM converted to SD.

Figure S62. Bright Light vs Control (Excessive Sleepiness, EEG-Beta) [CMT = Not Established] RCT (Healthy participants)

| | Bri | ght Ligh | nt | C | ontrol | | Mean Difference | | Mean Difference | |
|-------------------|-------|----------|-------|-------|--------|-------|--------------------|------|-------------------------------------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 95% CI | |
| 6.7.1 Lab Study | | | | | | | | | | |
| Figueiro 2016 | 1.131 | 0.157 | 17 | 1.115 | 0.136 | 17 | 0.02 [-0.08, 0.11] | | - | |
| | | | | | | | | | | - |
| | | | | | | | | -0.5 | -0.25 0 0.25 | 0.5 |
| | | | | | | | | | Favours Control Favours Bright Ligh | nt |

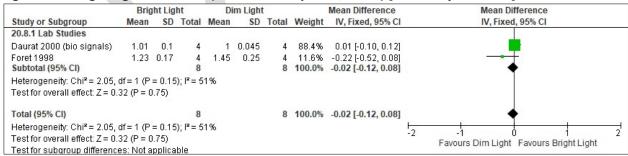
^{*}Figueiro 2016: White Light- 361±4 lux, Dim Light < 5 lux. Cross-over study (acceptable washout period). SEM converted to SD.

Figure S63. Bright Light vs Control (Excessive Sleepiness, EEG-Theta) [CMT = Not Established] RCT (Healthy participants)

| | Bri | ght Ligh | nt | C | ontrol | | Mean Difference | Mean Difference | | |
|-------------------|-------|----------|-------|-------|--------|-------|--------------------|--------------------------------------|--|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | | |
| 6.5.1 Lab Studies | | | | | | | | | | |
| Figueiro 2016 | 1.145 | 0.297 | 17 | 1.118 | 0.148 | 17 | 0.03 [-0.13, 0.18] | | | |
| | | | | | | | L | | | |
| | | | | | | | 12- | 1 -0.5 Ö 0.5 | | |
| | | | | | | | | Favours Bright Light Favours Control | | |

^{*}Figueiro 2016: White Light- 361±4 lux, Dim Light < 5 lux. Cross-over study (acceptable washout period). SEM converted to SD.

Figure S64. Bright Light vs Control (Excessive Sleepiness, GADS) [CMT = any decrease] RCT



^{*}Daurat 2000: data extracted from Figure 2, data averaged across the night, data from experiment A used Foret 1998: 2000-2400 vs 400-800, data extracted from the graph, data averaged across the night 1

Figure S65. Bright Light vs Control (Accident Risk, Variability of Lane Position) [CMT = any decrease] RCT (Healthy participants)

| | Brig | ht Lig | ht | C | ontrol | | Mean Difference | Mean Difference | | | | | |
|-------------------|------|--------|-------|------|--------|-------|--------------------|---|--|--|--|--|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | | | | | |
| 20.11.1 Lab Study | | | | | | | | | | | | | |
| Weisgerber 2017 | 0.27 | 0.07 | 19 | 0.27 | 0.09 | 19 | 0.00 [-0.05, 0.05] | - | | | | | |
| | | | | | | | - | | | | | | |
| | | | | | | | | -0.2 -0.1 0 0.1 0.2 Favours Bright Light Favours Dim Light | | | | | |

^{*}Weisgerber 2017: BL-5600 lux, dim light <50 lux, Crossover study, all participants in both arms, acceptable washout period. Data averaged across laps; SEM converted SD

Figure S66. Bright Light vs Control (Accident Risk, Number of Accidents) [CMT = any decrease] RCT (Healthy participants)

| | Bright Light | | | | | | Mean Difference | Mean Difference IV, Fixed, 95% CI | | | | |
|-------------------|------------------|-------|----|-------|---------|----|----------------------|---|--|--|--|--|
| Study or Subgroup | up Mean SD Total | | | | Mean SD | | IV, Fixed, 95% CI | | | | | |
| 6.9.1 Lab Study | | | | | | | | 1 | | | | |
| Weisgerber 2017 | 11.2 | 13.08 | 19 | 20.18 | 26.81 | 19 | -8.98 [-22.39, 4.43] | | | | | |
| | | | | | | | | 1 1 | | | | |
| | | | | | | | | -50 -25 0 25 Favours Bright Light Favours Control | | | | |

^{*}Weisgerber 2017: BL-5600 lux, dim light <50 lux, Crossover study (acceptable washout period). Data extracted from graph (total number of accidents and incidents); SEM converted SD for study.

Figure S67. Bright Light vs Control (Accident Risk, Steering Wheel Movements) [CMT = any decrease] RCT (Healthy participants)

| | Brig | ht Lig | ht | C | ontrol | | Mean Difference | Mean Difference |
|-------------------|------|--------|-------|------|--------|-------|---------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 6.13.1 Lab Study | | | | | | | | |
| Weisgerber 2017 | 4.55 | 4.01 | 19 | 8.64 | 10.5 | 19 | -4.09 [-9.14, 0.96] | |
| | | | | | | | | |
| | | | | | | | | -20 -10 0 10 20 Favours Bright Light Favours Control |

^{*}Weisgerber 2017: BL-5600 lux, dim light <50 lux, Crossover study, all participants in both arms, acceptable washout period. Data extracted from graphs and averaged across laps; SEM converted SD for stud

Figure S68. Bright Light vs Control (Sleep Quality, sleep quality index) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

| | Br | ight Ligh | t | D | im Light | | Mean Difference | | Mean Difference | | |
|---------------------|------|-----------|-------|------|----------|-------|--------------------|----|-------------------------------------|---------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 95% CI | | |
| 19.11.1 Field Study | | | | | | | | | | | |
| Bjorvatn 1999 | 3.4 | 0.4243 | 18 | 3.4 | 0.4243 | 18 | 0.00 [-0.28, 0.28] | | | | |
| | | | | | | | | _ | | | |
| | | | | | | | | -1 | -0.5 0 Favours Dim Light Favours | 0.5 Bright Light | |

Figure S69. Bright Light vs Control (Cognitive Performance, PVT lapses) [CMT = -1 lapse] RCT (Healthy participants)

| | Brig | ht Lig | ht | Co | ntro | I | Mean Difference | Mean Di | fference | |
|--------------------------|------|--------|-------|------|------|-------|---------------------|----------------------|----------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed | , 95% CI | |
| 20.33.1 Lab study | | | | | | | | | | |
| Lammers-vanderHolst 2021 | 1.6 | 3 | 7 | 4.1 | 5 | 10 | -2.50 [-6.31, 1.31] | - | | |
| | | | | | | | | -10 -5 (| 1 | 10 |
| | | | | | | | | Favours Bright Light | Favours Contro | 1 |

Figure S70. Bright Light vs Control (Cognitive Performance, GO/NOGO Normalized Reaction Time)
[CMT = Not Established] RCT (Healthy participants)

| | Brig | ht Ligh | t | C | ontrol | | Mean Difference | Mean Difference | |
|-------------------|--------|---------|-------|--------|--------|-------|-------------------------|------------------------------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | |
| 6.16.1 Lab Study | | | | | | | | 1 | |
| Figueiro 2016 | 502.42 | 16.78 | 17 | 530.14 | 15.26 | 17 | -27.72 [-38.50, -16.94] | | |
| | | | | | | | | | |
| | | | | | | | | -50 -25 0 25 | 50 |
| | | | | | | | | Favours Bright Light Favours Contr | ol |

^{*}Figueiro 2016: White Light 361±4 lux, Dim Light < 5 lux. Crossover study (acceptable washout period). SEM converted to SD, extracted from graphs.

Figure S71. Bright Light vs Control (Cognitive Performance, GO/NOGO 10% Best throughput) [CMT = Not Established] RCT (Healthy participants)

| | Bri | ght Ligh | nt | C | ontrol | | Mean Difference | | Mean Dif | ference | |
|-------------------|-------|----------|-------|-------|--------|-------|-------------------|------|----------------------------|------------------------|--------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed | , 95% CI | |
| 6.17.1 Lab Study | | | | | | | | | 1 | | |
| Figueiro 2016 | 0.261 | 0.008 | 17 | 0.246 | 0.012 | 17 | 0.02 [0.01, 0.02] | | | + | |
| | | | | | | | | -1- | 1 | - P | |
| | | | | | | | | -0.1 | -0.05 0 Favours Control | 0.05 Favours Bright | 0.1 Light |

^{*}Figueiro 2016: White Light 361±4 lux, Dim Light < 5 lux. Crossover study (acceptable washout period). SEM converted to SD, extracted from graphs.

Figure S72. Bright Light vs Control (Cognitive Performance, GO/NOGO 10% Worst throughput) [CMT =] RCT (Healthy participants)

| Bri | ght Ligh | nt | C | ontrol | | Mean Difference | Mean Difference |
|--------------------------------------|----------|---------|------------------------|--------------------|-----------------------|-----------------------------|---|
| or Subgroup Mean SD Tot Lab Study | | | | | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| | | | | | | | |
| 0.136 | 0.008 | 17 | 0.128 | 0.008 | 17 | 0.01 [0.00, 0.01] | |
| | | | | | | _ | |
| | | | | | | | -0.02 -0.01 0 0.01 0.02 Favours Control Favours Bright Light |
| | Mean | Mean SD | 594505038 40303740 PMA | Mean SD Total Mean | Mean SD Total Mean SD | Mean SD Total Mean SD Total | Mean SD Total Mean SD Total IV, Fixed, 95% CI |

^{*}Figueiro 2016: White Light 361±4 lux, Dim Light < 5 lux. Crossover study (acceptable washout period). SEM converted to SD, extracted from graphs.

Figure S73. Bright Light vs Control (Cognitive Performance, PVT mean reaction time, msec) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)

| | Brig | ght light | t | C | ontrol | | Mean Difference | | Me | ean Differen | ce | |
|----------------------|-------------|-----------|-------|--------|--------|-------|-----------------------|------|--------------|--------------|-------------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV | , Fixed, 95% | CI | |
| 19.14.2 No Diagnosis | s, Field St | udy | | | | | | | | 189 | | |
| Griepentrog 2018 | 252.86 | 55.97 | 43 | 255.14 | 98.92 | 43 | -2.28 [-36.25, 31.69] | | | • | | |
| | | | | | | | | -100 | -50 | | 50 | 100 |
| | | | | | | | | Fa | vours Bright | Light Favou | urs Control | |

Griepentrog 2018: Bright Light (1500-2000 lux). Ambient Light (300 lux). RCT. Crossover, all participants split counted in both arms (acceptable washout period). Data extracted from graph; mean & SD calculated from median, range, and sample size using Hozo et al 2005 calculation.

Figure S74. Bright Light vs Control (Cognitive Performance, PVT mean reaction time, msec) [CMT = Not Established] RCT (Healthy participants)

| | Bri | ght Light | | (| Control | | | Mean Difference | Mean Difference |
|--|-----------------|-------------|----------|-------------|---------|-------|--------|-------------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| 20.26.1 Lab Study | | | | | | | | | |
| Lammers-vanderHolst 2021 | 269 | 54 | 7 | 312 | 80 | 10 | 23.7% | -43.00 [-106.71, 20.71] | - • |
| Weisgerber 2017 | 585.41 | 225.92 | 19 | 590.14 | 224.27 | 19 | 4.7% | -4.73 [-147.87, 138.41] | |
| Wright 1997 | 320.59 | 37.22 | 10 | 327.39 | 43.59 | 9 | 71.6% | -6.80 [-43.45, 29.85] | |
| Subtotal (95% CI) | | | 36 | | | 38 | 100.0% | -15.28 [-46.29, 15.73] | • |
| Heterogeneity: Tau ² = 0.00; Ch | $ni^2 = 0.95$, | df = 2 (P : | = 0.62); | $I^2 = 0\%$ | | | | | |
| Test for overall effect: Z = 0.97 | (P = 0.33) | | | | | | | | |
| Total (95% CI) | | | 36 | | | 38 | 100.0% | -15.28 [-46.29, 15.73] | • |
| Heterogeneity: Tau ² = 0.00; Ch | $ni^2 = 0.95$, | df = 2 (P : | = 0.62); | $I^2 = 0\%$ | | | | | 100 100 100 |
| Test for overall effect: $Z = 0.97$ | (P = 0.33) | | | | | | | | -200 -100 0 100 200 Favours Bright Light Favours Dim Light |
| Test for subgroup differences: | Not appli | cable | | | | | | | ravouis biigiit Ligiit ravouis Diii Ligiit |

^{*} Weisgerber 2017: BL 5600 lux, dim light <50 lux, Crossover study, all participants in both arms, acceptable washout period. SEM converted SD for study, data (post-light and post-drive) extracted from graph and averaged.

Wright 1997: Modified-PVT. BL-2500 lux, dim light<100 lux, data averaged across night 1; data extracted from graph; SEM converted to SD.

Figure S75. Bright Light vs Control (Cognitive Performance, Choice Reaction Time) [CMT = Not Established] RCT (shift workers without a diagnosis of SWD)

| | Bri | ight Ligh | t | C | control | | Mean Difference | | Mea | an Differe | ence | |
|-------------------|-------|-----------|-------|-------|---------|-------|--------------------------|------|---------------|------------|--------------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, | Fixed, 959 | % CI | |
| 19.15.1 Lab Study | | | | | | | | | | 88 | | |
| Babkoff 2002 | 693.9 | 136.45 | 11 | 821.6 | 264.8 | 11 | -127.70 [-303.74, 48.34] | | + | 1 24 10 | | |
| | | | | | | | | _ | | | | _ |
| | | | | | | | | -500 | -250 | Ó | 250 | 500 |
| | | | | | | | | Fav | ours Bright L | ight Fav | ours Control | |

^{*}Babkoff 2002: Bright Light (3000 lux for 1 hr from 0130-0230). Dim Light (~20-50 lux). Testing took place in dim light (<50 lux). Crossover (acceptable washout period). Data extracted from graph; SEM converted to SD.

Figure S76. Bright Light vs Control (Cognitive Performance, Wilkinson Four Choice Reaction Time (Throughput)) [CMT = Not Established] RCT (Healthy participants)

| | Bri | ght Light | | C | ontrol | | Mean Difference | | Mea | an Differ | rence | |
|--------------------|--------|-----------|-------|--------|--------|-------|----------------------|-----|-------------|-----------|----------------|------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, I | | | |
| 6.27.1 Lab Studies | | | | | | | | | | 8 | | |
| Wright 1997 | 168.35 | 15.843 | 10 | 158.25 | 19.64 | 10 | 10.10 [-5.54, 25.74] | | | 10 T | 1 | |
| | | | | | | | | _ | - 1 | _ | | |
| | | | | | | | | -50 | -25 | 0 | 25 | 50 |
| | | | | | | | | | Favours Cor | ntrol Fa | vours Bright L | ight |

^{*}Wright 1997: BL-2500 lux, dim light<100 lux, data averaged across night 1; SEM converted SD for study.

Figure S77. Bright Light vs Control (Cognitive Performance, Wilkinson Four Choice Reaction Time (percent improvement)) [CMT = Not Established] RCT (Healthy participants)

| | Bri | ight Ligh | t | | Control | | Mean Difference | | Mean | Differe | ence | |
|---------------------|------|-----------|-------|------|---------|-------|-----------------------|-----|---------------|---------|---------------|------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fix | ced, 95 | % CI | |
| 20.15.1 Lab Studies | | | | | | | | | | | | |
| Campbell 1990 | 3.1 | 5.1962 | 12 | 9 | 39.8372 | 12 | -5.90 [-28.63, 16.83] | | 10 | - | | |
| | | | | | | | | | | | - 4 | - |
| | | | | | | | | -50 | -25 | 0_ | 25 | 50 |
| | | | | | | | | | Favours Contr | ol Fav | ours Bright L | ight |

^{*}Campbell 1990: data extracted from the graph. SEM converted to SD, data presented as percent improvement

Figure S78. Bright Light vs Control (Cognitive Performance, Response Time to More Difficult Visuospatial Discrimination) [CMT = Not Established] RCT (shift workers without a diagnosis of SWD)

| Brig | ht Lig | ht | C | ontrol | | Mean Difference | Mean Difference |
|------|--------|-------|------------------------|--------------------|-----------------------|-----------------------------|---|
| Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| | | | | | | | 9 |
| 3.89 | 1.03 | 11 | 3.65 | 0.98 | 11 | 0.24 [-0.60, 1.08] | |
| | | | | | | | |
| | | | | | | 1 | 2 -1 0 1 2 |
| | | | | | | | Favours Bright Light Favours Control |
| | Mean | | 96/96/12/10 (16/12/12) | Mean SD Total Mean | Mean SD Total Mean SD | Mean SD Total Mean SD Total | Mean SD Total Mean SD Total IV, Fixed, 95% CI |

^{*}Babkoff 2002: Bright Light (3000 lux for 1 hr from 0130-0230). Dim Light (~20-50 lux). Testing took place in dim light (<50 lux). Crossover (acceptable washout period). Data extracted from graph; SEM converted to SD, msec converted to sec.

Figure S79. Bright Light vs Control (Cognitive Performance, Response Time to Less Difficult Visuospatial Discrimination) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

| | Brig | ht Lig | ht | C | ontrol | | Mean Difference | Mean Difference |
|-------------------|------|--------|-------|------|--------|-------|---------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 19.18.1 Lab Study | | | | | | | | 2 |
| Babkoff 2002 | 3.62 | 0.82 | 11 | 3.67 | 0.98 | 11 | -0.05 [-0.81, 0.71] | + |
| | | | | | | | | |
| | | | | | | | | -1 -0.5 0 0.5 1 Favours Bright Light Favours Control |

^{*}Babkoff 2002: Bright Light (3000 lux for 1 hr from 0130-0230). Dim Light (~20-50 lux). Testing took place in dim light (<50 lux). Crossover (acceptable washout period). Data extracted from graph; SEM converted to SD, msec converted to sec.

Figure S80. Bright Light vs Control (Cognitive Performance, Letter Cancellation Task with no false alarms) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

| Bright Light | | | ht | C | ontrol | | Mean Difference | Mean Difference | | | | |
|-------------------|------|------|-------|------|--------|-------|----------------------|-----------------|-----------------------------|------------------------------|--|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, | 95% CI | | |
| 19.16.1 Lab Study | | | | | | | | | 100 | | | |
| Babkoff 2002 | 5.61 | 0.09 | 11 | 6.11 | 0.33 | 11 | -0.50 [-0.70, -0.30] | | - | | | |
| | | | | | | | | | | 1 1 | | |
| | | | | | | | | -1 | -0.5 Ó Favours Control F | 0.5 1 avours Bright Light | | |

^{*}Babkoff 2002: Bright Light (3000 lux for 1 hr from 0130-0230). Dim Light (~20-50 lux). Testing took place in dim light (<50 lux). Crossover (acceptable washout period). Data extracted from graph; SEM converted to SD.

Figure S81. Bright Light vs Control (Cognitive Performance, Search and Memory test (Reaction time)) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

| Expe | rimen | tal | C | ontrol | | Mean Difference | Mean Dit | ference | |
|-------|-------|-------|---------------|--------------------|-----------------------|-----------------------------|---|--|--|
| Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed | , 95% CI | |
| | | | | | | | | | |
| 183.5 | 18.6 | 15 | 190.8 | 22.9 | 15 | -7.30 [-22.23, 7.63] | -+ | | |
| | | | | | | | - | - | |
| | | | | | | | | Company of the Compan | 100 |
| | Mean | | Mean SD Total | Mean SD Total Mean | Mean SD Total Mean SD | Mean SD Total Mean SD Total | Mean SD Total Mean SD Total IV, Fixed, 95% CI | Mean SD Total Mean SD Total IV, Fixed, 95% CI IV, Fixed 183.5 18.6 15 190.8 22.9 15 -7.30 [-22.23, 7.63] -100 -50 0 | Mean SD Total Mean SD Total IV, Fixed, 95% CI 183.5 18.6 15 190.8 22.9 15 -7.30 [-22.23, 7.63] |

^{*}Costa 1993: end of shift, first night, no diagnosis

Figure S82. Bright Light vs Control (Cognitive Performance, Search and Memory test (Reaction time)) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

| | Expe | erimen | tal | C | ontrol | | Mean Difference | Mean Difference |
|---------------------|------|--------|-------|------|--------|-------|----------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 19.19.1 Field Study | | | | | | | | |
| Costa 1993 | 180 | 16.6 | 15 | 188 | 24.5 | 15 | -8.00 [-22.98, 6.98] | + |
| | | | | | | | | |
| | | | | | | | | -100 -50 0 50 10 |
| | | | | | | | | Favours Bright Light Favours Dim Light |

^{*}Costa 1993: end of shift, second night, no diagnosis

Figure S83. Bright Light vs Control (Cognitive Performance, Search and Memory test (Score)) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

| | Expe | erimen | tal | C | ontrol | | Mean Difference | Mean Difference | | | | | |
|---------------------|-------|--------|-------|-------|--------|-------|-------------------|-----------------|--------------|-----------|------------|-------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, F | ixed, 95% | CI | | |
| 19.21.1 Field Study | | | | | | | | | | 1 | | | |
| Costa 1993 | 5.489 | 0.76 | 15 | 4.742 | 0.55 | 15 | 0.75 [0.27, 1.22] | | | - | 94 | | |
| | | | | | | | _ | - 1. | | \perp | 1 | | |
| | | | | | | | | -4 | -2 | 0_ | 2 | 4 | |
| | | | | | | | | Fav | vours Dim Li | ght Favor | urs Bright | Light | |

^{*}Costa 1993: end of shift, first night, no dx

Figure S84. Bright Light vs Control (Cognitive Performance, Search and Memory test (Score)) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

| Expe | erimen | tal | C | ontrol | | Mean Difference | Mean Difference | | | | | |
|-------|--------|-------|-------------------------|--------------------|-----------------------|-----------------------------|---|--|--|--|--|--|
| Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fix | ced, 95% CI | | | | |
| | | | | | | | | | | | | |
| 5.165 | 0.68 | 15 | 4.842 | 1.11 | 15 | 0.32 [-0.34, 0.98] | | +- | | | | |
| | | | | | | _ | | | - 1 | | | |
| | | | | | | | -4 -2 | 0 2 | t Liabt | | | |
| | Mean | | 1245050128 0014924 MO10 | Mean SD Total Mean | Mean SD Total Mean SD | Mean SD Total Mean SD Total | Mean SD Total Mean SD Total IV, Fixed, 95% CI | Mean SD Total Mean SD Total IV, Fixed, 95% CI IV, Fix 5.165 0.68 15 4.842 1.11 15 0.32 [-0.34, 0.98] | Mean SD Total Mean SD Total IV, Fixed, 95% CI IV, Fixed, 95% CI 5.165 0.68 15 4.842 1.11 15 0.32 [-0.34, 0.98] | | | |

^{*}Costa 1993: end of shift, second night

Figure S85. Bright Light vs Control (Cognitive Performance, Search and memory test 3) [CMT = Not Established] RCT (Healthy participants)

| Bright Light | | | ht | Din | n Ligh | nt | Mean Difference | Mean Difference | | | | |
|-------------------|------|------|-------|------|--------|-------|--------------------|-----------------|----------------------|-----------|----------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixe | d, 95% CI | | |
| 20.31.1 Lab Study | | | | | | | | | | | | |
| Foret 1998 | 1 | 0.12 | 4 | 1 | 0.1 | 4 | 0.00 [-0.15, 0.15] | | <u> </u> | | | |
| | | | | | | | | _ | | | 1 | |
| | | | | | | | | -1 | -0.5 | Ó | 0.5 | |
| | | | | | | | | | Favours Bright Light | Favours D | im Light | |

^{*}Foret 1998: data extracted from the graph, night one averaged across the night, SEM converted to SD

Figure S86. Bright Light vs Control (Cognitive Performance, Search and memory test 5) [CMT = Not Established] RCT (Healthy participants)

| | Bright Light | | | | | t | Mean Difference | Mean Difference |
|-------------------|--------------|-----|-------|------|------|-------|---------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 20.32.1 Lab Study | | | | | | | | 1 |
| Foret 1998 | 1 | 0.1 | 4 | 1.01 | 0.12 | 4 | -0.01 [-0.16, 0.14] | 1 — |
| | | | | | | | | |
| | | | | | | | | -1 -0.5 0 0.5 Favours Bright Light Favours Dim Light |

^{*}Foret 1998: data extracted from the graph, night one averaged across the night, SEM converted to SD

Figure S87. Bright Light vs Control (Cognitive Performance, Reduced performance (%)) [CMT = Not Established] RCT (shift workers without a diagnosis of SWD)

| | Brig | ht Lig | ht | Dir | n Ligh | t | Mean Difference | Mean Difference | | | | |
|---------------------|------|--------|-------|------|--------|-------|------------------------|---|--|--|--|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | | | | |
| 19.23.1 Field Study | | | | | | | | | | | | |
| Bjorvatn 1999 | 14.5 | 9.8 | 18 | 24.9 | 13.6 | 18 | -10.40 [-18.14, -2.66] | - | | | | |
| | | | | | | | 100 | | | | | |
| | | | | | | | | -20 -10 0 10 20 Favours Bright Light Favours Dim Light | | | | |

Figure S88. Bright Light vs Control (Cognitive Performance, Dual Task control losses) [CMT = Not Established] RCT (Healthy participants)

| | Bri | ght Ligh | nt | (| Control | | Mean Difference | | N | lean Di | fference | | |
|--------------------|-------|----------|-------|-------|---------|-------|----------------------|-----|----------------------|---------------|----------------|----------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | ľ | V, Fixed | , 95% CI | | |
| 6.26.1 Lab Studies | | | | | | | | | | | | | |
| Wright 1997 | 24.07 | 11.13 | 10 | 28.34 | 12.84 | 10 | -4.27 [-14.80, 6.26] | | 30 | + | | | |
| | | | | | | | | + | | | | 1 | |
| | | | | | | | | -20 | -10 Favours Brigh | d it Light | ; Favours (| 1'0 Control | 20 |

^{*}Wright 1997: BL-2500 lux, dim light<100 lux, data averaged across night 1; SEM converted SD for study.

Figure S89. Bright Light vs Control (Cognitive Performance, Manikin (percent improvement)) [CMT = Not Established] RCT (Healthy participants)

| | Brigl | nt Lig | ht | Dim Light | | | Mean Difference | Mean Difference | | | | |
|-------------------|-------|--------|-------|-----------|------|-------|---------------------|-----------------|-------------------|-----------|--------------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed | I, 95% CI | | |
| 20.16.1 Lab Study | | | | | | | | | | or . | | |
| Campbell 1990 | 23.9 | 9 | 12 | 6.6 | 11.8 | 12 | 17.30 [8.90, 25.70] | | | - | | |
| | | | | | | | | | - 1 | | - | |
| | | | | | | | | -100 | -50 (|) | 50 | 100 |
| | | | | | | | | | Favours Dim Light | Favours E | 3right Light | |

^{*}Campbell 1990: data extracted from the graph. SEM converted to SD, data presented as percent improvement

Figure S90. Bright Light vs Control (Cognitive Performance, Switching Task- Mannequin Throughput) [CMT = Not Established] RCT (Healthy participants)

| | Bright Light | | | C | ontrol | | Mean Difference | | Mean Difference | |
|--------------------|--------------|------|-------|------|--------|-------|--------------------|-----|--------------------------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 95% CI | |
| 6.28.1 Lab Studies | | | | | | | | | 1 | |
| Wright 1997 | 2.62 | 3.19 | 10 | 2.11 | 4.17 | 9 | 0.51 [-2.86, 3.88] | | - 1 | |
| | | | | | | | | 1 | | |
| | | | | | | | | -10 | -5 0 5 | |
| | | | | | | | | | Favours Control Favours Bright Light | |

^{*}Wright 1997: BL-2500 lux, dim light<100 lux, data averaged across night 1, data reported as change from baseline SEM converted SD for study.

Figure S91. Bright Light vs Control (Cognitive Performance, Switching Task- Math Throughput) [CMT = Not Established] RCT (Healthy participants)

| | Bright Light | | | Control | | | Mean Difference | | Mean Difference | | | |
|-------------------|---------------------|-----|-------|---------|-----|-------|---------------------|-----|-------------------------|----------------------|---|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, | 95% CI | | |
| 6.29.1 Lab Study | | | | | | | | | 9 | | | |
| Wright 1997 | 22.72 | 4.9 | 10 | 23.74 | 3.9 | 9 | -1.02 [-4.98, 2.94] | | 1 | Total Control | | |
| | | | | | | | | 10 | | <u>į</u> | - | |
| | | | | | | | | -10 | -5 U Favours Control | Favours Bright Light | 1 | |

^{*}Wright 1997: BL-2500 lux, dim light<100 lux, data averaged across night 1; SEM converted SD for study.

Figure S92. Bright Light vs Control (Cognitive Performance, Average tracking score in MAT tracking task) [CMT = Not Established] RCT (Healthy participants)

| | Bright Light | | | C | ontrol | | Mean Difference | Mean Difference | | | | | |
|-------------------|--------------|------|-------|------|--------|-------|-------------------|-----------------|-----------------|----------|----------|-------------|-------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | ľ | V, Fixed | , 95% CI | | |
| 6.19.1 Lab Study | | | | | | | | | | 0 | | | |
| Figueiro 2016 | 37.9 | 4.54 | 17 | 33.7 | 4.54 | 17 | 4.20 [1.15, 7.25] | | | | 20 | - | |
| | | | | | | | | | | | | 1 | |
| | | | | | | | | -10 | -5 Favours (| Control | Favours | 5 Bright | 10 Light |

^{*}Figueiro 2016: White Light 361±4 lux, Dim Light < 5 lux. Crossover study, all participants in both arms, acceptable washout period. SEM converted to SD.

Figure S93. Bright Light vs Control (Cognitive Performance, Night 1 % Correct SALT) [CMT = Not Established] RCT (Healthy participants)

| | Bri | ght Ligh | nt | Control | | | Mean Difference | | Mean Difference | | | |
|-------------------|------------------------|----------|----|---------|------|-------|----------------------|-----|---------------------|-------------------|----|--|
| Study or Subgroup | Subgroup Mean SD Total | | | Mean SD | | Total | IV, Fixed, 95% CI | | IV, Fixed, 95 | % CI | | |
| 6.20.1 Lab Study | | | | | | | | | | | | |
| Campbell 1995 | 83.81 | 12.26 | 13 | 85.52 | 13.2 | 13 | -1.71 [-11.50, 8.08] | | - 1 | 96 | | |
| | | | | | | | | | | - 1 | | |
| | | | | | | | | -20 | -10 Ó | 10 | 20 | |
| | | | | | | | | | Favours Control Fav | ours Bright Light | t | |

^{*}Campbell 1995: BL >5000 lux (during the first 4 hours of NS1), dim light- <100 lux; Night 1 data was the average of timepoint during 2300-0700 (acute). SEM converted to SD, extracted from graphs.

Figure S94. Bright Light vs Control (Cognitive Performance, Night 1 Time to respond SALT) [CMT = Not Established] RCT (Healthy participants)

| | Brig | ht Lig | ht | C | ontrol | | Mean Difference | | Me | ean Differer | ice | |
|-------------------|------|--------|-------|------|--------|-------|---------------------|----|--------------|--------------|-------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, | Fixed, 95% | CI | |
| 6.22.1 Lab Study | | | | | | | | | | 33 | | |
| Campbell 1995 | 6.22 | 2.92 | 13 | 6.28 | 2.52 | 13 | -0.06 [-2.16, 2.04] | | - | - | | |
| | | | | | | | | _ | - 1 | | - 1 | |
| | | | | | | | | -4 | -2 | Ó | 2 | 4 |
| | | | | | | | | Fa | vours Bright | Light Favo | urs Control | |

^{*}Campbell 1995: BL >5000 lux (during the first 4 hours of NS1), dim light <100 lux; Night 1 data was the average of timepoint during 2300-0700 (acute). SEM converted to SD, extracted from graphs.

Figure S95. Bright Light vs Control (Cognitive Performance, Logical Reasoning (percent improvement)) [CMT = Not Established] RCT (Healthy participants)

| | Brig | ht Lig | ht | Co | ntro | I | Mean Difference | | Mean Difference |
|---------------------|------|--------|-------|------|------|-------|---------------------|-----|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 95% CI |
| 20.26.1 Lab Studies | | | | | | | | | |
| Campbell 1990 | 12.9 | 9.4 | 12 | 0.6 | 0.3 | 12 | 12.30 [6.98, 17.62] | | - |
| | | | | | | | | | |
| | | | | | | | | -50 | -25 0 25 50 Favours Control Favours Bright Light |

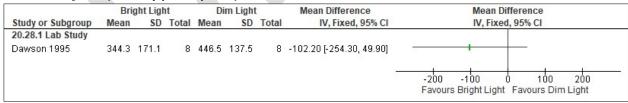
Campbell 1990: data extracted from the graph. SEM converted to SD, data presented as percent improvement

Figure S96. Bright Light vs Control (Cognitive Performance, Posner S-D AT Reaction Time (msec)) [CMT = Not Established] RCT (Healthy participants)

| | Brig | ht Lig | ht | Din | n Ligh | t | Mean Difference | | Mean Dif | ference | |
|-------------------|-------|--------|-------|-------|--------|-------|-------------------------|------|--------------------------------|--------------------------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed | , 95% CI | |
| 20.27.1 Lab Study | | | | | | | | | | | |
| Dawson 1995 | 580.9 | 93.6 | 8 | 673.9 | 82.9 | 8 | -93.00 [-179.64, -6.36] | | - | | |
| | | | | | | | | - | | | |
| | | | | | | | | -200 | -100 0 Favours Bright Light | 100 Favours Dim Light | 200 |

^{*}Dawson 1995: data extracted from graph, SEM converted to SD, data from night shift 1 used

Figure S97. Bright Light vs Control (Cognitive Performance, Posner Variability (msec)) [CMT = Not Established] RCT (Healthy participants)



^{*}Dawson 1995: data extracted from graph, SEM converted to SD, data from night shift 1 used

Figure S98. Bright Light vs Control (Cognitive Performance, Manikin Reaction Time (msec)) [CMT = Not Established] RCT (Healthy participants)

| | Brig | ht Light | t | Dim | Light | | Mean Difference | | Mean | Difference | <u> </u> | |
|-------------------|---------|----------|-------|----------|-------|-------|---------------------------|--------------|-------------------------|-----------------|------------------|------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fix | ed, 95% CI | | |
| 20.29.1 Lab Study | | | | | | | | | | 100 | | |
| Dawson 1995 | 1,309.6 | 336.3 | 8 | 1,454.49 | 283.7 | 8 | -144.89 [-449.78, 160.00] | 50 | - | | | |
| | | | | | | | | | - | | | - |
| | | | | | | | | -500 Favo | -250 ours Bright Lig | 0 ht Favour: | 250 s Dim Lig | 500 ght |

^{*}Dawson 1995: data extracted from graph, SEM converted to SD, data from night shift 1 used

Figure S99. Bright Light vs Control (Cognitive Performance, Manikin Throughput (msec)) [CMT = Not Established] RCT (Healthy participants)

| | Brigl | nt Light | | Dim | Light | | Mean Difference | Mean Difference |
|-------------------|----------|----------|-------|-----------|-------|-------|---------------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 20.30.1 Lab Study | | | | | | | | |
| Dawson 1995 | 1,442.31 | 565.7 | 8 | 1,688.462 | 467.8 | 8 | -246.15 [-754.82, 262.52] | - |
| | | | | | | | | -1000 -500 0 500 1000 |
| | | | | | | | | Favours Bright Light Favours Dim Light |

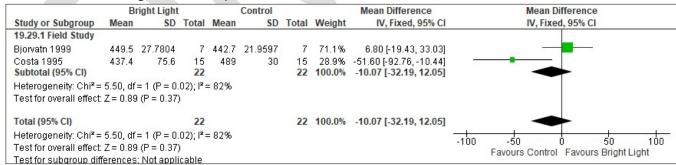
^{*}Dawson 1995: data extracted from graph, SEM converted to SD, data from night shift 1 used

Figure S100. Bright Light vs Control (Cognitive Performance, Simple reaction time) [CMT = Not Established] RCT

| | Bri | ght Ligh | nt | (| Control | | Mean Difference | | Mea | n Difference | |
|-------------------|-------|----------|-------|-------|---------|-------|-----------------------|------------|-----------------------|-----------------------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, F | ixed, 95% CI | |
| 20.34.1 Lab Study | | | | | | | | | | 9 (1) | |
| Smith 2008 | 26.31 | 25.77 | 12 | 47.52 | 41.47 | 12 | -21.21 [-48.83, 6.41] | · | 1 | | |
| | | | | | | | | | | | |
| | | | | | | | | -50 Fav | -25 ours Bright Li | 0 25 ght Favours Control | 50 |

Important Outcomes

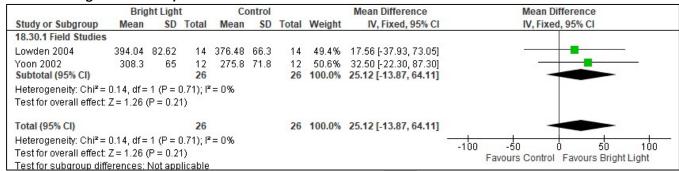
Figure S101. Bright Light vs Control (Total Sleep Time, Sleep Diary) [CMT = 15 min] non-RCT (shift workers without a diagnosis of SWD)



^{*}Costa 1995: Hours converted to minutes. Length of sleep between first- and second-night shifts.

Bjorvatn 1999: SEM converted to SD, at the platform data used

Figure S102. Bright Light vs Control (Total Sleep Time, Actigraphy) [CMT = 15 min] RCT (shift workers without a diagnosis of SWD)



^{*}Yoon 2002: Data averaged from 3 days, cross-over study (acceptable washout period), BL was 4-hour nocturnal light exposure of 4,000-6,000 lux.

Lowden 2004: Bright Light (2500 lux) or Normal light (300 lux) during their self-determined breaks during a night shift. Crossover, acceptable washout period. Data extracted from the graph and averaged; SEM converted to SD.

Figure S103. Bright Light vs Control (Total Sleep Time, Actigraphy) [CMT = 15 min] non-RCT (shift workers without a diagnosis of SWD)

| | Bri | ght Ligh | nt | C | ontrol | | Mean Difference | Mean Difference |
|-----------------------|-------|----------|-------|-------|--------|-------|------------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 18.31.1 Field Studies | | | | | | | | |
| Lowden 2012 | 259.6 | 85.19 | 7 | 277.4 | 60.8 | 16 | -17.80 [-87.59, 51.99] | |
| | | | | | | | | |
| | | | | | | | | -100 -50 0 50 100 Favours Control Favours Bright Light |

Lowden 2012: Bright light (650- 745 lux); pooled average from 3 nights. Control light (200 lux, weak yellow color); SEM converted to SD; hours converted to minutes

Figure S104. Bright Light vs Control (Mental Health, HADS) [CMT = Not Established] RCT (shift workers without a diagnosis of SWD)

| | Brig | ht Lig | ht | Co | ontro | ı | Mean Difference | Mean Diff | ference |
|--------------------|------|--------|-------|------|-------|-------|----------------------|----------------------|-----------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, | 95% CI |
| 7.29.1 Field Study | | | | | | | | | |
| Huang 2013 | 9.6 | 3.9 | 46 | 16.6 | 5.9 | 46 | -7.00 [-9.04, -4.96] | | |
| | | | | | | | | | |
| | | | | | | | | -10 -5 0 | 5 10 |
| | | | | | | | | Favours Bright Light | Favours Control |

^{*}Huang 2013: Bright light (7,000-10,000 lux for ≥ 30 min); Evening shift exposure took place between 19:30 and 20:30, while night shift exposure occurred between 23:00 and midnight. Higher scores on HADS indicate more severe impairment; used total score. No Dx.

Figure S105. Bright Light vs Control (Mental Health, Scale for shift-work complaints) [CMT = Not Established] non-RCT (shift workers without a diagnosis of SWD)

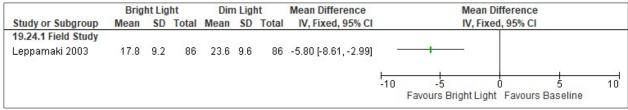


Figure S106. Bright Light vs Control (Mental Health, seven-point scale) [CMT = Not Established] RCT (shift workers without a diagnosis of SWD)

| Brigl | ht Lig | ht | Din | Ligh | nt | Mean Difference | | Me | an Differer | ice | |
|-------|--------|---------|---------------|--------------------|-----------------------|-----------------------------|---|---|---|--|---|
| Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, | Fixed, 95% | CI | |
| | | | | | | | | | 20 | | |
| 3.9 | 1.6 | 15 | 3.78 | 1.4 | 15 | 0.12 [-0.96, 1.20] | | | + | | |
| | | | | | | 85 ⁻ | - | | | | - |
| | Mean | Mean SD | Mean SD Total | Mean SD Total Mean | Mean SD Total Mean SD | Mean SD Total Mean SD Total | Mean SD Total Mean SD Total IV, Fixed, 95% CI | Mean SD Total Mean SD Total IV, Fixed, 95% CI | Mean SD Total Mean SD Total IV, Fixed, 95% CI IV, | Mean SD Total Mean SD Total IV, Fixed, 95% CI IV, Fixed, 95% | Mean SD Total Mean SD Total IV, Fixed, 95% CI IV, Fixed, 95% CI |

^{*}Costa 1993: end of shift, first night

Figure S107. Bright Light vs Control (Mental Health, seven-point scale) [CMT = Not Established] RCT (shift workers without a diagnosis of SWD)

| g. | ht Lig | nt | Din | n Ligh | nt | Mean Difference | Mean Difference |
|------|--------|-------------|--------------------|-----------------------------|--|---------------------------------|--|
| Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| | | | | | | | |
| 4.2 | 1.4 | 15 | 3.9 | 1.3 | 15 | 0.30 [-0.67, 1.27] | |
| | | | | | | 8 | -4 -2 0 2 4 |
| _ | 252 | 100 M 100 M | \$175 KR 8F 98000E | \$1500 89 99 WASSES 3019988 | CATTOL AND ANY MANAGES AND SHIPPING CATTOL | STOR AR BY WARREN SHOPPER STORY | Mean SD Total Mean SD Total IV, Fixed, 95% CI 4.2 1.4 15 3.9 1.3 15 0.30 [-0.67, 1.27] |

^{*}Costa 1993: end of shift, second night

Figure S108. Bright Light vs Control (Circadian Adaptation, MMSE) [CMT = Not Established], RCT (Healthy participants)

| | Brig | ht Lig | ht | C | ontrol | | Mean Difference | | Mean Di | fference | |
|--------------------|------|--------|-------|------|--------|-------|-------------------|-----|-------------------------|--------------------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed | 1, 95% CI | |
| 20.45.1 Free Sleep | | | | | | | | | | | |
| Horowitz 2001 | 5.07 | 4.07 | 13 | 0.94 | 2.21 | 14 | 4.13 [1.63, 6.63] | | | | |
| | | | | | | | | + | L | 1 | |
| | | | | | | | | -10 | -5 Favours Dim Light | 0 5 Favours Bright Light | 10 |

Figure S109. Bright Light vs Control (Circadian Adaptation, Phase shift MEL25%up (hours)) [CMT = Not Established], RCT (Healthy participants)

| | Brig | ht | Control | | | Mean Difference | Mean Difference | |
|--------------------------|------|-----|---------|------|-----|-----------------|--------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 20.43.1 Lab study | | | | | | | | V |
| Lammers-vanderHolst 2021 | 7.15 | 3.7 | 12 | 6.42 | 3.1 | 13 | 0.73 [-1.96, 3.42] | - |
| | | | | | | | - | |
| | | | | | | | | -4 -2 0 2 4 Favours Control Favours Bright Light |

Figure S110. Bright Light vs Control (Circadian Adaptation, Phase shift MEL25%down (hours)) [CMT = Not Established], RCT (Healthy participants)

| | Brig | ht | Control | | | Mean Difference | Mean Difference | | | |
|--------------------------|------|-----|---------|------|-----|-----------------|--------------------|--|--|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | | |
| 20.44.1 Lab study | | | | | | | | 9 | | |
| Lammers-vanderHolst 2021 | 6.47 | 3.6 | 12 | 4.76 | 3.4 | 13 | 1.71 [-1.04, 4.46] | · · | | |
| | | | | | | | - | | | |
| | | | | | | | | -4 -2 0 2 4 Favours Control Favours Bright Light | | |

Figure S111. Bright Light vs Control (Circadian Alignment, Overlap melatonin-sleep (hours)) [CMT = Not Established], RCTs (Healthy participants)

| | Brig | ht Lig | ht | Co | ntro | l i | Mean Difference | Mean Difference | | | | |
|--------------------------|------|--------|-------|------|------|-------|-------------------|-----------------|---------------|---------|--------------|-------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fix | ed, 95% | CI | |
| 20.45.1 Lab study | | | | | | | | | | | | |
| Lammers-vanderHolst 2021 | 4.9 | 2.8 | 12 | 2.62 | 2.8 | 13 | 2.28 [0.08, 4.48] | | | 7.0 | - | |
| | | | | | | | _ | - 4 | - i | | - 1 | 7 |
| | | | | | | | | -4 | -2 | Ò | 2 | 4 |
| | | | | | | | | | Favours Contr | ol Favo | urs Bright I | _ight |

Figure S112. Bright Light vs Control (Quality of life, Karolinska sleep diary) [CMT = Not Established] non-RCT (shift workers without a diagnosis of SWD)

| Bright Light | | | ht | Din | n Ligi | ht | Mean Difference | Mean Difference | | | | | |
|---------------------|------|-----|-------|------|--------|-------|----------------------|---------------------------------------|---|--|--|--|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | | | | | |
| 19.27.1 Field Study | | | | | | | | 80 | | | | | |
| Bjorvatn 1999 | 3.9 | 0.1 | 7 | 4.2 | 0.2 | 7 | -0.30 [-0.47, -0.13] | | | | | | |
| | | | | | | | 1 | | | | | | |
| | | | | | | | 3 | -1 -0.5 0 0.5 | | | | | |
| | | | | | | | | Favours Bright Light Favours Dim Ligh | t | | | | |

^{*}Bjorvatn 1999: SEM converted to SD, at the platform data used, (1, very good; 9, very bad)

Figure S113. Bright Light vs Control (Disease severity, ISI) [CMT = 8] RCT (shift workers without a diagnosis of SWD)

| | | | | | ontro | I | Mean Difference | Mean Difference | |
|--------------------|------|----|-------|------|-------|-------|------------------------|---|---------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | |
| 7.10.1 Field Study | | | | | | | | | |
| Huang 2013 | 5.7 | 5 | 46 | 16.9 | 3.2 | 46 | -11.20 [-12.92, -9.48] | + | |
| | | | | | | | | + | 1 1 |
| | | | | | | | | -20 -10 0 | 10 20 |
| | | | | | | | | Favours Bright Light Favours | Control |

^{*}Huang 2013: Nurses with ISI >14. Bright light (7,000-10,000 lux for \geq 30 min) 19:30- 20:30 (for evening shift) or 23:00- midnight (for night shift); ISI= insomnia severity index, lower is better.

Figure S114. Bright Light vs Control (WASO, Karolinska sleep diary) [CMT = Not Established] non-RCT (shift workers without a diagnosis of SWD)

| | Brig | ht Lig | ht | Din | Ligh | ht | Mean Difference | | Mea | n Difference | • | |
|---------------------|------|--------|-------|------|------|-------|--------------------|----|----------------|--------------|----------------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, F | ixed, 95% Cl | | |
| 19.28.1 Field Study | | | | | | | | | | | | |
| Bjorvatn 1999 | 3.9 | 0.1 | 7 | 3.8 | 0.1 | 7 | 0.10 [-0.00, 0.20] | | | - | | |
| | | | | | | | ŀ | | - | | | |
| | | | | | | | 1- | -1 | -0.5 | Ó | 0.5 | 185 |
| | | | | | | | | | Favours Dim Li | ght Favour | s Bright Light | |

^{*}Bjorvatn 1999: SEM converted to SD, at the platform data used, (1, many hours; 4, a few; 5, not awake), No dx

Figure S115. Bright Light vs Control (Wake After Sleep Onset, EEG) [CMT= 20 min], RCTs (Healthy participants)

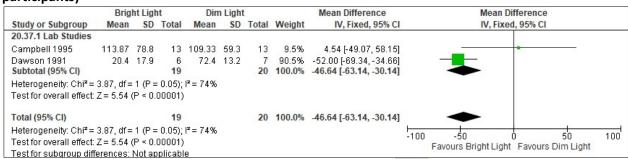


Figure S116. Bright Light vs Control (Sleep Latency, Karolinska sleep diary) [CMT = 20 min] RCT (shift workers without a diagnosis of SWD)

| | Bright Light | | | | n Ligi | ht | Mean Difference | Mean Difference | | | | |
|---------------------|--------------|-----|-------|------|--------|-------|--------------------|-----------------|---------------|---------------|---------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | ľ | V, Fixed, 95% | CI | |
| 19.31.1 Field Study | | | | | | | | | | 100 | | |
| Bjorvatn 1999 | 20.1 | 2.3 | 18 | 18.9 | 2.1 | 18 | 1.20 [-0.24, 2.64] | | | + | - | |
| | | | | | | | | _ | - | 700 | | |
| | | | | | | | | -10 | -5 | 0 | 5 | 11 |
| | | | | | | | | | Favours Brigh | nt Light Favo | ours Dim Ligh | it |
| | | | | | | | | | | | | |

Figure S117. Bright Light vs Control (Sleep Latency, Actigraphy) [CMT = 15 min] RCT (shift workers without a diagnosis of SWD)

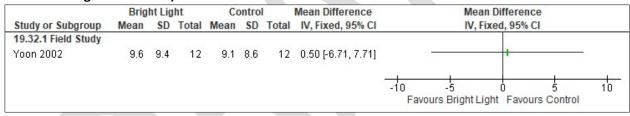
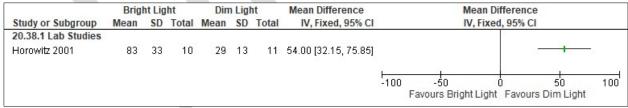
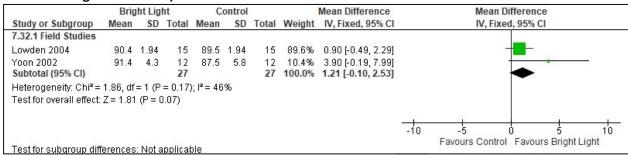


Figure S118. Bright Light vs Control (Sleep Latency, PSG/EEG) [CMT= 20 min], RCTs (Healthy participants)



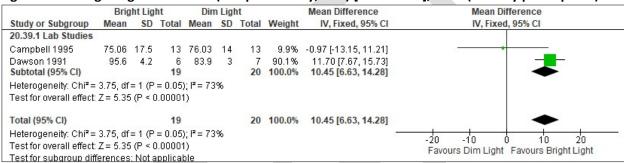
Horowitz 2001: free sleep, SD of sleep start, hours converted to minutes, healthy

Figure S119. Bright Light vs Control (Sleep Efficiency, Actigraphy) [CMT = 10%] RCT (shift workers without a diagnosis of SWD)



*Yoon 2002: Data from Days 2-3, cross-over study (acceptable washout period), BL was 4-hour nocturnal light exposure of 4,000-6,000 lux. Lowden 2004: Bright Light (2500 lux) or Normal light (300 lux) during their self-determined breaks during a night shift. Crossover, all participants counted in both arms (acceptable washout period). SEM converted to SD. No Dx.

Figure S120. Bright Light vs Control (Sleep Efficiency, EEG) [CMT= 10%], RCTs (Healthy participants)



Caffeine

Summary of Findings (GRADE)

Table S9. Caffeine in adults with shiftwork disorder

References: Schweitzer 2006, Wright 1997, Dagan 2006, Muehlbach 1995, McHill 2014, Babkoff 2002, Carrier 2007, Centofanti 2020

| Outcomes [Tool] | Certainty of the evidence (GRADE) | Absolute Difference Caffeine vs Control | No of Participants (studies) |
|--|-----------------------------------|---|---------------------------------|
| Excessive sleepiness or alertness [MWT] ^a | ⊕⊖⊖⊖ VERY LOW ^{b,c,d} | The mean difference in the caffeine group was 1.81 minutes more (0.13 more to 3.50 more) compared to control | 53 (2 RCTs) |
| Excessive sleepiness or alertness [SSS]e | LOM _p ,c | The mean difference in the caffeine group was 0.82 points lower (0.97 lower to 0.66 lower) compared to control | 68 (2 RCTs) |
| Excessive sleepiness or alertness [KSS]e | ⊕⊖⊖⊖ VERY LOW ^{b,c,d} | The mean difference in the caffeine group was 1.40 points lower (2.60 lower to 0.20 lower) compared to control | 33 (1 RCT) |
| Excessive sleepiness or alertness [MSLT]a | ⊕⊖⊖⊖ VERY LOW ^{b,c,d} | The mean difference in the caffeine group was 3.25 minutes higher (0.37 higher to 6.13 higher) compared to control | 30 (1 RCT) |
| Excessive sleepiness or alertness [VAS (arousal)]a,f | LOMc²ĕ ⊕⊕⊖⊖ | The mean difference in the caffeine group was 0.35 more (13.51 fewer to 14.21 more) compared to control | 22 (1 RCT) |

| Excessive sleepiness or alertness [VAS (alertness)]a,f | ⊕⊕⊖⊖ LOW ^{b,c} | The mean difference in the caffeine group was 14.12 higher (6.58 higher to 21.65 higher) compared to control | 60 (2 RCTs) |
|---|-----------------------------------|--|----------------|
| Excessive sleepiness or alertness [Samn Perelli Fatigue Scale] ^{e,f} | ⊕⊕⊖⊖ LOW ^{b,c} | The mean difference in the caffeine group was 1.62 lower (3.13 lower to 0.11 lower) compared to control | 12 (1 RCT) |
| Cognitive performance [PVT lapses] e | ⊕○○○ VERY LOW ^{b,c,d} | The mean difference in the caffeine group was 3.20 lapses fewer (5.53 fewer to 0.88 fewer) compared to control | 45 (2 RCTs) |
| Cognitive performance [multiple tests] f | ⊕⊕⊖⊖ LOW ^{b,d} | The evidence suggests caffeine increases cognitive performance slightly. 4 studies reported on the effect of caffeine on cognitive performance using the following tests: Torrance test of creative thinking, PVT mean reaction time, dual task, switching task, Wilkinson four choice reaction time, SALT, and a Flight simulator. The following studies were analyzed: Wright 1997, Muehlbach 1995, Dagan 2006, Babkoff 2002 | (4 RCTs) |

- a. Higher values favor the intervention
- b. Indirectness is due to the fact that participants included in the studies are healthy individuals. The effect in adults with SWD may be different.
- c. Imprecision due to small sample size (<200 participants)
- d. Imprecision due to 95% CI crossing the CMT
- e. Lower values favor the intervention
- f. CMT was not established by the TF
- g. Imprecision due to 95% CI crossing the null

Study Characteristics

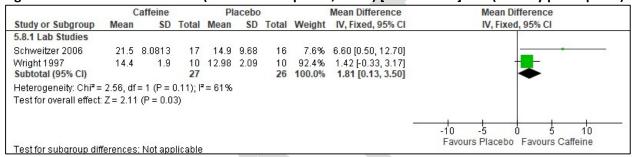
Table S10. Caffeine in adults with shiftwork disorder

| Study Citation | Study Design | Number of Participants (% Female) | Age in years | Population | Intervention (intensity) | Comparator | Time of Intervention Delivery | Duration of Follow-up |
|--------------------|-------------------|---|------------------------|---|---|--------------------|--|--------------------------|
| Babkoff 2002 | RCT, crossover | 12 (42) | 19-36 (Av: 24.6) | Shift workers without SWD diagnosis | Caffeine (200 mg) | placebo | caffeine or placebo given at 01:40 | 1 day |
| Carrier 2007 | RCT, | 17 (59) | 37.2 ±3.5 | Shift workers without SWD diagnosis | caffeine (200 mg) | Placebo | 1 capsule (100mg) 3h prior to bedtime and 2nd capsule (100mg) 1 hr prior to bedtime | 1 night |
| Centofanti 2020 | RCT, | 6 (67) | 21–36 y | Healthy participants | caffeine (200 mg) and nap (30 min) | Placebo and no nap | 3:30 | |
| Dagan 2006 | RCT, crossover | 24 (0) | 25 –31 | Healthy participants | Modafinil (200 mg) Caffeine (200 mg) | Placebo | 23:00 | 1 night |
| McHill 2014 | RCT | 30 (3) | 21.6 ± 3.5 | Healthy participants | Caffeine (200 mg) | Placebo | 5 hours before daytime sleep | 1 night |
| Muehlbach 1995 | RCT | 30 (47) | 24.3 | Healthy participants | Caffeine (2 mg/kg) | Placebo | between 01:20 and 01:50 | 5 nights |

| Schweitzer 2006 | RCT | 68 (53) | 31.3 | Healthy participants | caffeine (4 mg/kg) | placebo | caffeine taken 30 minutes prior to night shifts | 4 nights |
|--------------------|-----|---------|---------|-------------------------|---|---|---|----------|
| Wright 1997 | RCT | 46 (0) | 18–25 y | Healthy participants | Dim Light- Caffeine (≤100 lux/200 mg caffeine) | Dim Light- Placebo (≤100 lux/200 mg sugar) | bright light from 20.00 to 08.00 hours Caffeine at 20.00 and 02.00 hours each night | 2 nights |

Critical Outcomes

Figure S121. Caffeine vs Placebo (Excessive Sleepiness, MWT) [CMT= 2 min] RCT (Healthy participants)



^{*}Wright 1997: 200 mg caffeine was administered at 2000 and 0200. MWT data averaged over first night. SEM converted to SD. Schweitzer 2006: 4 mg/kg of caffeine taken 30 minutes prior to night shifts. MWT data night one study. Data extracted from graph; SEM converted to SD. Healthy

Figure S122. Caffeine vs Placebo (Excessive Sleepiness, SSS) [CMT= 1pt] RCT (Healthy participants)

| | Ca | ffeine | | Pl | acebo | | | Mean Difference | Mean Difference |
|-------------------------------------|----------|--------|---------|--------------------|-------|-------|--------|----------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 5.7.1 Lab Studies | | | | | | | | | |
| Dagan 2006 | 2.53 | 0.22 | 24 | 3.35 | 0.33 | 24 | 93.5% | -0.82 [-0.98, -0.66] | |
| Wright 1997 | 3.57 | 0.76 | 10 | 4.33 | 0.6 | 10 | 6.5% | -0.76 [-1.36, -0.16] | - |
| Subtotal (95% CI) | | | 34 | | | 34 | 100.0% | -0.82 [-0.97, -0.66] | • |
| Heterogeneity: Chi ² = (| 0.04, df | = 1 (P | = 0.85) | $ \cdot ^2 = 09$ | 6 | | | | |
| Test for overall effect: 2 | Z = 10.4 | 3 (P < | 0.0000 | 01) | | | | | |
| | | | | 100 | | | | | |
| | | | | | | | | _ | _ |
| | | | | | | | | | -2 -1 U 1 2 |
| Test for subgroup diffe | | | | | | | | | Favours Caffeine Favours Placebo |

^{*}Dagan 2006: 200 mg of caffeine administered at 23:00 h, data extracted from the figure, SSS Wright 1997: 200 mg total caffeine was administered at 100 mg at 20:00 h and 100 mg at 02:00 h. Used SSS data on first night. SEM converted to SD.

Figure S123. Caffeine vs Placebo (Excessive Sleepiness, KSS) [CMT= 1pt] RCT (Healthy participants)

| | Ca | ffein | е | Placebo | | | Mean Difference | Mean Difference | | | | | |
|--------------------|------|--|----|-------------------|-------------------|----|----------------------|-----------------|-------------|-----------|----------|-------|--|
| Study or Subgroup | Mean | an SD Total Mean SD Total IV, Fixed, 959 | | IV, Fixed, 95% CI | IV, Fixed, 95% CI | | | | | | | | |
| 5.77.1 Lab Studies | | | | | | | | | | 20 | | | |
| Schweitzer 2006 | 5.4 | 1.9 | 17 | 6.8 | 1.6 | 16 | -1.40 [-2.60, -0.20] | | - | | | | |
| | | | | | | | - | -4 | - 1 | | 1 | + | |
| | | | | | | | | т - | vours Caffe | eine Favo | urs Plac | ebo 4 | |

Schweitzer 2006: 4 mg/kg of caffeine taken 30 minutes prior to night shifts. KSS data only available on night 1.

Figure S124. Caffeine vs Placebo (Excessive Sleepiness, MSLT) [CMT= 1 min] RCT (Healthy participants)

| | C | affeine | | P | lacebo | | Mean Difference | Mean Difference |
|-------------------|-------|---------|-------|------|--------|-------|-------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| Muehlbach 1995 | 10.08 | 4.1828 | 15 | 6.83 | 3.873 | 15 | 3.25 [0.37, 6.13] | -10 -5 0 5 10 Favours Placebo Favours Caffeine |

^{*}Muehlbach 1995: Caffeine group received a mean of 142 mg (range: 98-197 mg) of caffeine at each nightly administration (2220 and 0120 hours), SEM converted to SD, data extracted from figure, data from night one, Healthy

Figure S125. Caffeine vs Placebo (Excessive Sleepiness/Alertness, VAS-arousal) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)

| | C | affeine | | P | lacebo | | Mean Difference | Mean Difference |
|-------------------|------|---------|-------|-------|--------|-------|----------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 5.9.1 Lab Study | | | | | | | | |
| Babkoff 2002 | 46.5 | 17.41 | 11 | 46.15 | 15.72 | 11 | 0.35 [-13.51, 14.21] | |
| | | | | | | | | |
| | | | | | | | | -20 -10 0 10 20 Favours Placebo Favours Caffeine |

^{*}Babkoff 2002: 200 mg caffeine given at 0140. Higher values mean higher arousal. Crossover study, acceptable washout period. Data extracted from graph (0230- end of shift); SEM converted to SD. No diagnosis

Figure S126. Caffeine vs Placebo (Excessive Sleepiness, VAS-Alertness) [CMT = Not Established] RCT (Healthy participants)

| | Ca | ffeine | | Pla | acebo | | | Mean Difference | Mean Difference | | |
|--------------------------|----------|--------|---------|--------------|----------------------------------|-----------------|--------|---------------------|-------------------|--|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI | | |
| McHill 2014 | 35.95 | 11.4 | 10 | 21.2 | 16.1 | 20 | 56.9% | 14.75 [4.76, 24.74] | | | |
| Muehlbach 1995 | 52.41 | 20.1 | 15 | 39.13 | 10.5 | 15 | 43.1% | 13.28 [1.80, 24.76] | | | |
| Total (95% CI) | | | 25 | | | 35 | 100.0% | 14.12 [6.58, 21.65] | | | |
| Heterogeneity: Chi2= | 0.04, df | = 1 (P | = 0.85) | $ I^2 = 09 $ | | -20 -10 0 10 20 | | | | | |
| Test for overall effect: | Z = 3.67 | (P = 0 | .0002) | | Favours Placebo Favours Caffeine | | | | | | |

^{*}Muehlbach 1995: Caffeine group received a mean of 142 mg (range: 98-197 mg) of caffeine at each nightly administration (2220 and 0120 hours), SEM converted to SD, data extracted from figure, data from night one, Healthy

Figure S127. Caffeine vs Placebo (Excessive Sleepiness, Samn Perelli Fatigue Scale) [CMT = Not Established] RCT (Healthy participants)

| | Caffeir | ne and | Nap | Placeb | o and | Nap | Mean Difference | | Me | an Difference | ce | |
|-------------------|---------|--------|-------|--------|-------|-------|----------------------|------|-----------------|---------------|---------------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, | Fixed, 95% (| CI | |
| 5.15.1 Lab Study | | | | | | | | | | | | |
| Centofanti 2020 | 3.6 | 1.27 | 6 | 5.22 | 1.4 | 6 | -1.62 [-3.13, -0.11] | | 200 | + | | |
| | | | | | | | | | | | - | |
| | | | | | | | | -10 | -5 | Ó | 5 | 10 |
| | | | | | | | | Favo | ours Caffeine & | Nap Favou | irs Placebo & | Nap |

^{*}Centofanti 2020: Caffeine give at 0325 (and 30 min nap at 0330). SP Fatigue Scale, higher numbers represent sleepier. Crossover study, acceptable washout period. Data extracted from graph (post-nap 0400-0445); SEM converted to SD.

Figure S128. Caffeine vs Placebo (Cognitive Performance, PVT lapses) [CMT= 1 lapse] RCTs (Healthy participants)

| | Ca | affeine | | PI | acebo | | | Mean Difference | | Mean Difference | |
|-----------------------------------|----------|---------|---------|-------------------------|-------|-------|--------|----------------------|-----|-----------------------------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | | IV, Fixed, 95% CI | |
| 6.22.1 Lab Studies | | | | | | | | | | | |
| Centofanti 2020 | 1.49 | 3.6 | 6 | 6.67 | 3.55 | 6 | 33.0% | -5.18 [-9.23, -1.13] | 64 | - | |
| Schweitzer 2006 | 5.45 | 4.16 | 17 | 7.68 | 4.16 | 16 | 67.0% | -2.23 [-5.07, 0.61] | | | |
| Subtotal (95% CI) | | | 23 | | | 22 | 100.0% | -3.20 [-5.53, -0.88] | | - | |
| Heterogeneity: Chi ² = | 1.37, df | = 1 (P | = 0.24) | $ \mathbf{r} ^2 = 27$ | % | | | | | | |
| Test for overall effect | Z = 2.70 | (P = 0 |).007) | | | | | | | | |
| Total (95% CI) | | | 23 | | | 22 | 100.0% | -3.20 [-5.53, -0.88] | | • | |
| Heterogeneity: Chi² = | 1.37, df | = 1 (P | = 0.24) | $ \mathbf{r} ^2 = 27$ | % | | | | 10 | <u> </u> | 40 |
| Test for overall effect: | Z = 2.70 | P = 0 | 0.007) | Ä. | | | | | -10 | Favours Caffeine Favours Placebo | 10 |
| Test for subgroup dif | ferences | : Not a | pplical | ole | | | | | | ravours Callellie Favours Placebo | |

^{*}Centofanti 2020: Caffeine give at 0325 (and 30 min nap at 0330). Crossover study, acceptable washout period. Data extracted from graph (post-nap 0400-0445); SEM converted to SD.

Schweitzer 2006: 4 mg/kg of caffeine taken 30 minutes prior to night shifts. Use PVT lapse ave (night 4). Data extracted from graph; SEM converted to SD.

Figure S129. Caffeine vs Placebo (Cognitive Performance, Torrance test of creative thinking (verbal/figural)) [CMT = Not Established] RCT (Healthy participants)

| Placebo Mean Difference Mean Difference | Placebo Mean Difference | | | | | Caffeine | | | | |
|---|-------------------------|------|-------|--------------------------------|-------|----------|------------------|--|--|--|
| Mean SD Total IV, Fixed, 95% CI IV, Fixed, 95% CI | Total | SD | Mean | tudy or Subgroup Mean SD Total | | | | | | |
| | | | | | | | 5.47.1 Lab Study | | | |
| -8.79 9.44 16 3.79 [-2.95, 10.53] | 16 | 9.44 | -8.79 | 17 | 10.31 | -5 | Schweitzer 2006 | | | |
| | | | | | | | | | | |
| | | | | | | | | | | |
| -10 -5 0 5 Favours Placebo Favours Caff | | | | | | | | | | |

^{*}Schweitzer 2006: 4 mg/kg of caffeine taken 30 minutes prior to night shifts. Torrance test of creative thinking was measured by change from baseline for standard score for fluency. (There were no significant group effects for the Torrance test in flexibility or originality). Only night average was given. Data extracted from graph; SEM converted to SD.

Figure S130. Caffeine vs Placebo (Cognitive Performance, modified PVT (mean reaction time)) [CMT = Not Established] RCT (Healthy participants)

| Ca | affeine | | Pla | acebo | | Mean Difference | Mean Difference | | | | |
|--------|---------|----------------------------|---------------|--------------------|-----------------------|-----------------------------|--|--|--|--|--|
| | | | | | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | | | | |
| | | | | | | | | | | | |
| 295.22 | 27.78 | 9 | 327.39 | 43.59 | 9 | -32.17 [-65.94, 1.60] | | | | | |
| | | | | | | | | | | | |
| | | | | | | | -100 -50 0 50 10 Favours Caffeine Favours Placebo | | | | |
| | Mean | 1577907 15902 - (7003-W100 | Mean SD Total | Mean SD Total Mean | Mean SD Total Mean SD | Mean SD Total Mean SD Total | Mean SD Total Mean SD Total IV, Fixed, 95% CI | | | | |

^{*}Wright 1997: 200 mg caffeine was administered at 2000 and 0200. Cognitive performance data averaged over first night (0030-0630). Data extracted from graphs; SEM converted to SD.

Figure S131. Caffeine vs Placebo (Cognitive Performance, dual task (control losses)) [CMT = Not Established] RCT (Healthy participants)

| | C | affeine | | P | lacebo | | Mean Difference | | Mea | n Differen | ce | |
|-------------------|-------|---------|-------|-------|--------|-------|----------------------|-----|----------------------|-----------------|------------------|---------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, F | ixed, 95% | CI | |
| 5.52.1 Lab Study | | | | | | | | | | | | |
| Wright 1997 | 19.21 | 14.01 | 10 | 28.34 | 12.84 | 10 | -9.13 [-20.91, 2.65] | 100 | + | | | |
| | | | | | | | | _ | | | | |
| | | | | | | | | -20 | -10 Favours Caffe | Ö eine Favoi | 10 urs Placeb | 20 0 |

^{*}Wright 1997: 200 mg caffeine was administered at 20:00 and 02:00. Cognitive performance data averaged over the first night (0030-0630). Data extracted from graphs; SEM converted to SD.

Figure S132. Caffeine vs Placebo (Cognitive Performance, switching task, mannequin (throughputchange from baseline)) [CMT = Not Established] RCT (Healthy participants)

| | Ca | ffeine | | Pla | acebo | | Mean Difference | Mean Difference |
|-------------------|------|--------|-------|------|-------|-------|--------------------|----------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 5.54.1 Lab Study | | | | | | | | 8 |
| Wright 1997 | 4.56 | 3.96 | 9 | 2.11 | 4.17 | 9 | 2.45 [-1.31, 6.21] | - |
| | | | | | | | | |
| | | | | | | | | -10 -5 0 5 10 |
| | | | | | | | | Favours Placebo Favours Caffeine |

^{*}Wright 1997: data averaged over the first night (0030-0630). Data extracted from graphs; SEM converted to SD.

Figure S133. Caffeine vs Placebo (Cognitive Performance, Wilkinson four choice reaction time (throughput)) [CMT = Not Established] RCT (Healthy participants)

| | Ca | affeine | | PI | acebo | | Mean Difference | | Mea | an Differ | ence | |
|-------------------|--------|---------|-------|--------|-------|-------|----------------------|-----|---------------------|-------------|----------------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, I | Fixed, 95 | 5% CI | |
| 5.53.1 Lab Study | | | | | | | | | | 20 | | |
| Wright 1997 | 168.89 | 22.99 | 10 | 158.25 | 19.64 | 10 | 10.64 [-8.10, 29.38] | | | Ø 34 | + | |
| | | | | | | | | _ | | | | |
| | | | | | | | | -50 | -25 Favours Plac | Ó ebo Fa | 25 vours Caffeine | 50 |

^{*}Wright 1997: data averaged over the first night (00:30-06:30). Data extracted from graphs; SEM converted to SD.

Figure S134. Caffeine vs Placebo (Cognitive Performance, switching task- math (throughput)) [CMT = Not Established] RCT (Healthy participants)

| | Ca | ffeine | | Pla | cebo |) | Mean Difference | | Mean Di | fference | |
|-------------------|-------|--------|-------|-------|------|-------|--------------------|-----|-----------------|------------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed | , 95% CI | |
| 5.55.1 Lab Study | | | | | | | | | | 85 | |
| Wright 1997 | 27.57 | 7.53 | 9 | 23.74 | 3.9 | 9 | 3.83 [-1.71, 9.37] | | 100 | + | |
| | | | | | | | | 1 | 10 | | |
| | | | | | | | | -10 | -5 (| 5 | 10 |
| | | | | | | | | | Favours Placebo | Favours Caffeine | 9 |

^{*}Wright 1997: data averaged over the first night (0030-0630). Data extracted from graphs; SEM converted to SD.

Figure S135. Caffeine vs Placebo (Cognitive Performance, SALT (Correct Responses (%)) [CMT = Not Established] RCT (Healthy participants)

| | Ca | ffein | е | Pla | cebo |) | Mean Difference | | Mean D | ifference | |
|-------------------|------|-------|-------|------|------|-------|--------------------|-----|-----------------|------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixe | d, 95% CI | |
| Muehlbach 1995 | 93.5 | 7.2 | 15 | 89.5 | 6.1 | 15 | 4.00 [-0.78, 8.78] | | | 1 | 剱 |
| | | | | | | | | -10 | -5 | 0 5 | 1 |
| | | | | | | | | | Favours Placebo | Favours Caffeine | |

^{*}Muehlbach 1995: data from night one

Figure S136. Caffeine vs Placebo (Cognitive Performance, SALT (Correction time (seconds)) [CMT = Not Established] RCT (Healthy participants)

| | Ca | Caffeine Placebo | | | |) | Mean Difference | Mean Difference | | | | | |
|-------------------|------|-----------------------------|----|-----|-----|-------|---------------------|-------------------|-----------|-------------|--------------|----|--|
| Study or Subgroup | Mean | Mean SD Total Mean SD Total | | | | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | | | | | |
| Muehlbach 1995 | 6.8 | 2.4 | 15 | 7.7 | 2.6 | 15 | -0.90 [-2.69, 0.89] | | | -+- | | | |
| | | | | | | | | -10 | -5 | Ó | 5 | 10 | |
| | | | | | | | | | Favours C | affeine Fav | ours Placebo | | |

^{*}Muehlbach 1995: data from night one

Figure S137. Caffeine vs Placebo (Cognitive Performance, SALT (Nonfaulty items (%)) [CMT = Not Established] RCT (Healthy participants)

| | Ca | Caffeine | | Pla | cebo |) | Mean Difference | Mean Difference |
|-------------------|------|-------------------------------|----|---------------|------|----|---------------------|--|
| Study or Subgroup | Mean | Mean SD Total I 0.2 0.5 15 | | Mean SD Total | | | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| Muehlbach 1995 | 0.2 | 0.5 | 15 | 0.7 | 0.9 | 15 | -0.50 [-1.02, 0.02] | |
| | | | | | | | -2 | 2 -1 Ö 1 Favours Caffeine Favours Placebo |

^{*}Muehlbach 1995: data from night one

Figure S138. Caffeine vs Placebo (Cognitive Performance, SALT (Empty items (%)) [CMT = Not Established] RCT (Healthy participants)

| | Ca | Caffeine | | Pla | ceb |) | Mean Difference | Mean Difference | | | | |
|-------------------|------|----------|-------|------|-----|-------|----------------------|-----------------|---------------------------------|----|--|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 95% CI | | | |
| Muehlbach 1995 | 0.1 | 0.2 | 15 | 0.3 | 0.3 | 15 | -0.20 [-0.38, -0.02] | 200 | -+- | | | |
| | | | | | | | | -2 | -1 0 1 | | | |
| | | | | | | | | | Favours Caffeine Favours Placel | 00 | | |

^{*}Muehlbach 1995: data from night one

Figure S139. Caffeine vs Placebo (Cognitive Performance, Flight Simulator (deviation from altitude)) [CMT = Not Established] RCT (Healthy participants)

| | Ca | Caffeine | | Placebo | | | Mean Difference | Mean Difference | | | | |
|-------------------|-------|----------|-------|---------|------|-------|--------------------------|-----------------|-----------------|-----|--|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed | I, 95% CI | | | |
| Dagan 2006 | 556.9 | 38.5 | 24 | 637.1 | 53.5 | 24 | -80.20 [-106.57, -53.83] | - | 50 | 100 | | |
| | | | | | | | | | Favours Placebo | | | |

^{*}Dagan 2006: data extracted from the figure

Figure S140. Caffeine vs Placebo (Cognitive Performance, Flight Simulator (deviation from velocity)) [CMT = Not Established] RCT (Healthy participants)

| | Ca | Caffeine | | | acebo | | Mean Difference | Mean Difference | | | | | |
|-------------------|-------|----------|----|-------|-------|-------|----------------------|-----------------|-------------------|-----------------|---|--|--|
| Study or Subgroup | Mean | | | | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 95% CI | | | | |
| Dagan 2006 | 35.12 | 3.83 | 24 | 42.05 | 4.19 | 24 | -6.93 [-9.20, -4.66] | | ,— | | | | |
| | | | | | | | | -20 | -10 | 0 10 | 2 | | |
| | | | | | | | | | Favours Caffeine | Favours Placebo | | | |

^{*}Dagan 2006: data extracted from the figure, 5 am and 7 am data pooled

Figure S141. Caffeine vs Placebo (Cognitive Performance, choice reaction time) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)

| | C | affeine | | P | lacebo | | Mean Difference | Mean Difference |
|-------------------|--------|---------|-------|--------|--------|-------|--------------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Random, 95% CI | IV, Random, 95% CI |
| 6.21.1 Lab Study | | | | | | | | |
| Babkoff 2002 | 695.35 | 200.66 | 11 | 802.52 | 241.02 | 11 | -107.17 [-292.50, 78.16] | |
| | | | | | | | | |
| | | | | | | | | -500 -250 0 250 500 Favours Caffeine Favours Placebo |

^{*}Babkoff 2002: 200 mg caffeine given at 0140. Choice reaction timed measured in milliseconds. Crossover study, acceptable washout period. Data extracted from graph (0230- end of shift); SEM converted to SD. Also, side note the visuo-spatial discrimination did not differ over treatment conditions. No Diagnosis

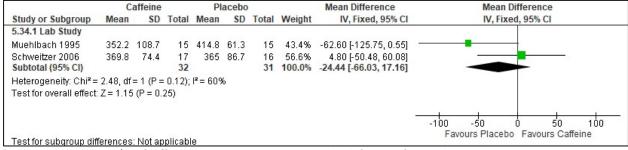
Figure S142. Caffeine vs Placebo (Cognitive Performance, trials without false alarms during the letter cancellation task) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)

| • | | | | | • | | | 0 , |
|-------------------|------|---------|-------|------|-------|-------|--------------------|----------------------------------|
| | Ca | affeine | | PI | acebo | | Mean Difference | Mean Difference |
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Random, 95% CI | IV, Random, 95% CI |
| 5.44.1 Lab Study | | | | | | | | |
| Babkoff 2002 | 6.4 | 0.07 | 11 | 6.11 | 0.33 | 11 | 0.29 [0.09, 0.49] | 2 |
| | | | | | | | | |
| | | | | | | | | -1 -0.5 0 0.5 1 |
| | | | | | | | | Favours Placebo Favours Caffeine |
| | | | | | | | | |

^{*}Babkoff 2002: 200 mg caffeine given at 0140. Number of trials without false alarms measured during letter cancellation task. Crossover study, acceptable washout period. Data extracted from graph (only night average given); SEM converted to SD. No Diagnosis

Important Outcomes

Figure S143. Caffeine vs Placebo (TST, PSG) [CMT= 15 min] RCT (Healthy participants)



^{*}Schweitzer 2006: 4 mg/kg of caffeine taken 30 minutes prior to night shifts. Data from night one

Muehlbach 1995: Caffeine group received a mean of 142 mg (range: 98-197 mg) of caffeine at each nightly administration (2220 and 0120 hours), data from night one, healthy

Figure S144. Caffeine vs Placebo (Total Sleep Time, PSG) [CMT= 15 min] RCT (Shift workers without SWD diagnosis)

| | C | affeine | | PI | acebo | | Mean Difference | Mean Difference | | | | | |
|-------------------|-------|---------|-------|---------------|-------|----|--------------------------|--|--|--|--|--|--|
| Study or Subgroup | Mean | SD | Total | al Mean SD To | | | IV, Fixed, 95% CI | IV, Fixed, 95% CI | | | | | |
| 5.38.1 Lab Study | | | | | | | | * | | | | | |
| Carrier 2007 | 264.5 | 93.59 | 17 | 346.2 | 67.2 | 17 | -81.70 [-136.47, -26.93] | - | | | | | |
| | | | | | | | | | | | | | |
| | | | | | | | | -200 -100 0 100 20 Favours Placebo Favours Caffeine | | | | | |

^{*}Carrier 2007: Day sleep group (n=17) sleep deprived for 25 hrs and recovery sleep started in the morning, 1 hr after their habitual wake time. Caffeine given in 2 capsules, 1 capsule (100mg) 3h prior to bedtime and 2nd capsule (100mg) 1 hr prior to bedtime. Crossover, acceptable washout period. SEM converted to SD. No diagnosis

Figure S145. Caffeine vs Placebo (TST, Subjective Questionnaire) [CMT= 15 min] RCT (Healthy participants)

| | C | affeine | | Placebo | | | Mean Difference | Mean Difference | | | | |
|-------------------|------|---------|-------|---------|------|-------|-------------------------|----------------------------------|--|--|--|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | | | | |
| 5.62.1 Lab Study | | | | | | | | | | | | |
| Muehlbach 1995 | 375 | 116.1 | 15 | 442 | 45.9 | 15 | -67.00 [-130.18, -3.82] | | | | | |
| | | | | | | | | -100 -50 0 50 100 | | | | |
| | | | | | | | | Favours Placebo Favours Caffeine | | | | |

Muehlbach 1995: Caffeine group received a mean of 142 mg (range: 98-197 mg) of caffeine at each nightly administration (2220 and 0120 hours), data from night one, healthy

Figure S146. Caffeine vs Placebo (WASO, Subjective Questionnaire) [CMT= 20 min] RCT (Healthy participants)

| | C | affeine | | Pla | acebo | | Mean Difference | Mean Difference |
|-------------------|-------|---------|-------|------|-------|-------|-----------------------|----------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 5.65.1 Lab Study | | | | | | | | ľ |
| Muehlbach 1995 | 103.4 | 108.3 | 15 | 67.2 | 61.7 | 15 | 36.20 [-26.88, 99.28] | - |
| | | | | | | | | |
| | | | | | | | | -100 -50 0 50 100 |
| | | | | | | | | Favours Caffeine Favours Placebo |

Muehlbach 1995: Caffeine group received a mean of 142 mg (range: 98-197 mg) of caffeine at each nightly administration (22:20 and 01:20 hours), data from night one, healthy

Figure S147. Caffeine vs Placebo (Sleep Latency, PSG) [CMT= 20 min] RCT (Healthy participants)

| | Ca | ffein | е | PI | acebo | Mean Difference | | | Mean Di | | | |
|-------------------|------|-------|-------|------|-------|-----------------|---------------------|-----|------------------|-----------|--------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed | 1, 95% CI | | |
| 5.63.1 Lab Study | | | | | | | | | | 9 | | |
| Muehlbach 1995 | 4.2 | 3.8 | 15 | 5.7 | 11.5 | 15 | -1.50 [-7.63, 4.63] | | - | | 76 | |
| | | | | | | | | - | - 1 | | 1 | |
| | | | | | | | | -10 | -5 | Ò | 5 | 1 |
| | | | | | | | | | Favours Caffeine | Favours P | lacebo | |

Muehlbach 1995: Caffeine group received a mean of 142 mg (range: 98-197 mg) of caffeine at each nightly administration (2220 and 0120 hours), data from night one, healthy

Figure S148. Caffeine vs Placebo (Sleep Latency, PSG) [CMT= 20 min] RCT (Shift workers without SWD diagnosis)

| | Ca | affeine | | Placebo | | | Mean Difference | Mean Difference | | | | | |
|-------------------|------|---------|-------|---------|------|-------|--------------------|-----------------|----------------|------|---------|---------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fi | xed, | 95% CI | | |
| 5.41.1 Lab Study | | | | | | | | | | 28 | | | |
| Carrier 2007 | 6.4 | 7.42 | 17 | 3.6 | 4.12 | 17 | 2.80 [-1.23, 6.83] | | | | + | | |
| | | | | | | | | _ | - | | | 1 | |
| | | | | | | | | -10 | -5 | Ó | | 5 | 10 |
| | | | | | | | | | Favours Caffei | ne | Favours | Placebo | |

^{*}Carrier 2007: Day sleep group (n=17) sleep deprived for 25 hrs and recovery sleep started in the morning, 1 hr after their habitual wake time. Caffeine given in 2 capsules, 1 capsule (100mg) 3h prior to bedtime and 2nd capsule (100mg) 1 hr prior to bedtime. Crossover, acceptable washout period. SEM converted to SD. No diagnosis

Figure S149. Caffeine vs Placebo (Sleep Latency, Subjective Questionnaire) [CMT= 20 min] RCT (Healthy participants)

| | Caffeine | | Pla | cebo |) | Mean Difference | Mean Difference | |
|-------------------|----------|-------|-------|------|----------|-----------------|-----------------------|----------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD Total | | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 5.64.1 Lab Study | | | | | | | | |
| Muehlbach 1995 | 49 | 119.7 | 15 | 14.3 | 9 | 15 | 34.70 [-26.05, 95.45] | - |
| | | | | | | | | |
| | | | | | | | | -100 -50 Ó 50 10 |
| | | | | | | | | Favours Caffeine Favours Placebo |

Muehlbach 1995: Caffeine group received a mean of 142 mg (range: 98-197 mg) of caffeine at each nightly administration (22:20 and 01:20 hours), data from night one, healthy

Figure S150. Caffeine vs Placebo (Sleep Efficiency, PSG) [CMT= 10%] RCT (Healthy participants)

| C | affeine | Placebo | | | Mean Difference | Mean Difference | |
|------|---------|---------------------------------|---------------|--------------------|-----------------------|-----------------------------|--|
| Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| | | | | | | | |
| 73 | 11.31 | 8 | 81 | 11.31 | 8 | -8.00 [-19.08, 3.08] | - + + |
| | | | | | | 1000 M | |
| | | | | | | | 50 -25 0 25 50 |
| | | | | | | | Favours Placebo Favours Caffeine |
| | Mean | Caffeine Mean SD 73 11.31 | Mean SD Total | Mean SD Total Mean | Mean SD Total Mean SD | Mean SD Total Mean SD Total | Mean SD Total Mean SD Total IV, Fixed, 95% CI 73 11.31 8 81 11.31 8 -8.00 [-19.08, 3.08] |

^{*}Batejat 2006: 300 mg caffeine given at midnight. Sleep efficiency index (%) measured by PSG during recovery sleep (0900-1500). Crossover, acceptable washout period. SEM converted to SD. healthy

Figure S151. Caffeine vs Placebo (Sleep Efficiency, PSG) [CMT= 10%] RCT (Shift workers without SWD diagnosis)

| | C | Caffeine Pla | | | Placebo Mean Difference | | | | Mean Difference | | | |
|-------------------|------|---------------|----|------|-------------------------|-------|------------------------|------------|-------------------|------------------|----------------|----|
| Study or Subgroup | Mean | SD Total Mean | | | | Total | IV, Fixed, 95% CI | | IV, F | Fixed, 95% CI | | |
| 5.42.1 Lab Study | | | | | | | | | | | | |
| Carrier 2007 | 58.5 | 22.68 | 17 | 76.5 | 16.08 | 17 | -18.00 [-31.22, -4.78] | 18 | - | | | |
| | | | | | | | | + | | | - | |
| | | | | | | | | -50 Far | -25 vours Plac | 0 ebo Favours | 25 Caffeine | 50 |

^{*}Carrier 2007: Day sleep group (n=17) sleep deprived for 25 hrs and recovery sleep started in the morning, 1 hr after their habitual wake time. Caffeine given in 2 capsules, 1 capsule (100mg) 3h prior to bedtime and 2nd capsule (100mg) 1 hr prior to bedtime. Crossover, acceptable washout period. SEM converted to SD. No diagnosis

Clockwise rotating shift schedule

Summary of Findings (GRADE)

Table S11. Clockwise rotating shift schedule in adults with shiftwork disorder

References: Tucker 2000, Viitasalo 2008, Viitasalo 2015, Vangelova 2008, Shon 2016, DiMuzio 2021, Lavie 1992, Shiffer 2018, Cruz 2003 (Part 1), Cruz 2003 (Part II)

| Outcomes [Tool] | Certainty of the evidence (GRADE) | Absolute Difference Clockwise shift vs Counterclockwise shift | No of Participants (studies) |
|---|-----------------------------------|---|---------------------------------|
| Excessive sleepiness or alertness [KSS] ^a | ⊕○○○ VERY LOW ^{b,c,d} | The mean difference in the clockwise shift was 1.45 points fewer (2.08 fewer to 0.83 fewer) compared to counterclockwise shift | 170 (2 non-RCTs) |
| Excessive sleepiness or alertness [ESS] ^a | ⊕⊖⊖⊖ VERY LOW ^{c,e} | The mean difference in the clockwise shift was 0.85 points fewer (1.93 fewer to 0.23 more) compared to counterclockwise shift | 166 (2 non-RCTs) |
| Excessive sleepiness or alertness [SSS] ^a | ⊕○○○ VERY LOW ^{c,d,f} | The mean difference in the clockwise shift was 1.2 points fewer (2.43 fewer to 0.03 more) compared to counterclockwise shift | 23 (1 non-RCT) |
| Excessive sleepiness or alertness [morning questionnaire]g,h | ⊕○○○ VERY LOW ^c | The mean difference in the clockwise shift was 17.3 higher (2.37 higher to 32.23 higher) compared to counterclockwise shift | 33 (1 non-RCT) |
| Excessive sleepiness or alertness [Correct responses during Bakan Vigilance Task] ^{a,g} | ⊕○○○ VERY LOW ^{c,f,i} | The mean difference in the clockwise shift was 8.56 lower (28.02 lower to 10.9 higher) compared to counterclockwise shift | 23 (1 non-RCT) |
| Sleep quality [Karolinska Sleep Diary] ^{g,h} | ⊕○○○ VERY LOW ^{c,i} | The mean difference in the clockwise shift was 0.58 points higher (0.01 lower to 1.17 higher) compared to counterclockwise shift | 25 (1 non-RCT) |
| Sleep Quality [PSQI] ^a | ⊕⊕○○ LOW | The mean difference in the clockwise group was 0.6 lower (0.84 lower to 0.36 lower) compared to counterclockwise | 4750 (1 non-RCT) |
| Sleep quality [Modified SSI] ^{a,g} | ⊕○○○ VERY LOWb,i | The mean difference in the clockwise group was 0 (0.15 lower to 0.15 higher) compared to counterclockwise | 611 (1 non-RCT) |
| Cognitive performance [multiple tests] ^g | ⊕○○○ VERY LOW ^c | The evidence is very uncertain about the effect of clockwise shift rotation on cognitive performance. Cognitive performance was measured using mean reaction time on PVT, speed on PVT, fastest 10% on PVT, slowest 10% on PVT, and a subjective report on the difficulty concentrating at work. The studies included were DIMuzzio 2021 and Shiffer 2018 | (2 non-RCTs) |

- a. Lower values favor the intervention
- b. There was unexplained inconsistency that was supported by nonoverlapping confidence intervals, high I2 values, and statistically significant heterogeneity of effect estimates.
- c. Imprecision due to small sample size (<200 participants)
- d. Imprecision due to the 95% CI crossing the CMT
- e. Risk of bias concerns due to lack of allocation concealment
- f. Indirectness is due to the fact that participants included in the studies are healthy individuals. The effect in adults with SWD may be different
- g. CMT was not established by the TF
- h. Higher values favor the intervention
- i. Imprecision due to the 95% CI crossing the null

Study Characteristics

Table S12. Clockwise rotating shift schedule in adults with shiftwork disorder

| Study Citation | Study Design | Number of Participants (% Female) | Age in years | Population | Intervention | Comparator | Duration of Follow- up |
|-------------------|--------------|---|------------------|---|--------------------------|---------------------------------|------------------------------|
| Cruz 2003 (I) | non-RCT | 28 (57) | 41.2 | Healthy participants | Clockwise shift rotation | Counterclockwise shift rotation | 1 week |
| Cruz 2003 (II) | non-RCT | 28 (57) | 41.2 | Healthy participants | Clockwise shift rotation | Counterclockwise shift rotation | 1 week |
| Di Muzio 2021 | non-RCT | 144 (64) | 41.3 (0.8) | Shift workers without SWD diagnosis | Clockwise shift rotation | Counterclockwise shift rotation | 3 days |
| Lavie 1992 | non-RCT | 33 (27) | 28.3 ± 5.03 | Shift workers without SWD diagnosis | Clockwise shift rotation | Counterclockwise shift rotation | 20 days |
| Shiffer 2018 | non-RCT | 100 (100) | 30 ± 5.5 | Shift workers without SWD diagnosis | Clockwise shift rotation | Counterclockwise shift rotation | 6 days |
| Shon 2016 | non-RCT | 4750 (63) | 27.5 ± 4.4 | Shift workers without SWD diagnosis | Clockwise shift rotation | Counterclockwise shift rotation | |
| Tucker 2000 | non-RCT | 611 (2) | 39.8 ± 0.85(SE) | Shift workers without SWD diagnosis | Clockwise shift rotation | Counterclockwise shift rotation | 28 days |
| Vangelova 2008 | non-RCT | 25 (68) | 48.3 ± 6.7 | Shift workers without SWD diagnosis | Clockwise shift rotation | Counterclockwise shift rotation | 2 weeks |
| Viitasalo 2008 | non-RCT | 84 (0) | 42.7 | Shift workers without SWD diagnosis | Clockwise shift rotation | Counterclockwise shift rotation | 8 months |
| Viitasalo 2015 | non-RCT | 319 (0) | not specified | Shift workers without SWD diagnosis | Clockwise shift rotation | Counterclockwise shift rotation | 2.5 years |

Critical Outcomes

Figure S152. Clockwise rotating shift vs Counterclockwise rotating shift (Excessive Sleepiness, KSS) [CMT = 1 pt] Non-randomized studies (shift workers without SWD diagnosis)

| | Clo | ckwis | e | Counte | rclocky | vise | | Mean Difference | Mean Difference |
|-----------------------------------|----------|----------|---------|--------------------------|---------|-------|--------|----------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 8.1.1 Field Study (No | Diagnos | is) | | | | | | | |
| DiMuzzio 2021 | 6.9 | 2.7 | 80 | 8.9 | 1.6 | 65 | 77.0% | -2.00 [-2.71, -1.29] | |
| Vangelova 2008 | 7.1 | 1.33 | 13 | 6.73 | 1.9 | 12 | 23.0% | 0.37 [-0.93, 1.67] | - • |
| Subtotal (95% CI) | | | 93 | | | 77 | 100.0% | -1.45 [-2.08, -0.83] | • |
| Heterogeneity: Chi ² = | 9.90, df | = 1 (P | = 0.003 | 2); $I^2 = 909$ | % | | | | |
| Test for overall effect | Z = 4.59 | 9 (P < 0 | 0.00001 |) | | | | | |
| Total (95% CI) | | | 93 | | | 77 | 100.0% | -1.45 [-2.08, -0.83] | • |
| Heterogeneity: Chi²= | 9.90, df | = 1 (P | = 0.000 | 2); I ² = 909 | % | | | - | |
| Test for overall effect | Z = 4.59 |) (P < 0 | 0.00001 |) | | | | | Favours Clockwise Favours Counterclockwise |
| Test for subaroup dif | ferences | : Not a | pplicat | ole | | | | | Favours Clockwise Favours Counterclockwise |

^{*}Vangelova 2008: Data extracted from graph, averaged over Night Shift DiMuzzio 2021: SEM converted to SD, data extracted from figure

Figure S153. Clockwise rotating shift vs Counterclockwise rotating shift (Excessive Sleepiness, ESS) [CMT = 2 pt] Non-randomized studies (Shift workers without SWD diagnosis)

| | Clo | ckwis | e | Counte | rclocky | wise | | Mean Difference | Mean Difference |
|-----------------------------------|------------|----------|---------|------------------|---------|-------|--------|----------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 8.2.1 Field Study (No | Diagnos | sis) | | | | | | | |
| Viitasalo 2008 | 6.2 | 3.5 | 40 | 8.3 | 3.9 | 22 | 30.4% | -2.10 [-4.06, -0.14] |] |
| Viitasalo 2015 | 5.6 | 3.13 | 61 | 5.9 | 3.44 | 43 | 69.6% | -0.30 [-1.59, 0.99] | <u> </u> |
| Subtotal (95% CI) | | | 101 | | | 65 | 100.0% | -0.85 [-1.93, 0.23] | • |
| Heterogeneity: Chi ² = | = 2.26, df | = 1 (P | = 0.13 | $ ^2 = 56\%$ | 6 | | | | |
| Test for overall effect | : Z= 1.54 | (P = 0 | 0.12) | | | | | | |
| Total (95% CI) | | | 101 | | | 65 | 100.0% | -0.85 [-1.93, 0.23] | 1 |
| Heterogeneity: Chi ² = | = 2.26, df | = 1 (P | = 0.13) | $ ^2 = 56\%$ | 6 | | | | 10 1 |
| Test for overall effect | Z = 1.54 | I(P = 0) | 0.12) | di. | | | | | -10 -5 0 5 1 Favours Clockwise Favours Counterclockwise |
| Test for subaroup dif | fferences | : Not a | pplical | ole | | | | | Favours Clockwise Favours Counterclockwise |

^{*}Viitasalo 2008: Rapidly rotating (Forward/CW) vs the old shift (Backward/CCW).

Viitasalo 2015: both age groups (<45 yrs and >45 yrs were averaged together)

Figure S154. Clockwise rotating shift vs Counterclockwise rotating shift (Excessive Sleepiness, SSS) [CMT = 1 pt] Non-randomized study (Healthy participants)

| | Favours | Clocky | vise | Counte | rclocky | vise | Mean Difference | Mean Difference | | | | |
|-----------------------|-------------|---------|-----------|---|---------|------|---------------------|-----------------|---------------|------------|-------------|-----------|
| Study or Subgroup | Mean | SD | Total | I Mean SD Total IV, Fixed, 95% CI IV, Fixed | | | | | | | CI | |
| 11.2.2 Lab Study (Not | t typically | perforn | ning shif | ftwork) | | | | | | 10 | | |
| Cruz 2003 (Part I) | 4.9 | 1.7 | 9 | 6.1 | 1 | 14 | -1.20 [-2.43, 0.03] | - | | | | |
| | | | | | | | _ | 9 | | | | |
| | | | | | | | | -4 | -2 | Ó | Ż | 4 |
| | | | | | | | | | Favours Clock | wise Favor | urs Counter | clockwise |

^{*}Cruz 2003 (Part I): Clockwise vs Counterclockwise; SSS (higher is sleepier)

Figure S155. Clockwise rotating shift vs Counterclockwise rotating shift (Excessive Sleepiness, morning questionnaire) [CMT = Not Established] Non-randomized study (Shift workers without SWD diagnosis)

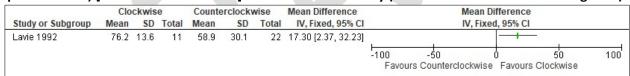
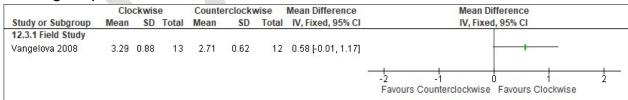


Figure S156. Clockwise rotating shift vs Counterclockwise rotating shift (Sleep Quality, Karolinska Sleep Diary: Sleep Qual Index) [CMT = Not Established] Non-randomized study (Shift workers without SWD diagnosis)



^{*}Vangelova 2008: CW (Forward) vs CCW (Backward) rotation. Sleep Quality Index (1= poor sleep, 5= no problems with sleep).

Figure S157. Clockwise rotating shift vs Counterclockwise rotating shift (Sleep Quality, PSQI) [CMT = 3 pts] Non-randomized study (Shift workers without SWD diagnosis)

| | Clockwise | | | | | vise | Mean Difference | Mean Difference | | | | |
|--------------------|-----------|-----|-------|------|-----|-------|----------------------|---------------------|-------------------------|--|--|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 9 | 95% CI | | | |
| 12.4.1 Field Study | | | | | | | | 1 | | | | |
| Shon 2016 | 4.3 | 2.7 | 4238 | 4.9 | 2.6 | 512 | -0.60 [-0.84, -0.36] | | | | | |
| | | | | | | | | | | | | |
| | | | | | | | | -1 -0.5 0 | 0.5 1 | | | |
| | | | | | | | | Favours Clockwise F | avours Counterclockwise | | | |

Figure S158. Clockwise rotating shift vs Counterclockwise rotating shift (Sleep Quality, Modified SSI) [CMT = Not Established] Non-randomized study (Shift workers without SWD diagnosis)

| | Clo | ckwis | e | Counte | erclocky | wise | | Mean Difference | Mean Difference |
|-----------------------------------|------------|-----------|----------|-----------------|----------|---------------|--------|----------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 12.7.1 Continuous (F | ield Stud | dy) | | | | | | | |
| Tucker 2000 | 3.28 | 0.92 | 133 | 3.05 | 0.84 | 143 | | 0.23 [0.02, 0.44] | |
| Subtotal (95% CI) | | | 133 | | | 143 | 54.8% | 0.23 [0.02, 0.44] | |
| Heterogeneity: Not a | pplicable | 9 | | | | | | | |
| Test for overall effect | Z = 2.18 | 6 (P = 0 | 0.03) | | | | | | |
| 12.7.2 Discontinuou | s (Field S | Study) | | | | | | | |
| Tucker 2000 | 2.96 | 0.81 | 65 | 3.24 | 0.99 | 270 | 45.2% | -0.28 [-0.51, -0.05] | |
| Subtotal (95% CI) | | | 65 | | | 270 | 45.2% | -0.28 [-0.51, -0.05] | |
| Heterogeneity: Not a | pplicable | 9 | | | | | | | |
| Test for overall effect | Z = 2.39 | 9 (P = 0) | 0.02) | | | | | | |
| Total (95% CI) | | | 198 | | | 413 | 100.0% | -0.00 [-0.15, 0.15] | |
| Heterogeneity: Chi ² = | 10.39, 0 | df = 1 (l | P = 0.00 | $(01); I^2 = 9$ | 0% | | | | -0.5 -0.25 0 0.25 0.5 |
| Test for overall effect | Z = 0.00 | (P = 1 | 1.00) | | | | | | -0.5 -0.25 0 0.25 0.6 Favours Clockwise Favours Counterclockwise |
| Test for subgroup dif | ferences | : Chi2: | = 10.39 | df = 1 (F) | 0.00 | 1), $I^2 = 9$ | 30.4% | | Tavours Ciockwise Tavours Counterclockwise |

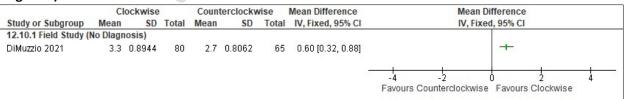
^{*}Tucker 2000: Adjusted means data used; SEM converted to SD. Higher scores may be associated with experiencing more sleep disturbances.

Figure S159. Clockwise rotating shift vs Counterclockwise rotating shift (Cognitive Performance, PVT (mean RT, ms)) [CMT = Not Established] Non-randomized study (Shift workers without SWD diagnosis)

| | Clo | ckwis | e | Counte | rclocky | vise | Mean Difference | Mean Difference | | | | |
|------------------------|----------|-------|-------|--------|---------|-------|-------------------------|-----------------|-------------------|--------------------|---------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixe | d, 95% CI | | |
| 12.9.1 Field Study (No | o Dlagno | sis) | | | | | | | | | | |
| DiMuzzio 2021 | 309.4 | 98.4 | 80 | 375.7 | 66.9 | 65 | -66.30 [-93.31, -39.29] | | + | | | |
| | | | | | | | | - | - | | | |
| | | | | | | | | -100 | -50 | Ö 50 | 100 | |
| | | | | | | | | | Favours Clockwise | Favours Countercle | ockwise | |

^{*}DiMuzzio 2021: SEM converted to SD, data extracted from figure

Figure S160. Clockwise rotating shift vs Counterclockwise rotating shift (Cognitive Performance, PVT (speed,1/RT ms)) [CMT = Not Established] Non-randomized study (Shift workers without SWD diagnosis)



^{*}DiMuzzio 2021: SEM converted to SD, data extracted from figure

Figure S161. Clockwise rotating shift vs Counterclockwise rotating shift (Cognitive Performance, PVT (fastest 10%, RT in ms)) [CMT = Not Established] Non-randomized study (Shift workers without SWD diagnosis)

| | Clo | ckwis | e | Counte | rclocky | vise | Mean Difference | Mean Difference | | | | | |
|------------------------|----------|-------|-------|--------|---------|-------|-------------------------|-----------------|-------------------|-----------|------------|-------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 95% CI | | | | |
| 12.11.1 Field Study (I | No Dlagn | osis) | | | | | | | | | | | |
| DiMuzzio 2021 | 231.5 | 50.1 | 80 | 286 | 53.2 | 65 | -54.50 [-71.46, -37.54] | -+ | | | | | |
| | | | | | | | | — | | | - 1 | | |
| | | | | | | | | -100 -50 | | Ö | 50 | 100 | |
| | | | | | | | | Favours | Clockwise | Favours C | ountercloc | kwise | |

^{*}DiMuzzio 2021: SEM converted to SD, data extracted from figure

Figure S162. Clockwise rotating shift vs Counterclockwise rotating shift (Cognitive Performance, PVT (slowest 10%, RT in ms)) [CMT = Not Established] Non-randomized study (Shift workers without SWD diagnosis)

| | (| Clockwise | | Cour | nterclockwi | se | Mean Difference | | Mean D | ifference | | |
|------------------------|----------|-----------|-------|-------|-------------|-------|--------------------------|------|---------------------------|-----------|-----|-------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixe | d, 95% CI | | |
| 12.12.1 Field Study (I | No Dlagr | nosis) | | | | | | | | (8) | | |
| DiMuzzio 2021 | 720 | 1,007.125 | 80 | 921.5 | 644.9806 | 65 | -201.50 [-472.22, 69.22] | | - | 100 | | |
| | | | | | | | | -500 | -260 | | 250 | 50 |
| | | | | | | | | -500 | -250 Favours Clockwise | Favours | | ckwis |

^{*}DiMuzzio 2021: SEM converted to SD, data extracted from figure

Figure S163. Clockwise rotating shift vs Counterclockwise rotating shift (Cognitive Performance, Difficulty in concentrating at work) [CMT = Not Established] Non-randomized study (Shift workers without SWD diagnosis)

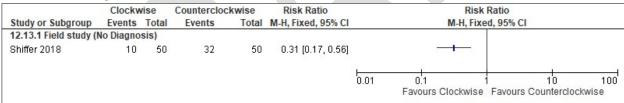
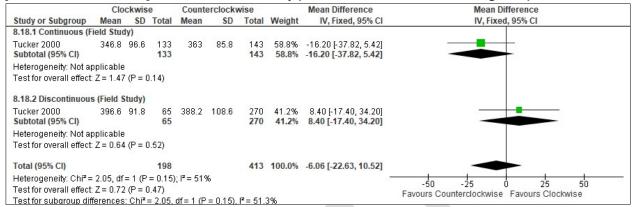


Figure S164. Clockwise rotating shift vs Counterclockwise rotating shift (Cognitive Performance, number of correct responses during the Bakan Vigilance Task) [CMT = Not Established] Non-randomized study (Healthy participants)

| | Cle | ockwise | 9 | Counte | erclocky | vise | Mean Difference | Mean Difference |
|---------------------|-------|---------|-------|--------|----------|-------|-----------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 11.1.1 Lab Study | | | | | | | | |
| Cruz 2003 (Part II) | 88.24 | 27.66 | 14 | 96.8 | 24.8 | 14 | -8.56 [-28.02, 10.90] | - 1 |
| | | | | | | | | |
| | | | | | | | | -50 -25 0 25 |
| | | | | | | | | Favours Counterclockwise Favours Clockwise |

Important Outcomes

Figure S165. Clockwise rotating shift vs Counterclockwise rotating shift (Total Sleep Time, Revised SSI) [CMT = Not Established] Non-randomized study (Shift workers without SWD diagnosis)



^{*}Tucker 2000: Both CW (delaying) and CCW (advancing) on both continuous and discontinuous shifts. Adjusted means used (no other data available); SEM converted to SD. hours converted to minutes

Figure S166. Clockwise rotating shift vs Counterclockwise rotating shift (Total Sleep Time, Self-report) [CMT = 15 min] Non-randomized studies (Shift workers without SWD diagnosis)

| | Clo | ockwise | е | Counte | erclocky | vise | | Mean Difference | Mean Difference |
|-----------------------------------|-----------|--------------------|----------|----------|-----------|-------|--------|-----------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| 12.14.1 Field Study | | | | | | | | | |
| Shiffer 2018 | 298.8 | 90 | 50 | 246 | 78 | 50 | 37.0% | 52.80 [19.79, 85.81] | |
| Vangelova 2008 | 476.4 | 103.2 | 13 | 469.2 | 52.8 | 12 | 19.8% | 7.20 [-56.36, 70.76] | - · · · · · · · · · · · · · · · · · · · |
| Viitasalo 2015 | 442.2 | 58.2 | 61 | 438 | 66.6 | 43 | 43.1% | 4.20 [-20.49, 28.89] | and the second s |
| Subtotal (95% CI) | | | 124 | | | 105 | 100.0% | 22.80 [-12.68, 58.28] | |
| Heterogeneity: Tau ² = | = 601.06; | Chi ² = | 5.52, df | = 2 (P = | 0.06); l² | = 64% | | | |
| Test for overall effect | Z = 1.28 | P = 0.3 | 21) | | | | | | |
| | | | | | | | | | |
| | | | | | | | | | -100 -50 0 50 100 |
| | | | | | | | | | Favours Counterclockwise Favours Clockwise |
| Test for subgroup dif | ferences | : Not ap | plicabl | e | | | | | |

^{*}Viitasalo 2015: CW (Forward) vs CCW (Backward) both were three-shift, both age groups (<45 yrs and >45 yrs were averaged together), hours converted to minutes

Vangelova 2008: CW (Forward) vs CCW (Backward) rotation, hours converted to minutes

Shiffer 2018: sleep duration after nightshift, hours converted to minutes

Figure S167. Clockwise rotating shift vs Counterclockwise rotating shift (Total Sleep Time, Actigraphy) [CMT = 15 min] Non-randomized study (Healthy participants)

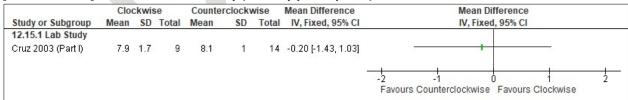


Figure S168. Clockwise rotating shift vs Counterclockwise rotating shift (Total Sleep Time, Actigraphy) [CMT = 15 min] Non-randomized study (Shift workers without SWD diagnosis)

| | Clo | ckwis | se | Counte | rclocky | vise | Mean Difference | | Mean [| Differen | nce | |
|---------------------|------|-------|-------|--------|---------|-------|--------------------------|--------------------|------------------------|-------------|-------------------|-------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixe | ed, 95% | CI | |
| 12.18.1 Field Study | | | | | | | | | | 7 | | |
| Lavie 1992 | 396 | 138 | 11 | 450 | 366 | 22 | -54.00 [-227.32, 119.32] | 25 | + | | | |
| | | | | | | | | - | - | | | |
| | | | | | | | | -200 Favours Co | -100 unterclockwise | Ö e Favo | 100 ours Clock | 200 wise |

^{*}Lavie 1992: Day 2 night data used, hours converted to minutes

Figure S169. Clockwise rotating shift vs Counterclockwise rotating shift (Mental Health, General health questionnaire) [CMT = Not Established] Non-randomized study (Shift workers without SWD diagnosis)

| | Clo | ckwis | e | Counte | rclocky | vise | | Mean Difference | Mean Difference |
|-----------------------------------|-----------|----------------------|---------|-------------|----------|-------------|--------|---------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 13.22.1 Continuous (| Field Stu | udy) | | | | | | | |
| Tucker 2000 | 11 | 6.34 | 133 | 11.28 | 5.5 | 143 | 57.0% | -0.28 [-1.68, 1.12] | |
| Subtotal (95% CI) | | | 133 | | | 143 | 57.0% | -0.28 [-1.68, 1.12] | |
| Heterogeneity: Not ap | oplicable | 9 | | | | | | | |
| Test for overall effect: | Z = 0.39 | 9 (P = 0) | 0.70) | | | | | | |
| 13.22.2 Discontinuou | us (Field | Study |) | | | | | | |
| Tucker 2000 | 11.01 | 5.72 | 65 | 11.84 | 6.9 | 270 | 43.0% | -0.83 [-2.45, 0.79] | - |
| Subtotal (95% CI) | | | 65 | | | 270 | 43.0% | -0.83 [-2.45, 0.79] | |
| Heterogeneity: Not ap | oplicable | 9 | | | | | | | |
| Test for overall effect: | Z = 1.01 | P = 0 | 0.31) | | | | | | |
| Total (95% CI) | | | 198 | | | 413 | 100.0% | -0.52 [-1.58, 0.54] | |
| Heterogeneity: Chi ² = | 0.25, df | = 1 (P | = 0.61) | z = 0% | | | | | + + + + + |
| Test for overall effect: | Z = 0.98 | 6(P=0) | 0.34) | | | | | | Favours Clockwise Favours counterclockwise |
| Test for subgroup diff | ferences | : Chi ² : | = 0.25. | df = 1 (P = | = 0.61). | $I^2 = 0\%$ | | | Favours Ciockwise Favours counterclockwise |

^{*}Tucker 2000: Both CW (delaying) and CCW (advancing) on both continuous and discontinuous shifts. GHQ score, low score = high well-being. SEM converted to SD.

Figure S170. Clockwise rotating shift vs Counterclockwise rotating shift (Mental Health, Stress scale) [CMT = Not Established] Non-randomized study (Shift workers without SWD diagnosis)

| | Cloc | kwis | se | Counte | erclocky | wise | Mean Difference | | Me | ean Diff | ference | |
|---------------------|------|------|-------|--------|----------|-------|--------------------|----|---------------------|------------|-----------------------|---------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV | , Fixed, | 95% CI | |
| 12.20.1 Field Study | | | | | | | | | | - 9 | | |
| Vangelova 2008 | 5.13 | 1.1 | 13 | 4.85 | 0.93 | 12 | 0.28 [-0.52, 1.08] | | 100 | | + | |
| | | | | | | | | | | | | <u> </u> |
| | | | | | | | | -2 | -1 Favours Clock | 0 kwise | 1 Favours Counterc | 2 lockwise |

^{*}Vangelova 2008: CW (Forward) vs CCW (Backward) rotation. Night shift data extracted from graph; timepoints (0000-0600) averaged. Stress scale (1= very low, to 9= very high).

Figure S171. Clockwise rotating shift vs Counterclockwise rotating shift (Sleep Onset Latency, Actigraphy) [CMT = 15 min] Non-randomized study (Shift workers without SWD diagnosis)

| Cloc | ckwis | se | Counte | rclocky | vise | Mean Difference | | Mean Differ | ence |
|------|-------|---------|---------------------|--------------------|-----------------------|-----------------------------|---|---|--|
| Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 95 | 5% CI |
| | | | | | | | | 1 | |
| 9.15 | 0.9 | 11 | 12.64 | 3.16 | 22 | -3.49 [-4.91, -2.07] | | | |
| | | | | | | | | | 9- |
| | | | | | | | -10 | -5 0 | 5 1 vours Counterclockwise |
| | Mean | Mean SD | 90-0000 E0000 E0000 | Mean SD Total Mean | Mean SD Total Mean SD | Mean SD Total Mean SD Total | Mean SD Total Mean SD Total IV, Fixed, 95% CI | Mean SD Total Mean SD Total IV, Fixed, 95% CI | Mean SD Total IV, Fixed, 95% CI IV, Fixed, 95% CI 9.15 0.9 11 12.64 3.16 22 -3.49 [-4.91, -2.07] |

^{*}Lavie 1992: Night data used

Figure S172. Clockwise rotating shift vs Counterclockwise rotating shift (Sleep Efficiency, Actigraphy) [CMT = 10%] Non-randomized study (Shift workers without SWD diagnosis)

| | Clo | ckwis | е | Counte | rclocky | vise | Mean Difference | | | Mean Dif | fference | | |
|---------------------|-------|-------|-------|--------|---------|-------|---------------------|---------|---------|-----------|-----------|-----------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | | IV, Fixed | , 95% CI | | |
| 12.19.1 Field Study | | | | | | | | | | | | | |
| Lavie 1992 | 87.81 | 5.89 | 11 | 88.54 | 4 | 22 | -0.73 [-4.59, 3.13] | | jū. | - | 2 | | |
| | | | | | | | | - | -1 | | | | 1 |
| | | | | | | | | -10_ | -5 | |) | . 5 | 10 |
| | | | | | | | | Favours | Counter | clockwise | Favours C | Clockwise | |

^{*}Lavie 1992: Night data used

Additional evidence on planned work schedule

The following data was not included in the decision-making process (S173-S176).

Figure S173. Planned Work Schedule (Fast CW) vs Control (CW) (Sleep Quality, VAS-sleep quality) [CMT = Not Established] Observational

| Fast C | lockw | rise | Clo | ckwis | e | Mean Difference | | Mean | Difference | |
|--------|-------|-------|--|--------------------|-----------------------|-----------------------------|---|---|---|--|
| Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixe | ed, 95% CI | |
| | | | | | | | | | 1 | |
| 53.83 | 3.91 | 33 | 49.63 | 4.06 | 34 | 4.20 [2.29, 6.11] | | | - | |
| | | | | | | | | 1 | | - 1 |
| | | | | | | | -10 | -5 Favours Clockwis | 0 5 R Favoure Fact Clock | 10 |
| | Mean | | AN SACES SALES SAL | Mean SD Total Mean | Mean SD Total Mean SD | Mean SD Total Mean SD Total | Mean SD Total Mean SD Total IV, Fixed, 95% CI | Mean SD Total Mean SD Total IV, Fixed, 95% CI 53.83 3.91 33 49.63 4.06 34 4.20 [2.29, 6.11] | Mean SD Total Mean SD Total IV, Fixed, 95% CI IV, Fixed 53.83 3.91 33 49.63 4.06 34 4.20 [2.29, 6.11] | Mean SD Total Mean SD Total IV, Fixed, 95% CI IV, Fixed, 95% CI 53.83 3.91 33 49.63 4.06 34 4.20 [2.29, 6.11] ———————————————————————————————————— |

^{*}Fischer 1997: Fast CW (faster forward) versus CW (Forward, slower rotation is the control). VAS (0= very bad sleep, 100= very good sleep).

Figure S174. Planned Work Schedule (Fast CW) vs Control (CW) (Total Sleep Time, Sleep diary) [CMT = 15 min] Observational

| | Fast C | lockw | ise | Clo | ckwis | e | Mean Difference | | Mean Differe | nce | |
|---------------------|--------|-------|-------|------|-------|-------|----------------------|------|-----------------------|------------------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 959 | 6 CI | |
| 12.17.1 Field Study | | | | | | | | | | | |
| Fischer 1997 | 4.77 | 0.28 | 34 | 5.53 | 0.52 | 33 | -0.76 [-0.96, -0.56] | | - | | |
| | | | | | | | | - 10 | | | - |
| | | | | | | | | -2 | -i Ó | i | ż |
| | | | | | | | | | Favours Clockwise Fav | ours Fast Clockw | ise |

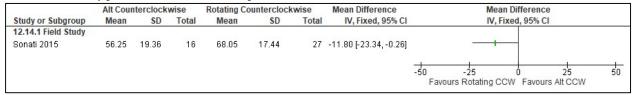
^{*}Fischer 1997: Fast CW (faster forward) versus CW (Forward, slower rotation). Last night of night shifts, mean sleep duration (hours).

Figure S175. Planned Work Schedule (Alternate CCW) vs Control (Rotating CCW) (Sleep Quality, WHOQOL-BREF: how satisfied are you with your sleep) [CMT = Not Established] Observational

| Alt Count | erclock | wise | Rotating Co | unterclock | wise | Mean Difference | Mean Difference | e |
|-----------|---------|---------|--|--------------------|-----------------------|-----------------------------|---|---|
| Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% C | 3 |
| | | | | | | | | |
| 3.12 | 0.8 | 16 | 3.25 | 1.09 | 27 | -0.13 [-0.70, 0.44] | | |
| | | | | | | | | |
| | | | | | | | -2 -1 0 Favours Rotating CCW Favou | 1 2 rs Alt CCW |
| | Mean | Mean SD | 1995 TO 1995 T | Mean SD Total Mean | Mean SD Total Mean SD | Mean SD Total Mean SD Total | Mean SD Total Mean SD Total IV, Fixed, 95% CI | Mean SD Total Mean SD Total IV, Fixed, 95% CI IV, Fixed, 95% CI |

^{*}Sonati 2015: Alternate CCW shift versus rotating CCW (comparator). Scores based on a modified Likert scale, where 5= very satisfied.

Figure S176. Planned Work Schedule (Alternate CCW) vs Control (Rotating CCW) (Quality of Life, WHOQOL-BREF) [CMT = Not Established] Observational



^{*}Sonati 2015: Alternate CCW shift versus rotating CCW. Overall score used. Facets of WHO QoL pertaining to concentration, energy, and sleep satisfaction were assessed with a Likert scale (1-5, with 5 being very satisfied) and the overall score was transformed to a 0-100 scale (100 being very satisfied).

Naps prior to the first night shift

Summary of Findings (GRADE)

Table S13. Naps prior to the first night shift in adults with shiftwork disorder

References: Schweitzer 2006, Macchi 2002, Rosa 1993

| Outcomes [Tool] | Certainty of the evidence (GRADE) | Absolute Difference Naps prior to the shift vs Control | No of Participants (studies) |
|--|-------------------------------------|---|------------------------------|
| Excessive sleepiness or alertness [MWT] ^a | ⊕○○○ VERY LOW ^{b,c,d,e} | The mean difference in the nap group was 5.24 minutes higher (1.13 lower to 11.61 higher) compared to control | 33 (1 RCT) |
| Excessive sleepiness or alertness [VAS-alertness] ^{f,g} | ⊕○○○ VERY LOW ^{d,h} | The mean difference in the nap was 0.63 lower (1.35 lower to 0.09 higher compared to control | 16 (1 non-RCT) |
| Sleep quality [9-point scale] ^{a,f} | ⊕○○○ VERY LOW ^{d,h} | The mean difference in the nap group was 0.55 points lower (2.25 lower to 1.15 higher) compared to control | 18 (1 non-RCT) |
| Cognitive performance [PVT lapses] ^{f,g} | ⊕○○○ VERY LOW ^{b,c,d,e} | The mean difference in the nap group was 2.44 lapses fewer (4.63 fewer to 0.25 fewer) compared to control | 33 (1 RCT) |
| Cognitive performance [Torrance of creative thinking] ^{a,f} | ⊕○○○ VERY LOW ^{b,c,h} | The mean difference in the nap group was 0.65 units fewer (7.86 fewer to 6.56 more) compared to control | 33 (1 RCT) |
| Cognitive performance [multiple tests] ^f | ⊕○○○ VERY LOW ^{d,e} | The evidence suggests that planned naps result in little to no difference in cognitive performance including Four-choice serial reaction time (sec), Two-Letter Memory and Search Test, and Head Steadiness reported as percent of time off target. | 17 (1 non-RCT) |

- a. Higher values favor the intervention
- b. Risk of bias concerns due to lack of allocation concealment
- c. Indirectness is due to the fact that participants included in the studies are healthy individuals. The effect in adults with SWD may be different
- d. Imprecision due to small sample size (<200 participants)
- e. Imprecision due to the 95% CI crossing the CMT
- f. CMT was not established by the TF
- g. Lower values favor the intervention
- h. Imprecision due to the 95% CI crossing the null

Study Characteristics

Table S14. Naps prior to the first night shift in adults with shiftwork disorder

| Study Citation | Study Design | Number of Participants (% Female) | Age (years) | Population | Intervention (duration) | Comparator | Time of Intervention Delivery | Duration of Follow- up |
|--------------------|-------------------|---|--------------------|---|----------------------------|------------|--|------------------------------|
| Macchi 2002 | RCT, crossover | 8 (13) | 40.9 ± 2.1 (SE) | Shift workers without SWD diagnosis | Nap (3 hours) | No nap | 14:00 - 17:00 | 3 days |
| Rosa 1993 | non-RCT | 19 (0) | 25 to 59 | Shift workers without SWD diagnosis | Nap (2.11-2.20 hours) | No nap | Prior to the night shift | 5-7 days |
| Schweitzer 2006 | RCT | 68 (53) | 31.3 | healthy individuals | nap (2.5 hours) | No nap | nap from 19:30- 22:00 plus placebo taken 30 minutes prior to night shifts; | 4 nights |

Critical Outcomes

Figure S177. Naps prior to the first night shift vs Control (Excessive Sleepiness, MWT) [CMT = 2 min] RCT (Healthy participants)

| | | Nap | | N | o Nap | | Mean Difference | Mean Difference |
|-------------------|-------|--------|-------|-------|-------|-------|---------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 16.19.1 Lab Study | | | | | | | | |
| Schweitzer 2006 | 20.17 | 8.9471 | 17 | 14.93 | 9.68 | 16 | 5.24 [-1.13, 11.61] | + + - |
| | | | | | | | _ | |
| | | | | | | | | -10 -5 0 5 10 Favours No Nap Favours Nap |

^{*}Schweitzer 2006: Data (on night shift 1 averaged from 2345-0630) extracted from graph; SEM converted to SD.

Figure S178. Naps prior to the first night shift vs Control (Excessive Sleepiness, VAS-Alertness) [CMT = Not Established], non-randomized study (Healthy participants)

| | | Nap | | | No Nap | | Mean Difference | Mean Difference |
|-------------------|--------|--------|-------|-------|--------|-------|---------------------|----------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 17.20.1 Lab Study | | | | | | | | |
| Macchi 2002 | -0.092 | 0.8259 | 8 | 0.538 | 0.6392 | 8 | -0.63 [-1.35, 0.09] | |
| | | | | | | | - | |
| | | | | | | | | Favours Nap Favours No Nap |

^{*}Machhi 2002: z-scored data

Figure S179. Naps prior to the first night shift vs Control (Sleep Quality, 9-point scale) [CMT = Not Established] non-randomized study (Shift workers without SWD diagnosis)

| - | • | | | , , | | | | <u> </u> | | | | |
|-------------------|------|------|-------|------|-------|-------|---------------------|----------|-------------------|-----------|-------|---|
| | Nap | | | N | o Nap | | Mean Difference | | Me | ean Diffe | rence | |
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 95% CI | | | |
| Rosa 1993 | 5.97 | 1.93 | 9 | 6.52 | 1.75 | 9 | -0.55 [-2.25, 1.15] | | 100 | 1 | | |
| | | | | | | | | | | | - 1 | 1 |

^{*}Rosa 1993: Data from First Night and other workdays were pooled, data extracted from figure.

Figure S180. Naps prior to the first night shift vs Control (Cognitive Performance, PVT lapses) [CMT = 1 lapse] RCT (Healthy participants)

| | Nap | | | No | No Nap Mean Dit | | | | Mean Difference | | |
|-------------------|------|------|-------|------|-----------------|-------|----------------------|-------------|-----------------------|---------------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 95% CI | | |
| 12.22.1 Lab Study | | | | | | | | | 1 | | |
| Schweitzer 2006 | 3.6 | 2.43 | 17 | 6.04 | 3.8 | 16 | -2.44 [-4.63, -0.25] | | - | | |
| | | | | | | | | | | 1 | - 1 |
| | | | | | | | | -10 | -5 0 Favours Nap F | avours No Nap | 10 |

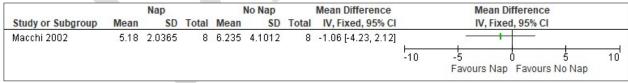
^{*}Schweitzer 2006: Data (on night shift 1 averaged from 2345-0630) extracted from graph; SEM converted to SD.

Figure S181. Naps prior to the first night shift vs Control (Cognitive Performance, Torrance test of creative thinking-fluency, mean change from baseline) [CMT = Not Established] RCT (Healthy participants)

| | | Nap | | No | o Nap | | Mean Difference | | Mea | an Differe | nce | |
|-------------------|-------|-------|-------|-------|-------|-------|---------------------|------------|-----------------|--------------|---------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, F | Fixed, 959 | 6 CI | |
| 12.21.1 Lab Study | | | | | | | | | | 18 | | |
| Schweitzer 2006 | -9.44 | 11.63 | 17 | -8.79 | 9.44 | 16 | -0.65 [-7.86, 6.56] | 200 | | - | | |
| | | | | | | | | - 1 | | | - 1 | |
| | | | | | | | | -10 Fav | -5 ours No I | Ö Nap Fav | 5 ours Nap | 10 |

^{*}Schweitzer 2006: Data extracted from graph; SEM converted to SD

Figure S182. Naps prior to the first night shift vs Control (Cognitive Performance, Four choice serial reaction time (sec)) [CMT = Not Established] non-randomized study (Healthy participants)



^{*}Macchi 2002: data extracted from graph, SEM converted to SD, data averaged across the night

Figure S183. Naps prior to the first night shift vs Control (Cognitive Performance, Two-Letter Memory and Search Test (reaction time in sec)) [CMT = Not Established] non-randomized study (Healthy participants)

| | Nap | | | | No Nap | | Mean Difference | Mean Difference |
|-------------------|--------|--------|-------|-------|--------|-------|---------------------|----------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| Macchi 2002 | 0.4725 | 0.1344 | 8 | 0.515 | 0.2051 | 8 | -0.04 [-0.21, 0.13] | |
| | | | | | | | | -1 -0.5 0 0.5 |
| | | | | | | | | Favours Nap Favours No Nap |

^{*}Macchi 2002: data extracted from graph, SEM converted to SD, data averaged across the night

Figure S184. Naps prior to the first night shift vs Control (Cognitive Performance, Hand steadiness (percent time off target)) [CMT = Not Established] non-randomized study (Shift workers without SWD diagnosis)

| | Nap | | | | lo Nap | | Mean Difference | | Mean | Difference | | |
|-------------------|------|-----|-------|------|--------|-------|---------------------|-----|-------------------|------------------|---|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 95% CI | | | |
| Rosa 1993 | 9.34 | 9.8 | 9 | 7.55 | 10.42 | 9 | 1.79 [-7.56, 11.14] | | | | | |
| | | | | | | | | -50 | -25 | 0 25 | 5 | |
| | | | | | | | | | Favours na | p Favours no nap | | |

^{*}Rosa 1993: Data from first half and second half of night shift were pooled

Important Outcomes

Figure S185. Naps prior to the first night shift vs Control (Total sleep time, Subjective) [CMT = 15 min] non-randomized studies (Healthy participants)

| | Nap | | | N | lo Nap | | Mean Difference | Mean Difference | | | | | |
|-------------------|-------|-------|-------|-------|--------|-------|------------------------|-----------------|-------------------|-----------|-----------------|-----------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 95% CI | | | | |
| Rosa 1993 | 448.8 | 125.4 | 9 | 391.8 | 112.2 | 9 | 57.00 [-52.93, 166.93] | | | | | | - |
| | | | | | | | | -200 F | -100 avours No | 0 Naps | 1 Favours Na | 00 aps | 200 |

^{*}Rosa 1993: 8-hour night shift, hours converted to minutes, nap time included

Diet and meal timing

Summary of Findings (GRADE)

Table S15. Diet and meal timing in adults with shiftwork disorder

References: Grant 2017, Gupta 2019, Gupta 2017

| Outcomes [Tool] | Certainty of the evidence (GRADE) | Absolute Difference | No of Participants (studies) |
|---|-------------------------------------|---|------------------------------|
| | | Eating a snack or not eating vs Eating a full meal | |
| Excessive sleepiness or alertness [KSS] ^a | ⊕○○○ VERY LOW ^{b,c,d} | The mean difference in the snacking or not eating at night group was 3.24 points fewer (5.68 fewer to 0.80 fewer) compared to eating a full meal | 10 (1 RCT) |
| Excessive sleepiness or alertness [SSS] ^a | ⊕○○○ VERY LOW ^{b,c,d} | The mean difference in the snacking or not eating at night group was 0.79 points fewer (1.30 fewer to 0.27 fewer) compared to eating a full meal | 39 (1 RCT) |
| Accident risk [Driving Simulator (% of time in safe zone)]e | ⊕⊖⊖⊖ VERY LOW ^{b,c,f,g} | The mean difference in the snacking or not eating group was 5.49 percent higher (0.34 lower to 11.32 higher) compared to eating a full meal | 49 (2 RCTs) |

| Accident risk [Driving Simulator (speed variability]a | ⊕⊖⊖⊖ VERY LOW ^{b,c,f,g} | The mean difference in the snacking or not eating at night group was 1.92 km/h lower (3.92 lower to 0.08 higher) compared to eating a full meal | 49 (2 RCTs) |
|---|-------------------------------------|--|----------------|
| Accident risk [Driving Simulator (lane variability)] ^a | LOM _p ,c | The mean difference in the snacking or not eating group was 0.06 meters fewer (0.11 fewer to 0.01 fewer) compared to eating a full meal | 49 (2 RCTs) |
| Cognitive performance [PVT lapses] ^a | LOM _p ,c | The mean difference in the snacking or not eating group was 3.07 points fewer (4.21 fewer to 1.93 fewer) compared to eating a full meal | 49 (2 RCTs) |
| Cognitive performance [multiple tests] ^h | rom _{p'c} ⊕⊕⊖⊖ | The evidence suggests that not eating (or snacking at night) results in little difference in cognitive performance tests (PVT, DSST, Choice Reaction Time Task, Running Memory continuous performance task). | 39 (3 RCTs) |

- a. Lower values favor the intervention
- b. Indirectness is due to the fact that participants included in the studies are healthy individuals. The effect in adults with SWD may be different
- c. Imprecision due to small sample size (<200 participants)
- d. Imprecision due to the 95% CI crossing the CMT
- e. Higher values favor the intervention
- f. There was unexplained inconsistency that was supported by nonoverlapping confidence intervals, high I2 values, and statistically significant heterogeneity of effect estimates.
- g. Imprecision due to the 95% CI crossing the null
- h. CMT was not determined the TF

Study Characteristics

Table S16. Diet and meal timing in adults with shiftwork disorder

| | Study Design | Number of Participants (% Female) | Age (years) | Population | Intervention | Comparator | Time of Intervention Delivery | Duration of Follow- up |
|---------------|-----------------|-----------------------------------|-----------------------------------|----------------------|--------------------|-----------------------------|---|------------------------------|
| Grant 2017 | DOT | 12 (0) | 24.70 1.555 | Healthy | N 1 | P.H. J | meal at 19:00, 01:30, and 07:00 meal at 19:00 and 07:00 and snacks at 09:30 and | 4 . 1 |
| Gupta 2017 | RCT RCT | 13 (0) | 24.70 ± 5.55 24.70 ± 5.55 | Healthy participants | No meal | Full meal | 14:10 meal at 19:00, 01:30, and 07:00 meal at 19:00 and 07:00 and snacks at 09:00 and 16:00 | 4 nights |
| Gupta 2019 | RCT | 39 (41) | 24.5 ± 5.0 | Healthy participants | Snack No meal | Full meal | meal at 19:00, 0:30 and 07:00 meal at 19:00 and 07:00 and snacks at 0:30 and 17:00 Meal at 19:00 and 07:00 and snacks at 09:30 and | Ĭ |
| Oian 2022 | RCT | 19 (37) | 24.5 ± 3.0 26.5 ± 4.1 | Healthy participants | Daytime only meals | Daytime and Nighttime meals | 17:00 | 4 nights 4 days |

Critical Outcomes

Figure S186. Diet and Meal Timing vs Control (Excessive Sleepiness, KSS) [CMT = 1 pt] RCT (Healthy participants)

| | Not | t Eatin | g | Eatin | g at Ni | ght | Mean Difference | Mean Difference |
|--------------------|------|---------|-------|-------|---------|-------|----------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 13.1.1 Lab Studies | | | | | | | | |
| Grant 2017 | 5.41 | 1.97 | 5 | 8.65 | 1.97 | 5 | -3.24 [-5.68, -0.80] | - t |
| | | | | | | | | |
| | | | | | | | | -10 -5 0 5 10 |
| | | | | | | | | Favours Snack/Not Eating Favours Full Meal |

^{*}Grant 2017: Night shift 4 (used 0400 timepoint). KSS; SEM converted to SD.

Figure S187 Diet and Meal Timing vs Control (Excessive Sleepiness, SSS) [CMT = 1 pt] RCT (Healthy participants)

| | No | t Eatin | g | Eatin | g at Ni | ght | | Mean Difference | Mean Difference |
|-----------------------------------|-----------|-----------|---------|-----------------------|----------|------------------------|--------|----------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 13.2.1 Lab Studies | | | | | | | | | 9 |
| Gupta 2019 | 5.34 | 1.11 | 12 | 5.7 | 0.58 | 7 | 45.8% | -0.36 [-1.12, 0.40] | - |
| Subtotal (95% CI) | | | 12 | | | 7 | 45.8% | -0.36 [-1.12, 0.40] | • |
| Heterogeneity: Not ap | oplicable | 9 | | | | | | | |
| Test for overall effect | Z = 0.93 | B (P = 0) | 0.35) | | | | | | |
| 13.2.2 Lab Study, Sn | ack at N | light | | | | | | | |
| Gupta 2019 | 4.55 | 1.05 | 14 | 5.7 | 0.54 | 6 | 54.2% | -1.15 [-1.85, -0.45] | |
| Subtotal (95% CI) | | | 14 | | | 6 | 54.2% | -1.15 [-1.85, -0.45] | • |
| Heterogeneity: Not ap | oplicable | | | | | | | | |
| Test for overall effect: | Z = 3.22 | 2 (P = 0) | 0.001) | | | | | | |
| Total (95% CI) | | | 26 | | | 13 | 100.0% | -0.79 [-1.30, -0.27] | • |
| Heterogeneity: Chi ^z = | 2.24, df | = 1 (P | = 0.13 | ; I ² = 55 | % | | | 9 | |
| Test for overall effect: | Z = 3.00 | P = 0 | 0.003) | | | | | | Favours Snack/Not Eating Favours Full Meal |
| Test for subgroup dif | ferences | : Chi²: | = 2.24. | df = 1 (F | P = 0.13 | 3), $ \mathbf{r} = 6$ | 55.4% | | Favours Shacking Favours Full Weal |

^{*}Gupta 2019: (averaged 0130 & 0400 timepoints, across the 4-night shifts). Eating at night (n=13; halved the participants to not double count them in the total). SSS; SEM converted to SD.

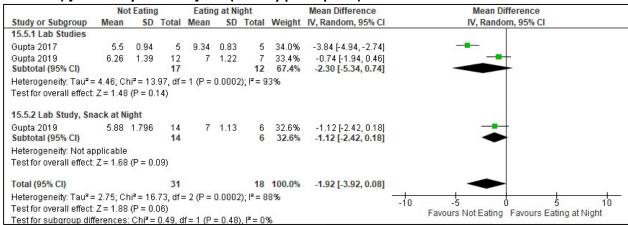
Figure S188. Diet and Meal Timing vs Control (Accident Risk, % of time spent in safe zone, in driving simulator) [CMT = any increase] RCT (Healthy participants)

| | Not | Eating | g | Eatin | g at Ni | ght | | Mean Difference | Mean Difference |
|-----------------------------------|----------|---------|----------|------------|---------|---------------------|--------|---------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| 15.4.1 Lab Studies | | | | | | | | | |
| Gupta 2017 | 82.8 | 7.13 | 5 | 68.24 | 6.22 | 5 | 24.3% | 14.56 [6.27, 22.85] | |
| Gupta 2019 | 88.4 | 6.58 | 12 | 85.75 | 3.7 | 7 | 36.9% | 2.65 [-1.97, 7.27] | • |
| Subtotal (95% CI) | | | 17 | | | 12 | 61.2% | 8.09 [-3.54, 19.71] | - |
| Heterogeneity: Tau ² = | 59.19; | Chi²= I | 6.04, di | f=1 (P= | = 0.01) | I ² = 83 | % | | |
| Test for overall effect: | Z=1.38 | (P = 0 | 1.17) | | | | | | |
| 15.4.2 Lab Study, Sn | ack at N | ight | | | | | | | |
| Gupta 2019 | 88.25 | 5.8 | 14 | 85.75 | 3.43 | 6 | 38.8% | 2.50 [-1.59, 6.59] | • - |
| Subtotal (95% CI) | | | 14 | | | 6 | 38.8% | 2.50 [-1.59, 6.59] | • |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z=1.20 | (P = 0 | 1.23) | | | | | | |
| Total (95% CI) | | | 31 | | | 18 | 100.0% | 5.49 [-0.34, 11.32] | • |
| Heterogeneity: Tau ^z = | 18.41; | Chi²= | 7.07, di | f = 2 (P = | = 0.03) | $l^2 = 72$ | % | | -50 -25 0 25 5 |
| Test for overall effect: | Z = 1.85 | (P = 0 | 1.06) | - 125 | į. | | | | Favours Eating at Night Favours Not Eating |
| Test for subgroup diff | erences | : Chi²: | = 0.79 | df = 1 (F | 9 = 0.3 | 7) $I^2 = 0$ | 1% | | ravours Eating at Might Pavours Mot Eating |

^{*}Gupta 2017: used 0300 timepoint, across the 4 night shifts. SEM converted to SD.

Gupta 2019: (averaged 0130 & 0400 timepoints, on night shift 4). Eating at night (n=13; halved the participants to not double count them in the total). SEM converted to SD.

Figure S189. Diet and Meal Timing vs Control (Accident Risk, Speed variability (km/h), in driving simulator) [CMT = any decrease] RCT (Healthy participants)



^{*}Gupta 2017: used 0300 timepoint, across the 4 night shifts. SEM converted to SD.

Gupta 2019: (averaged 0130 & 0400 timepoints, on night shift 4). Eating at night (n=13; halved the participants to not double count them in the total). SEM converted to SD.

Figure S190. Diet and Meal Timing vs Control (Accident Risk, Lane variability (m, in driving simulator) [CMT = any decrease] RCT (Healthy participants)

| | No | t Eatin | g | Eatin | g at Ni | ght | | Mean Difference | Mean Difference |
|-----------------------------------|----------|------------|---------|-----------|----------|------------------------|--------|----------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| 15.6.1 Lab Studies | | | | | | | | | |
| Gupta 2017 | 0.38 | 0.09 | 5 | 0.43 | 0.09 | 5 | 15.9% | -0.05 [-0.16, 0.06] | • |
| Gupta 2019 | 0.26 | 0.07 | 12 | 0.29 | 0.05 | 7 | 42.1% | -0.03 [-0.08, 0.02] | |
| Subtotal (95% CI) | | | 17 | | | 12 | 58.0% | -0.03 [-0.08, 0.01] | |
| Heterogeneity: Tau ^z = | 0.00; C | $hi^2 = 0$ | 10, df= | 1 (P= | 0.75); [| = 0% | | | |
| Test for overall effect: | Z=1.38 | (P = 0 | 1.17) | | | | | | |
| 15.6.2 Lab Study, Sn | ack at N | ight | | | | | | | |
| Gupta 2019 | 0.19 | 0.07 | 14 | 0.29 | 0.05 | 6 | 42.0% | -0.10 (-0.15, -0.05) | |
| Subtotal (95% CI) | | | 14 | | | 6 | 42.0% | -0.10 [-0.15, -0.05] | - |
| Heterogeneity: Not ap | plicable | 12 | | | | | | | |
| Test for overall effect: | Z= 3.61 | (P = 0 | .0003) | | | | | | |
| Total (95% CI) | | | 31 | | | 18 | 100.0% | -0.06 [-0.11, -0.01] | • |
| Heterogeneity: Tau ^z = | 0.00; C | $hi^2 = 3$ | 26, df= | 2 (P= | 0.20); (| ² = 399 | 6 | | -0.2 -0.1 0 0.1 0.2 |
| Test for overall effect: | Z = 2.49 | P = 0 | .01) | 161 | | | | | |
| Test for subaroup diff | | | | df = 1 (F | = 0.03 | $3), \mathbf{r} = 6$ | 88.4% | | Favours Not Eating Favours Eating at Night |

^{*}Gupta 2017: used 0300 timepoint, across the 4 night shifts. SEM converted to SD.

Gupta 2019: (averaged 0130 & 0400 timepoints, on night shift 4). Eating at night (n=13; halved the participants to not double count them in the total). SEM converted to SD.

Figure S191. Diet and Meal Timing vs Control (Cognitive Performance, PVT lapses) [CMT = 1 lapse] RCT (Healthy participants)

| | Not | Eating | g | Eatin | g at Nig | ght | | Mean Difference | Mean Difference |
|-----------------------------------|----------|--------------------|---------|------------|----------|---------|--------|----------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| 15.2.1 Lab Studies | | | | | | | | | |
| Grant 2017 | 9.02 | 7.63 | 5 | 9.58 | 8.34 | 5 | 1.3% | -0.56 [-10.47, 9.35] | |
| Gupta 2019 | 4.44 | 2.18 | 12 | 7.35 | 1.51 | 7 | 46.8% | -2.91 [-4.58, -1.24] | - |
| Subtotal (95% CI) | | | 17 | | | 12 | 48.1% | -2.85 [-4.49, -1.20] | • |
| Heterogeneity: Tau ^z = | 0.00; C | hi² = 0. | 21, df= | 1 (P= | 0.65); [| = 0% | | | |
| Test for overall effect: | Z = 3.40 | (P = 0 | .0007) | | | | | | |
| 15.2.2 Lab Study, Sna | ack at N | ight | | | | | | | |
| Gupta 2019 | 4.07 | 2.13 | 14 | 7.35 | 1.4 | 6 | 51.9% | -3.28 [-4.86, -1.70] | . |
| Subtotal (95% CI) | | | 14 | | | 6 | 51.9% | -3.28 [-4.86, -1.70] | • |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z = 4.07 | (P < 0 | .0001) | | | | | | |
| Total (95% CI) | | | 31 | | | 18 | 100.0% | -3.07 [-4.21, -1.93] | • |
| Heterogeneity: Tau ^z = | 0.00; C | hi² = 0. | 35, df= | 2 (P= | 0.84); [| = 0% | | | -10 -5 0 5 10 |
| Test for overall effect: | Z = 5.28 | (P < 0 | .00001 |) | 8538 | | | | -10 -5 0 5 10 Favours Not Eating Favours Eating at Night |
| Test for subaroup diff | erences | Chi ² : | - 0 14 | df = 1 / F | = 0.71 | 1/2 = 0 | 196 | | ravours Not Eating Favours Eating at Night |

^{*}Grant 2017: Night shift 4 (used 0400 timepoint). SEM converted to SD.

Gupta 2019: (averaged 0130 & 0400 timepoints, on night shift 4). Eating at night (n=13; halved the participants to not double count them in the total). SEM converted to SD.

Figure S192. Diet and Meal Timing vs Control (Cognitive Performance, PVT (mean reciprocal reaction time)) [CMT = Not Established] RCT (Healthy participants)

| | No | t Eating | g | Eatin | g at Ni | ght | | Mean Difference | Mean Difference |
|-----------------------------------|----------|----------|---------|-----------|----------|--------------------|--------|--------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| 15.3.1 Lab Studies | | | | | | | | | 9 |
| Gupta 2017 | 4.27 | 0.13 | 5 | 4.22 | 0.16 | 5 | 35.8% | 0.05 [-0.13, 0.23] | - • - |
| Gupta 2019 | 4.43 | 0.28 | 12 | 4.09 | 0.16 | 7 | 33.7% | 0.34 [0.14, 0.54] | |
| Subtotal (95% CI) | | | 17 | | | 12 | 69.4% | 0.19 [-0.09, 0.48] | |
| Heterogeneity: Tau ² = | 0.03; C | hi² = 4. | 50, df= | 1 (P= | 0.03); [| ² = 789 | 6 | | |
| Test for overall effect: | Z = 1.32 | P = 0 | 1.19) | 86 | | | | | |
| 15.3.2 Lab Study, Sn | ack at N | ight | | | | | | | |
| Gupta 2019 | 4.41 | 0.3 | 14 | 4.09 | 0.2 | 6 | 30.6% | 0.32 [0.10, 0.54] | |
| Subtotal (95% CI) | | | 14 | | | 6 | 30.6% | 0.32 [0.10, 0.54] | |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z = 2.80 | (P = 0 | .005) | | | | | | |
| Total (95% CI) | | | 31 | | | 18 | 100.0% | 0.23 [0.04, 0.42] | - |
| Heterogeneity: Tau ² = | 0.02; C | hi² = 5. | 58, df= | 2 (P= | 0.06); (| = 649 | 6 | - | 1 1 |
| Test for overall effect: | Z = 2.34 | (P = 0 | .02) | | | | | | -1 -0.5 0 0.5 |
| Test for subgroup diff | foroncoo | · Chi² · | - 0.48 | df = 1 /F | - 0.40 | 3) 2 - 1 | 196 | | Favours Eating at Night Favours No Eating |

^{*}Gupta 2017: used 0300 timepoint, across the 4 night shifts. SEM converted to SD.

Gupta 2019: (averaged 0130 & 0400 timepoints, on night shift 4). Eating at night (n=13; halved the participants to not double count them in the total). SEM converted to SD.

Figure S193. Diet and Meal Timing vs Control (Cognitive Performance, DSST, # correct) [CMT = Not Established] RCT (Healthy participants)

| | Not Eating Eating a | | | | g at Ni | ght | Mean Difference | Mean Difference | | | | |
|-------------------|---------------------|------|-------|------|---------|-------|----------------------|-----------------|-------------------------|--------------------|----|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixe | d, 95% CI | | |
| 15.7.1 Lab Study | | | | | | | | | | | | |
| Grant 2017 | 101.79 | 9.19 | 5 | 97.9 | 16.9 | 5 | 3.89 [-12.97, 20.75] | | (a) | 1 | | |
| | | | | | | | | _ | 19 | | | |
| | | | | | | | | -50 | -25 | Ó 25 | 50 | |
| | | | | | | | | | Favours Eating at Night | Favours Not Eating | | |

^{*}Grant 2017: Night shift 4 (used 0400 timepoint). SEM converted to SD.

Figure S194. Diet and Meal Timing vs Control (Cognitive Performance, PVT (# errors)) [CMT = Not Established] RCT (Healthy participants)

| | No | t Eating | g | Eatin | g at Nig | ght | Mean Difference | Mean Difference | | | | |
|-------------------|------|----------|-------|-------|----------|-------|----------------------|-----------------|--------------------|-----------|-------------|-------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixe | d, 95% CI | | |
| 15.8.1 Lab Study | | | | | | | | | | | | |
| Grant 2017 | 0.09 | 0.51 | 5 | 8.01 | 11.81 | 5 | -7.92 [-18.28, 2.44] | 300 | - | 90 | | |
| | | | | | | | | -11 | Ti . | | | |
| | | | | | | | | -20 | -10 | Ó | 10 | 20 |
| | | | | | | | | | Favours Not Eating | Favours | Eating at N | light |

^{*}Grant 2017: Night shift 4 (used 0400 timepoint). SEM converted to SD.

Figure S195. Diet and Meal Timing vs Control (Cognitive Performance, Choice reaction time task, throughput) [CMT = Not Established] RCT (Healthy participants)

| | Not | Eating | | Eatin | g at Ni | ght | | Mean Difference | Mean Difference |
|-----------------------------------|---|----------------------|-----------|----------|---------|-------------|------------------------|--|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 15.9.1 Lab Study | | | | | | | | | |
| Gupta 2019 Subtotal (95% CI) | 133.2 | 9.7 | 12 12 | 123.9 | 6.35 | 7 7 | 57.5% 57.5 % | 9.30 [2.07, 16.53] 9.30 [2.07, 16.53] | |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: . | ••• | P = 0.0 | 1) | | | | | | |
| 15.9.2 Lab Study, Sna | ck at Nig | ht | | | | | | | |
| Gupta 2019 Subtotal (95% CI) | 140.45 | 13.29 | 14 14 | 123.9 | 5.88 | 6 | | 16.55 [8.15, 24.95] 16.55 [8.15, 24.95] | |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: . | • | P = 0.0 | 001) | | | | | | |
| Total (95% CI) | | | 26 | | | 13 | 100.0% | 12.38 [6.90, 17.86] | • |
| Heterogeneity: Chi ² = | 1.64, df= | 1 (P = 0) | 0.20); [3 | = 39% | | | | | -50 -25 0 25 |
| Test for overall effect: . | Z = 4.43 (I | P < 0.0 | 0001) | | | | | | Favours Eating at Night Favours Not Eating |
| Test for subgroup diffe | erences: (| Chi ² = 1 | .64, df | = 1 (P = | 0.20), | $I^2 = 39.$ | 2% | | Tavours Latting at Might Tavours Mot Latting |

^{*}Gupta 2019: (averaged 0130 & 0400 timepoints, on night shift 4). Eating at night (n=13; halved the participants to not double count them in the total). SEM converted to SD. Throughput (correct responses/ minute).

Figure S196. Diet and Meal Timing vs Control (Cognitive Performance, running memory continuous performance task, throughput) [CMT = Not Established] RCT (Healthy participants)

| | No | t Eating |] | Eatin | g at Ni | ght | | Mean Difference | Mean Difference |
|--------------------------|----------|--------------------|--------|--------------|---------|------------|--------|----------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 15.10.1 Lab Study | | | | | | | | | |
| Gupta 2019 | 109.5 | 10.74 | 12 | 100.3 | 8.47 | 7 | 56.2% | 9.20 [0.47, 17.93] | —— |
| Subtotal (95% CI) | | | 12 | | | 7 | 56.2% | 9.20 [0.47, 17.93] | • |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z = 2.08 | (P = 0. | 04) | | | | | | |
| 15.10.2 Lab Study, S | nack at | Night | | | | | | | |
| Gupta 2019 | 124 | 14.59 | 14 | 100.3 | 7.84 | 6 | 43.8% | 23.70 [13.81, 33.59] | |
| Subtotal (95% CI) | | | 14 | | | 6 | 43.8% | 23.70 [13.81, 33.59] | |
| Heterogeneity: Not ap | plicable | 8 | | | | | | | |
| Test for overall effect: | Z = 4.70 | (P < 0. | 00001) | | | | | | |
| Total (95% CI) | | | 26 | | | 13 | 100.0% | 15.56 [9.01, 22.10] | • |
| Heterogeneity: Chi²= | 4.64, df | = 1 (P = | 0.03); | $I^2 = 78\%$ | 5 | | | | -50 -25 0 25 5 |
| Test for overall effect: | Z = 4.68 | (P < 0. | 00001) | | | | | | -50 -25 0 25 5i Favours Eating at Night Favours Not Eating |
| Test for subaroup diff | erences | Chi ² = | 4 64 d | f=1 (P | = 0.03 | $1^2 = 78$ | 3 4% | | Favours Eating at Might Favours Mot Eating |

^{*}Gupta 2019: (averaged 0130 & 0400 timepoints, on night shift 4). Eating at night (n=13; halved the participants to not double count them in the total). SEM converted to SD. Throughput (correct responses/ minute).

Important Outcomes

Figure S197. Diet and Meal Timing vs Control (Total Sleep Time (min), PSG or EEG) [CMT = 15 min] RCT (Healthy participants)

| | No | t Eating |) | Eatir | g at Nig | ght | | Mean Difference | Mean Difference |
|-----------------------------------|-----------|-----------|--------|----------|-----------|----------|--------|-----------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| 15.11.1 Lab Studies | | | | | | | | | |
| Gupta 2017 | 332.2 | 12.24 | 5 | 329.3 | 12.25 | 5 | 82.2% | 2.90 [-12.28, 18.08] | - |
| Gupta 2019 | 377.8 | 34.8 | 12 | 382.5 | 54.3 | 7 | 9.4% | -4.70 [-49.49, 40.09] | |
| Subtotal (95% CI) | | | 17 | | | 12 | 91.7% | 2.12 [-12.26, 16.49] | • |
| Heterogeneity: Tau ^z = | 0.00; CI | hi² = 0.1 | 0, df= | 1 (P = 0 | .75); 2= | - 0% | | | |
| Test for overall effect: | Z = 0.29 | P = 0 | 77) | | | | | | |
| 15.11.2 Lab Study, Si | nack at l | Night | | | | | | | |
| Gupta 2019 | 378.6 | 37.4 | 14 | 382.5 | 54.3 | 6 | 8.3% | -3.90 [-51.56, 43.76] | |
| Subtotal (95% CI) | | | 14 | | | 6 | | -3.90 [-51.56, 43.76] | |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z = 0.16 | (P = 0. | 87) | | | | | | |
| Total (95% CI) | | | 31 | | | 18 | 100.0% | 1.62 [-12.15, 15.38] | • |
| Heterogeneity: Tau ² = | 0.00; CI | hi² = 0.1 | 6, df= | 2(P = 0) | .93); [2= | - 0% | | | |
| Test for overall effect: | | | | | 6000 | | | | -100 -50 0 50 100 |
| Test for subaroup diff | | , | | f= 1 (P | = 0.81) | 12 = 0.9 | | | Favours Eating at Night Favours Not Eating |

^{*}Gupta 2017: Day sleep after Night shift 2 (only data available during intervention).

Gupta 2019: Day sleep after Night shift 3. Eating at night (n=13; halved the participants to not double count them in the total).

Figure S198. Diet and Meal Timing vs Control (Total Sleep Time, actigraphy) [CMT = 15 min] RCT (Healthy participants)

| | Not | Eatin | g | Eating | at Ni | ght | | Mean Difference | Mean Difference |
|--------------------------|-----------|------------------|---------|-----------------|--------|--------------|--------|----------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 15.15.1 Lab Study | | | | | | | | | |
| Gupta 2019 | 415.4 | 5.5 | 8 | 414.2 | 5.3 | 5 | 83.0% | 1.20 [-4.81, 7.21] | - - |
| Subtotal (95% CI) | | | 8 | | | 5 | 83.0% | 1.20 [-4.81, 7.21] | • |
| Heterogeneity: Not ap | oplicable | | | | | | | | |
| Test for overall effect: | Z = 0.39 | (P = 0 | 0.70) | | | | | | |
| 15.15.2 Lab Study, S | nack at N | Night | | | | | | | |
| Gupta 2019 | 404.9 | 23.7 | 14 | 414.2 | 5.3 | 5 | 17.0% | -9.30 [-22.56, 3.96] | |
| Subtotal (95% CI) | | | 14 | | | 5 | 17.0% | -9.30 [-22.56, 3.96] | |
| Heterogeneity: Not ap | oplicable | | | | | | | | |
| Test for overall effect | Z=1.38 | (P = (| 0.17) | | | | | | |
| Total (95% CI) | | | 22 | | | 10 | 100.0% | -0.59 [-6.06, 4.88] | • |
| Heterogeneity: Chi²= | 2.00, df: | = 1 (P | = 0.16) | $ ^2 = 509$ | % | | | | -50 -25 0 25 5 |
| Test for overall effect: | Z = 0.21 | (P = 0) | 0.83) | | | | | | -50 -25 0 25 5 Favours Eating at Night Favours Not Eating |
| Test for subgroup dif | ferences: | Chi ² | = 2.00. | df = 1 (P) | = 0.11 | 6) $ z = 5$ | 50.0% | | 1 avours Lauring activity it Pavours (vol Eating |

^{*}Gupta 2019: Day sleep after Night shift 3. Eating at night (n=10; halved the participants to not double count them in the total)

Figure S199. Diet and Meal Timing vs Control (Mental Health, Depression-like Mood) [CMT = Not Established] RCT (Healthy participants)

| | Not | Eatin | g | Eating at Night | | | Mean Difference | Mean Difference | | | |
|-------------------|------|-------|-------|-----------------|-----|-------|----------------------|-----------------|---------------|-----------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fix | ced, 95% CI | |
| Qian 2022 | 99.7 | 3.7 | 10 | 86.5 | 3.4 | 9 | 13.20 [10.01, 16.39] | | | + | |
| | | | | | | | | -20 | -10 | 0 10 20 | |
| | | | | | | | | Favours E | Eating at Nig | ht Favours Not Eating | |

^{*}Qian 2022: averaged across each timepoint and averaged across Days 2-4, data presented as % of baseline, higher numbers=less depression, data extracted from the graph

Figure S200. Diet and Meal Timing vs Control (Mental Health, Anxiety-like Mood) [CMT = Not Established] RCT (Healthy participants)

| Not Eating | | g | Eating at Night | | | Mean Difference | Mean Difference | |
|-------------------|------|-----|-----------------|------|-----|-----------------|-------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| Qian 2022 | 102 | 3.6 | 10 | 96 | 4.3 | 9 | 6.00 [2.41, 9.59] | |
| | | | | | | | x = x_ | -20 -10 0 10 20 |
| | | | | | | | | Favours Eating at Night Favours Not Eating |

^{*}Qian 2022: averaged across each timepoint and averaged across Days 2-4, data presented as % of baseline, higher numbers=less anxiety, data extracted from the graph

Figure S201. Diet and Meal Timing vs Control (WASO, PSG or EEG) [CMT = 20 min] RCT (Healthy participants)

| | Not | t Eating | 9 | Eatin | g at Ni | ght | | Mean Difference | Mean [| Difference |
|-----------------------------------|----------|-------------|---------|-----------|----------|-------------------|--------|-----------------------|--|------------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Rand | om, 95% CI |
| 15.12.1 Lab Studies | | | | | | | | | | |
| Gupta 2017 | 23.6 | 12.2 | 5 | 24.5 | 12.2 | 5 | 82.0% | -0.90 [-16.02, 14.22] | Sec. 1 | - |
| Gupta 2019 | 37.5 | 34.7 | 12 | 32.3 | 53.8 | 7 | 9.5% | 5.20 [-39.23, 49.63] | - | - |
| Subtotal (95% CI) | | | 17 | | | 12 | 91.5% | -0.27 [-14.58, 14.05] | • | ~ |
| Heterogeneity: Tau ² = | 0.00; C | $hi^2 = 0.$ | 06, df= | 1 (P= | 0.80); (| z = 0% | | | | |
| Test for overall effect: | Z = 0.04 | P = 0 | .97) | | | | | | | |
| 15.12.2 Lab Study, Sn | ack at | Night | | | | | | | | |
| Gupta 2019 | 34.2 | 35.3 | 14 | 32.3 | 53.8 | 6 | 8.5% | 1.90 [-44.95, 48.75] | 9 | <u> </u> |
| Subtotal (95% CI) | | | 14 | | | 6 | 8.5% | 1.90 [-44.95, 48.75] | | |
| Heterogeneity: Not ap | plicable | 12 | | | | | | | | |
| Test for overall effect: | Z = 0.08 | P = 0 | .94) | | | | | | | |
| Total (95% CI) | | | 31 | | | 18 | 100.0% | -0.08 [-13.77, 13.61] | - | • |
| Heterogeneity: Tau ² = | 0.00; C | $hi^2 = 0.$ | 07, df= | 2 (P= | 0.96); (| ² = 0% | | | 100 -50 | <u> </u> |
| Test for overall effect: | Z = 0.01 | (P = 0) | .99) | | 800 | | | | THE CHARLES THE PARTY OF THE PA | Ó 50 10 Favours Eating at Night |
| Test for subgroup diffe | erences | : Chi²: | = 0.01 | df = 1 (F | 2 = 0.93 | 3), $ z = 1$ | 1% | | ravours Not Eating | ravours calling at Night |

^{*}Gupta 2017: Day sleep after Night shift 2 (only data available during intervention). Eating at night at 0130.

Gupta 2019: Day sleep after Night shift 3. Eating or Snack at night at 0030. Eating at night (n=13; halved the participants to not double count them in the total)

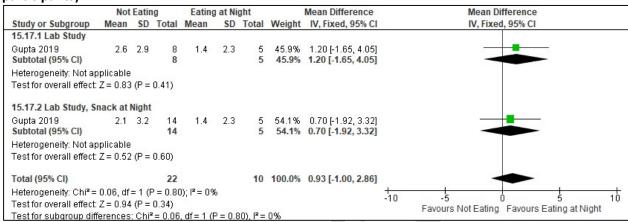
Figure S202. Diet and Meal Timing vs Control (Sleep Latency, PSG or EEG) [CMT = 20 min] RCT (Healthy participants)

| | Not | Eating | g | Eatin | g at Ni | ght | | Mean Difference | Mean Difference |
|-----------------------------------|-----------|--------------------|---------|------------|----------|-------------------|--------|--------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| 15.13.1 Lab Studies | | | | | | | | | |
| Gupta 2017 | 3.7 | 0.96 | 5 | 2.5 | 0.96 | 5 | 76.5% | 1.20 [0.01, 2.39] | |
| Gupta 2019 | 5.3 | 2.5 | 12 | 5.3 | 3.3 | 7 | 13.6% | 0.00 [-2.82, 2.82] | |
| Subtotal (95% CI) | | | 17 | | | 12 | 90.1% | 1.02 [-0.08, 2.12] | • |
| Heterogeneity: Tau ² = | 0.00; CI | hi² = 0. | 59, df= | 1 (P= | 0.44); [| = 0% | | | |
| Test for overall effect: | Z = 1.82 | (P = 0) |).07) | | | | | | |
| 15.13.2 Lab Study, Si | nack at l | Night | | | | | | | |
| Gupta 2019 | 6.6 | 3.8 | 14 | 5.3 | 3.3 | 6 | 9.9% | 1.30 [-2.01, 4.61] | - • |
| Subtotal (95% CI) | | | 14 | | | 6 | 9.9% | 1.30 [-2.01, 4.61] | |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z = 0.77 | (P = 0 | 0.44) | | | | | | |
| Total (95% CI) | | | 31 | | | 18 | 100.0% | 1.05 [0.01, 2.09] | • |
| Heterogeneity: Tau ² = | 0.00; CI | hi² = 0. | 61, df= | 2 (P= | 0.74); [| ² = 0% | | | -10 -5 0 5 10 |
| Test for overall effect: | Z = 1.97 | (P = 0 | 0.05) | 180 | 838 | | | | Favours Not Eating Favours Eating at Night |
| Test for subaroup diff | erences | Chi ² : | = 0.02 | df = 1 / F | 0 = 0.8 | 7) 2 = (| 196 | | ravours Not Eating Pavours Eating at Night |

^{*}Gupta 2017: Day sleep after Night shift 2 (only data available during intervention).

Gupta 2019: Day sleep after Night shift 3. Eating at night (n=13; halved the participants to not double count them in the total)

Figure S203. Diet and Meal Timing vs Control (Sleep Latency, actigraphy) [CMT = 15 min] RCT (Healthy participants)



^{*}Gupta 2019: Day sleep after Night shift 3. Eating at night (n=10; halved the participants to not double count them in the total)

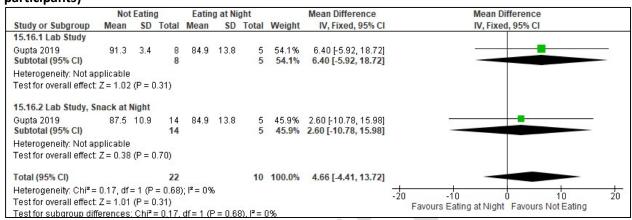
Figure S204. Diet and Meal Timing vs Control (Sleep Efficiency, PSG or EEG) [CMT = 10%] RCT (Healthy participants)

| | Not | Eating | 3 | Eatin | g at Ni | ght | | Mean Difference | Mean Difference |
|-----------------------------------|----------|--------------------|---------|----------|---------|-------------------------|--------|-----------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| 15.14.1 Lab Studies | | | | | | | | | 1 |
| Gupta 2017 | 92.4 | 3.35 | 5 | 92.42 | 3.35 | 5 | 80.8% | -0.02 [-4.17, 4.13] | |
| Gupta 2019 | 89.8 | 8.3 | 12 | 91.1 | 13.1 | 7 | 12.0% | -1.30 [-12.08, 9.48] | • |
| Subtotal (95% CI) | | | 17 | | | 12 | 92.8% | -0.19 [-4.06, 3.69] | • |
| Heterogeneity: Tau ² = | 0.00; CI | $hi^2 = 0.$ | 05, df= | 1 (P= | 0.83); | ² = 0% | | | |
| Test for overall effect: | Z = 0.09 | (P = 0 | .93) | 161 | 8333 | | | | |
| 15.14.2 Lab Study, Sr | ack at I | Night | | | | | | | |
| Gupta 2019 | 90.3 | 14 | 9 | 91.1 | 13.1 | 6 | 7.2% | -0.80 [-14.71, 13.11] | - |
| Subtotal (95% CI) | | | 9 | | | 6 | 7.2% | -0.80 [-14.71, 13.11] | |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z= 0.11 | (P = 0 | .91) | | | | | | |
| Total (95% CI) | | | 26 | | | 18 | 100.0% | -0.23 [-3.96, 3.50] | • |
| Heterogeneity: Tau ² = | 0.00; CI | hi² = 0. | 05, df= | 2 (P = | 0.97); | ² =0% | | | -20 -10 0 10 2 |
| Test for overall effect: | Z = 0.12 | (P = 0) | .90) | | | | | | -20 -10 0 10 2i Favours Eating at Night Favours Not Eating |
| Test for subgroup diff | erences | Chi ² = | 0.01 | df = 1/F | 9 = 0.9 | $3) \mathbf{F} = 0$ | 196 | | Favours Eating attrigit. Favours Not Eating |

^{*}Gupta 2017: Day sleep after Night shift 2 (only data available during intervention).

Gupta 2019: Day sleep after Night shift 3. Eating at night (n=13; halved the participants to not double count them in the total)

Figure S205. Diet and Meal Timing vs Control (Sleep Efficiency, actigraphy) [CMT = 10%] RCT (Healthy participants)



^{*}Gupta 2019: Day sleep after Night shift 3. Eating at night (n=10; halved the participants to not double count them in the total)

Bright light and caffeine

Summary of Findings (GRADE)

Table S17. Bright light and caffeine in adults with shiftwork disorder

References: Babkoff 2002, Wright 1997, Outcomes **Certainty of the Absolute Difference** No of Participants [Tool] evidence (studies) (GRADE) **Bright light and caffeine vs Control** The mean difference in the bright light and caffeine group **Excessive sleepiness or** 22 **Ф**ООО was 6.71 higher (7.43 lower to 20.85 higher) compared to (1 RCT) alertness VERY LOW^{c,d,e} [VAS (sleepiness)]a,b control **Excessive sleepiness or** The mean difference in the bright light and caffeine group 19 Θ alertness was 1.77 points lower (2.87 lower to 0.67 lower) compared (1 RCT) VERY LOW^{c,e,g,h} [SSS]f to control The mean difference in the bright light and caffeine group Excessive sleepiness or **Φ**()()() 20 alertness was 2.02 minutes more (1.48 more to 2.56 more) compared (1 RCT) VERY LOWc,e,g,h [MWT]a Cognitive performance **Ф**ООО The evidence (2 RCTs) is very uncertain about the effect of VERY LOW c,d,e,g [multiple tests]b bright light and caffeine on cognitive performance (2 RCTs) (performance tests include choice reaction time, letter cancellation, PVT, Dual Task control losses, Switching Task-Mannequin and -Math, and Wilkinson Four choice reaction time).

- a. Higher values favor the intervention
- b. CMT was not established by the TF
- c. Risk of bias concerns due to lack of blinding
- d. Imprecision due to the 95% CI crossing the null
- e. Imprecision due to small sample size (<200 participants)
- f. Lower values favor the intervention
- g. Indirectness is due to the fact that participants included in the studies are healthy individuals. The effect in adults with SWD may be different.
- h. Imprecision due to the 95% crossing the CMT

Study Characteristics

Table S18. Bright light and caffeine in adults with shiftwork disorder

| | | • | | | | | | |
|-------------------|-------------------|---|----------------------|---|--|---|--|---------------------------------|
| Study Citation | Study Design | Number of Participants (% Female) | Age range (years) | Population | Intervention (dose/intensity) | Comparator | Time of Intervention Delivery | Duration of Follow- up |
| Babkoff 2002 | RCT, crossover | 12 (42) | 19-36 | Shift workers without SWD diagnosis | Bright light (3,000 lux) and caffeine (200 mg) | Dim light (20-50 lux) and placebo | light exposure from 01:30- 02:30 caffeine or placebo given at 01:40 | 1 day |
| Wright 1997 | RCT | 46 (0) | 18–25 | Healthy participants | Bright Light- Caffeine (2500 lux/200 mg caffeine) | Dim Light- Placebo (≤100 lux/200 mg sugar) | bright light from 20.00 to 08.00 hours Caffeine at 20.00 and 02.00 hours each night | 2 nights |

Critical Outcomes

Figure S206. Bright Light + Caffeine vs Dim-light +placebo (Excessive Sleepiness, VAS-sleepiness) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

| | Bright | t Light + | Caf | Dim lig | ht + plac | ebo | Mean Difference | | | Mean Di | fference | | |
|-------------------|--------|-----------|-------|---------|-----------|-------|---------------------|-------|-----------------|-----------|-----------|----------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | | IV, Fixed | , 95% CI | | |
| 19.1.1 Lab Study | | | | | | | | | | | | | |
| Babkoff 2002 | 52.86 | 18.04 | 11 | 46.15 | 15.72 | 11 | 6.71 [-7.43, 20.85] | | | | + | | |
| | | | | | | | | | | 200 | | | |
| | | | | | | | | -50 | -25 | (|) | 25 | 50 |
| | | | | | | | | Favou | ırs Dim light + | placebo | Favours B | right Light +C | af |

^{*}Babkoff 2002: Data extracted from graph (0230-0830); SEM converted to SD. Higher value represents higher arousal

Figure S207. Bright Light + Caffeine vs Dim-Light + Caffeine (Excessive Sleepiness, VAS-sleepiness) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

| | Bright | t Light + | Caf | Dim- | light + (| Caf | Mean Difference | | | Mean D | ifference | | |
|-------------------|--------|-----------|-------|-------|-----------|-------|---------------------|-----|--------------|--------------|-----------|----------------|-------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | | IV, Fixe | d, 95% CI | | |
| 20.24.1 Lab Study | | | | | | | | | | | | | |
| Babkoff 2002 | 52.86 | 18.04 | 11 | 48.28 | 16.72 | 11 | 4.58 [-9.96, 19.12] | | | 50 | 1 | -93 | |
| | | | | | | | | _ | | | | | - 1 |
| | | | | | | | | -50 | -25 | | Ò | 25 | 50 |
| | | | | | | | | | Favours Dim- | -light + Caf | Favours | Bright Light - | + Caf |

^{*}Babkoff 2002: Data extracted from graph (0230-0830); SEM converted to SD. Higher value represents higher arousal

Figure S208. Bright Light + Caffeine vs Bright Light + Placebo (Excessive Sleepiness, VAS-sleepiness) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

| | Bright | Light + | Caf | Bright Li | ght + Plac | cebo | Mean Difference | Mean Difference |
|-------------------|--------|---------|-------|-----------|------------|-------|----------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 20.25.1 Lab Study | | | | | | | | |
| Babkoff 2002 | 52.86 | 18.04 | 11 | 40.57 | 17.35 | 11 | 12.29 [-2.50, 27.08] | + |
| | | | | | | | | |
| | | | | | | | | -50 -25 0 25 5 Favours BL + Placebo Favours BL + Caf |

Figure S209. Bright light + Caffeine vs Dim-light + Placebo (Excessive Sleepiness, SSS) [CMT = 1 pts] RCT (Healthy participants)

| | Bright | Light + | Caf | Dim-lig | ht + Plac | ebo | Std. Mean Difference | Std. Mean Difference | |
|-------------------|--------|---------|-------|---------|-----------|-------|----------------------|--------------------------------------|-------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | |
| 18.21.1 Lab Study | | | | | | | | 1 | |
| Wright 1997 | 2.82 | 0.98 | 10 | 4.33 | 0.57 | 9 | -1.77 [-2.87, -0.67] | | |
| | | | | | | | + | | |
| | | | | | | | -4 | -2 0 2 | 4 |
| | | | | | | | | Favours BL + Caf Favours Dim-I + Pla | acebo |

Figure S210. Bright light + Caffeine vs Dim-light + Caffeine (Excessive Sleepiness, SSS) [CMT = 1 pts] RCT (Healthy participants)

| | Bright | Light + | Caf | Dim-I | ight + (| Caf | Std. Mean Difference | Std. Mean | Difference |
|-------------------|--------|---------|-------|-------|----------|-------|----------------------|--|-------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed | , 95% CI |
| 20.38.1 Lab Study | | | | | | | | | |
| Wright 1997 | 2.82 | 0.98 | 10 | 3.57 | 0.72 | 9 | -0.83 [-1.77, 0.12] | - 1 | - |
| | | | | | | | + | | |
| | | | | | | | -4 | The second section of the second section is a second section of the second section of the second section of the second second section of the section of the second section of the second section of the second section of the second section of the section of th | 1 2 4 |
| | | | | | | | | Favours BL + Caf | Favours Dim-light + Caf |

Figure S211. Bright light + Caffeine vs Bright Light + Placebo (Excessive Sleepiness, SSS) [CMT = 1 pts] RCT (Healthy participants)

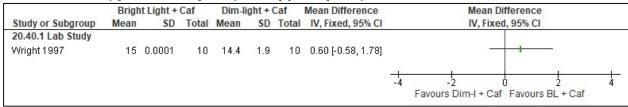
| | Bright | Light + | Caf | Bright Lig | ht + Plac | cebo 5 | Std. Mean Difference | Std. Mean Difference | |
|-------------------|--------|---------|-------|-------------------|-----------|--------|----------------------|---|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | |
| 20.39.1 Lab Study | | | | | | | | | |
| Wright 1997 | 2.82 | 0.98 | 10 | 4.33 | 0.6 | 10 | -1.78 [-2.85, -0.71] | - 1 | |
| | | | | | | | + | | |
| | | | | | | | -4 | -2 0 2 Favours BL + Caf Favours BL + Placebo | 4 |

^{*}Wright 1997: Night 1 data used; SEM converted to SD.

Figure S212. Bright light + Caffeine vs Dim-light + Placebo (Excessive Sleepiness, Maintenance of Wakefulness Test) [CMT = 2 min] RCT (Healthy participants)

| | Brigh | t Light + | Caf | Dim-lig | ht + Plac | ebo | Mean Difference | | N | Mean Dif | ference | |
|-------------------|-------|-----------|-------|---------|-----------|-------|-------------------|-------|--------------|----------|--------------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | ľ | V, Fixed | 95% CI | |
| 18.3.1 Lab Study | | | | | | | | | | | | |
| Wright 1997 | 15 | 0.0001 | 10 | 12.98 | 0.87 | 10 | 2.02 [1.48, 2.56] | | | | - | _ |
| | | | | | | | | 4 | | 70 | | |
| | | | | | | | | -4 | -2 | Ó | 2 | |
| | | | | | | | | Favou | rs Dim-I + P | lacebo | Favours BL + | Caf |

Figure S213. Bright light + Caffeine vs Dim-light + Caffeine (Excessive Sleepiness, Maintenance of Wakefulness Test) [CMT = 2 min] RCT (Healthy participants)



^{*}Babkoff 2002: Data extracted from graph (0230-0830); SEM converted to SD. Higher value represents higher arousal.

Figure S214. Bright light + Caffeine vs Bright Light + Placebo (Excessive Sleepiness, Maintenance of Wakefulness Test) [CMT = 2 min] RCT (Healthy participants)

| | Brigh | t Light + | Caf | Bright Li | ght + Pla | cebo | Mean Difference | | M | ean Differen | ce | |
|-------------------|-------|-----------|-------|-----------|-----------|-------|-------------------|-------|-------------|--------------|--------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV | , Fixed, 95% | CI | |
| 20.41.1 Lab Study | | | | | | | | | | 18 | | |
| Wright 1997 | 15 | 0.0001 | 10 | 13.49 | 2.31 | 10 | 1.51 [0.08, 2.94] | | | 8 | - | |
| | | | | | | | | + | - | | | - |
| | | | | | | | | -4 | -2 | 0_ | 2 | 4 |
| | | | | | | | | Favou | rs BL + Pla | cebo Favo | urs BL + Caf | |

^{*}Wright 1997: Used Night 1 data; SEM converted to SD.

Figure S215. Bright Light + Caffeine vs Dim-light + placebo (Cognitive Performance, choice reaction time) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

| | Bright | Light + | Caf | Dim-lig | ht + Plac | ebo | Mean Difference | | Mean | Difference | | |
|-------------------|--------|---------|-------|---------|-----------|-------|--------------------------|------|------------------------|-----------------|------------------|----------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fix | ed, 95% CI | | |
| 19.2.1 Lab Study | | | | | | | | | | 0 | | |
| Babkoff 2002 | 694.46 | 165.3 | 11 | 802.52 | 241.02 | 11 | -108.06 [-280.77, 64.65] | | - | 10.00 | | |
| | | | | | | | | | | 1 | -1- | -1- |
| | | | | | | | | -500 | -250 Favours BL + C | U af Favours | 250 Dim-l + F | 500 Placebo |

^{*}Babkoff 2002: Data extracted from graph (0230-0830); SEM converted to SD.

Figure S216. Bright light + Caffeine vs Dim-light + Placebo (Cognitive Performance, letter cancellation (number of trials without a false alarm)) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

| | Bright | Light + | Caf | Dim-lig | ht + Plac | ebo | Mean Difference | Mean Difference |
|-------------------|--------|---------|-------|---------|-----------|-------|-------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 19.3.1 Lab Study | | | | | | | | |
| Babkoff 2002 | 6.62 | 0.63 | 11 | 6.11 | 0.33 | 11 | 0.51 [0.09, 0.93] | |
| | | | | | | | | |
| | | | | | | | | -2 -1 0 1 2 |
| | | | | | | | | Favours Dim-I + Placebo Favours BL + Caf |

^{*}Babkoff 2002: Data extracted from graph (0230-0830), SEM converted to SD.

Figure S217. Bright light + Caffeine vs Dim-light + Placebo (Cognitive Performance, PVT reaction time) [CMT = Not Established] RCT (Healthy participants)

| | Bright | Light + | Caf | Dim-lig | ht + Plac | ebo | Mean Difference | Mean Difference | |
|-------------------|--------|---------|-------|---------|-----------|-------|-------------------------|-------------------------------------|-------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | |
| 18.8.1 Lab Study | | | | | | | | | |
| Wright 1997 | 265.84 | 14.48 | 10 | 327.39 | 43.59 | 9 | -61.55 [-91.41, -31.69] | - 1 | |
| 2.00206 | | | | | | | | | 1 |
| | | | | | | | | -100 -50 0 50 | 100 |
| | | | | | | | | Favours BL + Caf Favours Dim-I + PI | acebo |

^{*}Wright 1997: Data extracted (0030-0630 timepoints averaged); SEM converted to SD.

Figure S218. Bright light + Caffeine vs Dim-light + Placebo (Cognitive Performance, Dual task control losses) [CMT = Not Established] RCT (Healthy participants)

| | Bright | t Light + | Caf | Dim-lig | ht + Plac | cebo | Mean Difference | | Mean Differ | rence | |
|-------------------|--------|-----------|-------|---------|-----------|-------|------------------------|-----|---------------------|---------------------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 9 | 5% CI | |
| 18.9.1 Lab Study | | | | | | | | | 3 | | |
| Wright 1997 | 11.36 | 11.86 | 10 | 28.34 | 12.84 | 10 | -16.98 [-27.81, -6.15] | | - | | |
| | | | | | | | | | | - 1 | |
| | | | | | | | | -50 | -25 Ó | 25 | 50 |
| | | | | | | | | | Favours BL + Caf Fa | avours Dim-I + Plac | cbo |

^{*}Wright 1997: Data extracted (0030-0630 timepoints averaged); SEM converted to SD.

Figure S219. Bright light + Caffeine vs Dim-light + Placebo (Cognitive Performance, Switching Task-Mannequin throughput- change from baseline) [CMT = Not Established] RCT (Healthy participants)

| | | | | | | | | | - | | <u> </u> | |
|-------------------|--------|---------|-------|---------|-----------|-------|--------------------|-----------|-------------|-------------|------------|-----|
| | Bright | Light + | Caf | Dim-lig | ht + Plac | ebo | Mean Difference | | Me | an Differen | ice | |
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, | Fixed, 95% | CI | |
| 18.10.1 Lab Study | | | | | | | | | | 1 | | |
| Wright 1997 | 5.27 | 4.52 | 10 | 2.11 | 4.17 | 9 | 3.16 [-0.75, 7.07] | | | 564 | + | - |
| 10090 | | | | | | | | | | | | |
| | | | | | | | | -10 | -5 | - 6 | 5 | 10 |
| | | | | | | | | Favours [| Dim-I + Pla | cebo Favo | urs BL + C | Caf |
| | | | | | | | | | | | | |

^{*}Wright 1997: Data extracted (0030-0630 timepoints averaged); SEM converted to SD.

Figure S220. Bright light + Caffeine vs Dim-light + Placebo (Cognitive Performance, Wilkinson Four Choice Reaction Time) [CMT = Not Established] RCT (Healthy participants)

| | Bright | Light + | Caf | Dim-lig | ht + Plac | ebo | Mean Difference | Mean Di | fference |
|-------------------|--------|---------|-------|---------|-----------|-------|----------------------|-------------------------|------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed | , 95% CI |
| 18.11.1 Lab Study | | | | | | | | | |
| Wright 1997 | 185.45 | 4.75 | 10 | 158.25 | 19.64 | 10 | 27.20 [14.68, 39.72] | | |
| | | | | | | | | 11 10 | 7 1 |
| | | | | | | | | -50 -25 (|) 2'5 5'0 |
| | | | | | | | | Favours Dim-I + Placebo | Favours BL + Caf |

^{*}Wright 1997: Data extracted (0030-0630 timepoints averaged); SEM converted to SD.

Figure S221. Bright light + Caffeine vs Dim-light + Placebo (Cognitive Performance, Switching Task-Math throughput) [CMT = Not Established] RCT (Healthy participants)

| | Bright I | Light + | Caf | Dim-ligh | t + Plac | ebo | Mean Difference | | Me | ean Diff | ference | |
|-------------------|----------|---------|-------|----------|----------|-------|--------------------|------|-----------------|----------|------------------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV | , Fixed, | 95% CI | |
| 18.12.1 Lab Study | | | | | | | | | | 1910 | | |
| Wright 1997 | 30.02 | 7.4 | 10 | 23.74 | 3.9 | 9 | 6.28 [1.03, 11.53] | | | | | |
| | | | | | | | | | | | | - 1 |
| | | | | | | | | -20 | -10 | Ó | 1'0 | 20 |
| | | | | | | | | Favo | urs Dim-I + Pla | acebo | Favours BL + Caf | |

^{*}Wright 1997: Data extracted (0030-0630 timepoints averaged); SEM converted to SD.

None

Nap and caffeine

Summary of Findings (GRADE)

Table S19. Nap and caffeine in adults with shiftwork disorder

References: Schweitzer 2006 Outcomes Certainty of the **Absolute Difference** No of Participants [Tool] evidence (studies) (GRADE) Nap and caffeine vs Control The mean difference in the nap and caffeine group was 1.96 111 **Excessive sleepiness or** Θ alertness points lower (3.06 lower to 0.85 lower) compared to control (2 RCTs) VERY LOW^{b,c,d} [KSS]a **Excessive sleepiness or** $\Theta \bigcirc \bigcirc \bigcirc$ The mean difference in the nap and caffeine group was **7.12** 33 alertness min higher (0.45 higher to 13.79 higher) compared to (1 RCT) VERY LOWb,c,d,f [MWT]e control **Cognitive performance** The mean difference in the nap and caffeine group was 2.23 33 Θ lapses fewer (4.53 fewer to 0.07 more) compared to control (1 RCT) [PVT lapses]a VERY LOW^{b,c,d,f,g} **Cognitive performance** The evidence (2 RCTs) is very uncertain about the effect of Θ [multiple tests]h naps and caffeine on cognitive performance (measured by VERY LOW^{b,c,g} PVT and Torrence Test of Creative thinking).

- a. Lower values favor the intervention
- b. Risk of bias concerns due to lack of blinding
- c. Indirectness is due to the fact that participants included in the studies are healthy individuals. The effect in adults with SWD may be different
- d. Imprecision due to 95% CI crossing the CMT
- e. Higher values favor the intervention
- f. Imprecision due to small sample size (<200 participants)
- g. Imprecision due to 95% CI crossing the null
- h. CMT was not established by the TF

Study Characteristics

Table S20. Nap and caffeine in adults with shiftwork disorder

| | DIC CEC. ITUP | | | | | | | |
|--------------------|--|--|--|--|---|------------------------|---|------------------------------|
| Study Citation | Study Design | Number of Participant s (% Female) | Age (years) | Population | Intervention (duration /intensity) | Comparat or | Time of Intervention Delivery | Duration of Follow- up |
| Schweitzer 2006 | Lab study: RCT Field study: RCT, crossover | Lab Study: 68 (53) Field Study: 53 (21) | Lab study: 31.3 Field study: 33.5 | Lab Study: healthy individuals Field Study: shift workers without SWD diagnosis | (Lab) nap (2.5 hr) plus caffeine (4 mg/kg) (Field) nap (2 hr) plus caffeine (300 mg) | placebo and no naps | (Lab) nap from 19:30- 22:00 plus caffeine taken 30 minutes prior to night shifts; (Field) nap prior to the night shift starting approximately 3-4 hours before shift | 4 nights |

Critical Outcomes

Figure S222. Nap + Caffeine vs Control (Excessive Sleepiness, KSS) [CMT = 1 pt] RCT (Healthy participants)

| | Na | p + Caf | | P | lacebo | | | Mean Difference | Mean Difference |
|--------------------------|----------|----------------------|---------|-------------|----------|-------------|--------|----------------------|------------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 19.8.1 Field Study | | | | | | | | | |
| Schweitzer 2006 | 5.66 | 13.22 | 39 | 6.29 | 14.69 | 39 | 3.2% | -0.63 [-6.83, 5.57] | * |
| Subtotal (95% CI) | | | 39 | | | 39 | 3.2% | -0.63 [-6.83, 5.57] | |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z = 0.20 | P = 0.1 | 84) | | | | | | |
| 19.8.2 Lab Study | | | | | | | | | |
| Schweitzer 2006 | 4.8 | 1.7 | 17 | 6.8 | 1.6 | 16 | 96.8% | -2.00 [-3.13, -0.87] | - |
| Subtotal (95% CI) | | | 17 | | | 16 | 96.8% | -2.00 [-3.13, -0.87] | • |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z = 3.48 | (P = 0. | 0005) | | | | | | |
| Total (95% CI) | | | 56 | | | 55 | 100.0% | -1.96 [-3.06, -0.85] | • |
| Heterogeneity: Chi²= | 0.18, df | = 1 (P = | 0.67); | $I^2 = 0\%$ | | | | | -10 -5 0 5 1 |
| Test for overall effect: | Z = 3.46 | (P = 0.1) | 0005) | | | | | | Favours Nap + Caf Favours Placebo |
| Test for subgroup diff | erences | : Chi ² = | 0.18, d | f=1 (P | = 0.67), | $I^2 = 0.9$ | 6 | | Tavours Ivap - Odi Favours Flacebo |

 $^{{}^*}$ Schweitzer 2006 (Field): KSS data from end of shift; SD calculated from p-value.

Schweitzer 2006 (lab): KSS data only available for night 1.

Figure S223. Nap + Caffeine vs Caffeine (Excessive Sleepiness, KSS) [CMT = 1 pt] RCT (Healthy participants)

| | Nap | + Ca | af | Ca | ffeine | е | Mean Difference | | Mean D | ifference | |
|-------------------|------|------|-------|------|--------|-------|---------------------|------|----------------|-----------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixe | d, 95% CI | |
| 20.24.1 Lab Study | | | | | | | | | | 100 | |
| Schweitzer 2006 | 4.8 | 1.7 | 17 | 5.4 | 1.9 | 17 | -0.60 [-1.81, 0.61] | | - | 100 | |
| | | | | | | | | | 10 | | |
| | | | | | | | | -4 | -2 | Ó 2 | 4 |
| | | | | | | | | Favo | ours Nap + Caf | Favours C | af |

^{*}Schweitzer 2006 (lab): KSS data only available for night 1.

Figure S224. Nap + Caffeine vs Nap (Excessive Sleepiness, KSS) [CMT = 1 pt] RCT (Healthy participants)

| Nap | + Ca | af | 1 | Nap | | Mean Difference | | | Mean D | ifferen | ce | |
|------|------|---------|----------------------|--------------------|-----------------------|-----------------------------|----|---|--|---|--|---|
| Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | | IV, Fixe | d, 95% | CI | |
| | | | | | | | | | | 10 | | |
| 4.8 | 1.7 | 17 | 5.7 | 1.8 | 17 | -0.90 [-2.08, 0.28] | | 807 | - | 100 | | |
| | | | | | | | | | | | | |
| | | | | | | | -4 | -2 | | <u> </u> | | - |
| | | | | | | | | Favours Na | ap + Cat | Favor | urs Nap | |
| | Mean | Mean SD | \$2550 BPS 584 65150 | Mean SD Total Mean | Mean SD Total Mean SD | Mean SD Total Mean SD Total | | Mean SD Total Mean SD Total IV, Fixed, 95% CI | Mean SD Total Mean SD Total IV, Fixed, 95% CI 4.8 1.7 17 5.7 1.8 17 -0.90 [-2.08, 0.28] — -4 -2 -2 -2 -2 -4 -2 | Mean SD Total Mean SD Total IV, Fixed, 95% CI IV, Fixed 4.8 1.7 17 5.7 1.8 17 -0.90 [-2.08, 0.28] | Mean SD Total Mean SD Total IV, Fixed, 95% CI IV, Fixed, 95% 4.8 1.7 17 5.7 1.8 17 -0.90 [-2.08, 0.28] | Mean SD Total Mean SD Total IV, Fixed, 95% CI IV, Fixed, 95% CI |

^{*}Schweitzer 2006 (lab): KSS data only available for night 1.

Figure S225. Nap + Caffeine vs Control (Excessive Sleepiness, MWT) [CMT = 2 min] RCT (Healthy participants)

| | Nap | + Ca | af | P | lacebo | | Mean Difference | | Mean Difference |
|-------------------|-------|------|-------|-------|--------|-------|--------------------|-----|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 95% CI |
| 18.2.1 Lab Study | | | | | | | | | |
| Schweitzer 2006 | 25.98 | 5.9 | 17 | 18.86 | 12.36 | 16 | 7.12 [0.45, 13.79] | | |
| | | | | | | | | + | |
| | | | | | | | | -20 | -10 0 10 Favours Placebo Favours Nap + Caf |

^{*}Schweitzer 2006 (lab): MWT (data averaged and extracted from nightshift 2); SEM converted to SD.

Figure S226. Nap + Caffeine vs Caffeine (Excessive Sleepiness, MWT) [CMT = 2 min] RCT (Healthy participants)

| | Nap | + Ca | af | | Caf | | Mean Difference | Mean D | ifference |
|-------------------|-------|------|-------|-------|------|-------|--------------------|-------------|-------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixe | d, 95% CI |
| 20.24.1 Lab Study | | | | | | | | 7 | |
| Schweitzer 2006 | 25.98 | 5.9 | 17 | 22.94 | 6.51 | 17 | 3.04 [-1.14, 7.22] | 107 | 1 |
| | | | | | | | | | |
| | | | | | | | | -20 -10 | 0 10 20 |
| | | | | | | | | Favours Caf | Favours Nap + Caf |

^{*}Schweitzer 2006 (lab): MWT (data averaged and extracted from nightshift 2); SEM converted to SD.

Figure S227. Nap + Caffeine vs Nap (Excessive Sleepiness, MWT) [CMT = 2 min] RCT (Healthy participants)

| | Nap | + Ca | af . | | Nap | | Mean Difference | | Mean D | ifference | |
|-------------------|-------|------|-------|-------|------|-------|--------------------|-----|-------------|-------------|-------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixe | d, 95% CI | |
| 20.25.1 Lab Study | | | | | | | | | | | |
| Schweitzer 2006 | 25.98 | 5.9 | 17 | 21.62 | 8.82 | 17 | 4.36 [-0.68, 9.40] | | | +- | |
| | | | | | | | | _ | | 1 | |
| | | | | | | | | -20 | -10 | 0 10 | 20 |
| | | | | | | | | | Favours Nap | Favours Nap | + Caf |

^{*}Schweitzer 2006 (lab): MWT (data averaged and extracted from nightshift 2); SEM converted to SD.

Figure S228. Nap + Caffeine vs Control (Cognitive Performance, PVT lapses) [CMT = 1 lapse] RCT (Healthy participants)

| | Na | p + Ca | f | PI | acebo | | Mean Difference | Mean Difference |
|-------------------|------|--------|-------|------|-------|-------|---------------------|-----------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 18.7.1 Lab Study | | | | | | | | 9 |
| Schweitzer 2006 | 3.51 | 2.39 | 17 | 5.74 | 4.08 | 16 | -2.23 [-4.53, 0.07] | |
| | | | | | | | | |
| | | | | | | | | -10 -5 0 5 10 |
| | | | | | | | | Favours Nap + Caf Favours Placebo |

^{*}Schweitzer 2006 (lab): PVT # of lapses by sq root transformed; SEM converted to SD.

Figure S229. Nap + Caffeine vs Caffeine (Cognitive Performance, PVT lapses) [CMT = 1 lapse] RCT (Healthy participants)

| | Na | p + Ca | f | | Caf | | Mean Difference | | M | ean Dif | ference | |
|-------------------|------|--------|-------|------|-----|-------|---------------------|-----|------------|---------|-------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV | , Fixed | , 95% CI | |
| 20.24.1 Lab Study | | | | | | | | | | | 10 | |
| Schweitzer 2006 | 3.51 | 2.39 | 17 | 3.96 | 1.9 | 17 | -0.45 [-1.90, 1.00] | | | - | - | |
| | | | | | | | | | - 1 | | | |
| | | | | | | | | -10 | -5 | Ó | 5 | 10 |
| | | | | | | | | Fa | avours Nap | + Caf | Favours Caf | |

^{*}Schweitzer 2006 (lab): PVT # of lapses by sq root transformed; SEM converted to SD.

Figure S230. Nap + Caffeine vs Caffeine (Cognitive Performance, PVT lapses) [CMT = 1 lapse] RCT (Healthy participants)

| | Na | p + Ca | f | | Nap | | Mean Difference | Mean Difference |
|-------------------|------|--------|-------|------|------|-------|---------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 20.25.1 Lab Study | | | | | | | | |
| Schweitzer 2006 | 3.51 | 2.39 | 17 | 3.82 | 3.17 | 17 | -0.31 [-2.20, 1.58] | - - |
| | | | | | | | | |
| | | | | | | | | -10 -5 0 5 Favours Nap + Caf Favours Nap |

^{*}Schweitzer 2006 (lab): PVT # of lapses by sq root transformed; SEM converted to SD.

Figure S231. Nap + Caffeine vs Control (Cognitive Performance, PVT mean reaction time of the slowest 10%, reciprocally transformed) [CMT = Not Established] RCT (Shift workers without a SWD diagnosis)

| | Na | p + Ca | f | PI | acebo | | Mean Difference | Mean Difference |
|---------------------|------|--------|-------|------|-------|-------|--------------------|-----------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 19.14.1 Field Study | | | | | | | | |
| Schweitzer 2006 | 2.47 | 0.75 | 39 | 2.37 | 0.75 | 39 | 0.10 [-0.23, 0.43] | |
| | | | | | | | | |
| | | | | | | | | -1 -0.5 0 0.5 1 |
| | | | | | | | | Favours Placebo Favours Nap + Caf |

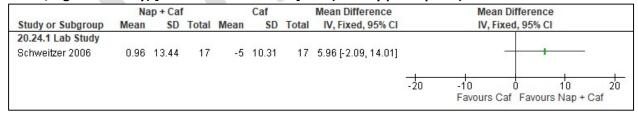
^{*}Schweitzer 2006 (Field): SEM converted to SD. PVT mean reaction times (reciprocally transformed).

Figure S232. Nap + Caffeine vs Control (Cognitive Performance, Torrance tests of creative thinking-verbal/ figural- fluency) [CMT = Not Established] RCT (Healthy participants)

| | Na | p + Caf | | PI | acebo | | Mean Difference | | Mean I | Difference | |
|-------------------|------|---------|-------|-------|-------|-------|--------------------|-----|-----------------|-------------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixe | ed, 95% CI | |
| 18.4.1 Lab Study | | | | | | | | | | 1 | |
| Schweitzer 2006 | 0.96 | 13.44 | 17 | -8.79 | 9.44 | 16 | 9.75 [1.86, 17.64] | | | | |
| | | | | | | | | _ | - 4 | | _ |
| | | | | | | | | -20 | -1'0 | Ó 1'O | 20 |
| | | | | | | | | | Favours Placebo | Favours Nap + Caf | |

^{*}Schweitzer 2006 (lab): Data extracted from graph; SEM converted to SD.

Figure S233. Nap + Caffeine vs Caffeine (Cognitive Performance, Torrance tests of creative thinking-verbal/ figural- fluency) [CMT = Not Established] RCT (Healthy participants)



^{*}Schweitzer 2006 (lab): Data extracted from graph; SEM converted to SD.

Figure S234. Nap + Caffeine vs Nap (Cognitive Performance, Torrance tests of creative thinking-verbal/figural-fluency) [CMT = Not Established] RCT (Healthy participants)

| | Na | p + Caf | F | | Nap | | Mean Difference | | Mea | an Difference | ce | |
|-------------------|------|---------|-------|-------|-------|-------|---------------------|-----|-----------|---------------|-----------|------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, F | Fixed, 95% | CI | |
| 20.25.1 Lab Study | | | | | | | | | | | | |
| Schweitzer 2006 | 0.96 | 13.44 | 17 | -9.44 | 11.63 | 17 | 10.40 [1.95, 18.85] | | | | - | - 10 |
| | | | | | | | | _ | 1 | | - | |
| | | | | | | | | -20 | -10 | Ó | 10 | 20 |
| | | | | | | | | | Favours 1 | Vap Favou | ırs Nap + | Caf |

^{*}Schweitzer 2006 (lab): Data extracted from graph; SEM converted to SD.

Figure S235. Nap + Caffeine vs Control (Total Sleep Time, PSG or Actigraphy) [CMT = 15 min] RCT

| | - | | | | | | | | |
|-----------------------------------|-----------|----------|---------|------------------------|----------|--------------|--------|-----------------------|--|
| | Na | p + Ca | f | P | lacebo | | | Mean Difference | Mean Difference |
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 18.20.1 Lab Study | | | | | | | | | |
| Schweitzer 2006 | 452.8 | 52.3 | 17 | 361.1 | 76.7 | 16 | 53.5% | 91.70 [46.64, 136.76] | |
| Subtotal (95% CI) | | | 17 | | | 16 | 53.5% | 91.70 [46.64, 136.76] | • |
| Heterogeneity: Not ap | oplicable | | | | | | | | |
| Test for overall effect | Z = 3.99 |) (P < 0 | 0.0001) | | | | | | |
| 18.20.2 Field Study | | | | | | | | | |
| Schweitzer 2006 | 358.5 | 99.4 | 33 | 342.2 | 100.8 | 33 | 46.5% | 16.30 [-32.00, 64.60] | - |
| Subtotal (95% CI) | | | 33 | | | 33 | 46.5% | 16.30 [-32.00, 64.60] | * |
| Heterogeneity: Not ap | oplicable | | | | | | | | |
| Test for overall effect | Z= 0.66 | 6 (P = 0 | 0.51) | | | | | | |
| Total (95% CI) | | | 50 | | | 49 | 100.0% | 56.61 [23.66, 89.56] | • |
| Heterogeneity: Chi ² = | 5.01, df | = 1 (P | = 0.03) |); I ² = 80 | % | | | | 100 |
| Test for overall effect | Z = 3.37 | (P = 0 | 0.0008) | | | | | | -200 -100 0 100 200 Favours Placebo Favours Nap + Caf |
| Test for subgroup dif | ferences | : Chi²: | = 5.01, | df = 1 (F | P = 0.03 |), $I^2 = 8$ | 0.0% | | Tavouis Flacebo Favouis Nap + Cal |

^{*}Schweitzer 2006 (Field): (actigraphy data from day sleep 2 and nap 2).

Schweitzer 2006 (lab): PSG data (from day sleep 2 and nap 2).

Figure S236. Nap + Caffeine vs Caffeine (Total Sleep Time, PSG) [CMT = 15 min] RCT (Healthy participants)

| Na | p + Ca | f | | Caf | | Mean Difference | | Mean Dif | ference | |
|-------|--------|---------|--|--------------------|-----------------------|-----------------------------|---|---|--|--|
| Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, | , 95% CI | |
| | | | | | | | | 1 | | |
| 452.8 | 52.3 | 17 | 360.4 | 77.2 | 17 | 92.40 [48.07, 136.73] | | | | |
| | | | | | | | | | 1 | - |
| | | | | | | | -200 | -100 Ó Favours Caf | The second of th | 200 f |
| | Mean | Mean SD | AND TO SEE STATE OF THE SECOND | Mean SD Total Mean | Mean SD Total Mean SD | Mean SD Total Mean SD Total | Mean SD Total Mean SD Total IV, Fixed, 95% CI | Mean SD Total Mean SD Total IV, Fixed, 95% CI 452.8 52.3 17 360.4 77.2 17 92.40 [48.07, 136.73] | Mean SD Total Mean SD Total IV, Fixed, 95% CI IV, Fixed 452.8 52.3 17 360.4 77.2 17 92.40 [48.07, 136.73] | Mean SD Total IV, Fixed, 95% CI IV, Fixed, 95% CI 452.8 52.3 17 360.4 77.2 17 92.40 [48.07, 136.73] ———————————————————————————————————— |

^{*}Schweitzer 2006 (lab):. PSG data (from day sleep 2 and nap 2).

Figure S237. Nap + Caffeine vs Nap (Total Sleep Time, PSG) [CMT = 15 min] RCT (Healthy participants)

| | | | - P (| | | -,, - | | The first of the f |
|-------|------------|---------------------|----------------------------|---------------------------------|--|--|-------------------------------|--|
| Na | p + Ca | f | | Nap | | Mean Difference | | Mean Difference |
| Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 95% CI |
| | | | | | | | | 7 |
| 452.8 | 52.3 | 17 | 405.3 | 81.6 | 17 | 47.50 [1.43, 93.57] | | - |
| | | | | | | | | |
| | | | | | | | -100 | -50 Ö 50 1Ö Favours Nap Favours Nap + Caf |
| | Na Mean | Nap + Ca Mean SD | Nap + Caf Mean SD Total | Nap + Caf Mean SD Total Mean | Nap + Caf Nap Mean SD Total Mean SD | Nap + Caf Nap Mean SD Total Mean SD Total | Nap + Caf Nap Mean Difference | Mean SD Total Mean SD Total IV, Fixed, 95% CI 452.8 52.3 17 405.3 81.6 17 47.50 [1.43, 93.57] |

^{*}Schweitzer 2006 (lab): PSG data (from day sleep 2 and nap 2).

(1 non-RCT)

Figure S238. Nap + Caffeine vs Control (Total Sleep Time, Sleep Diary) [CMT = 15 min] RCT

| | Na | p + Ca | f | PI | acebo | | Mean Difference | | Mean D | ifference | | |
|---------------------|-------|--------|-------|-------|-------|-------|-----------------------|------|-----------------|-----------|-----------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixe | d, 95% CI | | |
| 19.19.1 Field Study | | | | | | | | | | | | |
| Schweitzer 2006 | 415.6 | 67.7 | 39 | 401.6 | 80.1 | 39 | 14.00 [-18.92, 46.92] | | | 1 | | |
| | | | | | | | | T | 17 | | 1 | |
| | | | | | | | | -100 | -50 | Ó | 50 | 100 |
| | | | | | | | | | Favours Placebo | Favours N | lap + Caf | |

8-hour or 12-hour work shift

Summary of Findings (GRADE)

Table S21. 8-hour or 12-hour work shift in adults with shiftwork disorder

References: Axelsson 1998, Rosa 1989, Jaffe 1996 Outcomes **Certainty of the Absolute Difference** No of Participants [Tool] (studies) evidence (GRADE) 8-hour work shift vs 12-hour work shift The mean difference in the 8-hour work shift group was **0.2 Excessive sleepiness or** Θ alertness VERY LOWa,b higher (0.3 lower to 0.7 higher) compared to the 12-hour (1 non-RCT) [Modified SSI] work shift **Excessive sleepiness or** Θ The mean difference in the 8-hour work shift group was **0.6** 62 alertness points lower (0.88 lower to 0.32 lower) compared to the 12- (1 non-RCT) VERY LOWa,b [KSS] hour work shift group Sleep quality ФООО The mean difference in the 8-hour work shift group was **0.1** [Questionnaire] points higher (0.18 lower to 0.38 higher) compared to the (1 non-RCT) VERY LOW^{a,b} 12-hour work shift group Sleep quality The mean difference in the 8-hour work shift group was **0.15** 120 $\Theta \bigcirc \bigcirc \bigcirc$ [Questionnaire] VERY LOW^{a,b} points lower (0.69 lower to 0.39 higher) compared to the (1 non-RCT) 12-hour work shift group Sleep quality Θ The mean difference in the melatonin group was **0.7 higher** 214 [Shift work survey **VERY LOW^a** (0.83 lower to 2.23 higher) compared to control (1 non-RCT) questionnaire]

The mean difference in the melatonin group was 15 msec

lower (59.05 lower to 29.05 higher) compared to control

a. Imprecision due to the 95% CI crossing the line of no effect.

Φ()()()

VERY LOWa,b

b. Imprecision due to small sample size (<200 participants)

Study Characteristics

Cognitive performance

Test]

[Serial Simple Reaction Time

Table S22. 8-hour or 12-hour work shift in adults with shiftwork disorder

| Study Citation | Study Design | Number of Participants (% Female) | Age (years) | Population | Intervention | Comparator | Duration of Follow-up |
|-------------------|--------------------|---|--|---|-----------------------|---------------------|--------------------------|
| Axelsson 1998 | non-RCT, crossover | 31 (13) | M: 38 ± 2 (SE) F: 29 ± 2 (SE) | Shift workers without SWD diagnosis | 8-hour night shift | 12-hour night shift | 3 days |
| Jaffe 1996 | non-RCT | 214 (5) | 38.3 | Shift workers without SWD diagnosis | 8-hour night shift | 12-hour night shift | 12 days |

| Rosa 1989 | non-RCT | 120 | 25-35 (data only available for 49 participants) | Shift workers without SWD diagnosis | 8-hour night shift | 12-hour night shift | 5 weeks |
|--------------------|--------------------|---------|---|---|-----------------------|------------------------|---------|
| Tucker 1996 | non-RCT | 162 (0) | 42.1 | Shift workers without SWD diagnosis | 8-hour shift schedule | 12-hour shift schedule | 28 days |
| Williamson 1994 | non-RCT, crossover | 18 (NR) | 24.4 (4.35) | Shift workers without SWD diagnosis | 8-hour shift schedule | 12-hour shift schedule | 8 weeks |

Critical Outcomes

Figure S239. 8-hour Work Shift vs 12-hour Work Shift (Excessive Sleepiness, modified SSI: alertness rating) [CMT = Not Established] Non-randomized study (Shift workers without SWD diagnosis)

| | | 8hr | | Cont | rol (12 | hr) | Mean Difference | Mean Difference |
|--------------------|------|-----|-------|------|---------|-------|--------------------|--------------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 10.8.1 Field Study | | | | | | | | 7 |
| Tucker 1996 | 5.76 | 1.5 | 70 | 5.56 | 1.73 | 92 | 0.20 [-0.30, 0.70] | - |
| | | | | | | | | -1 -0.5 0 0.5 1 |
| | | | | | | | | Favours 8hr Shift Favours 12hr Shift |

^{*}Tucker 1996: Data extracted from graph and averaged from 2400-0600 timepoints, SEM converted to SD. Higher score is associated with less alertness.

Figure S240. 8-hour Work Shift vs 12-hour Work Shift (Excessive Sleepiness, KSS) [CMT = 1 pt] Non-randomized study (Shift workers without SWD diagnosis)

| | | 8hr | | | 12hr | | Mean Difference | | Mean Differen | ce | |
|---------------------|------|------|-------|------|------|-------|----------------------|----|------------------|----------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 95% | CI | |
| 10.30.1 Field Study | | | | | | | | | 0 | | |
| Axelsson 1998 | 5.1 | 0.56 | 31 | 5.7 | 0.56 | 31 | -0.60 [-0.88, -0.32] | | | | |
| | | | | | | | | | | | 1 |
| | | | | | | | | -2 | -ì ò | 1 | Ż. |
| | | | | | | | | | Favours 8hr Favo | urs 12hr | |

^{*}Axelsson 1998: SEM converted to SD.

Figure S241. 8-hour Work Shift vs 12-hour Work Shift (Sleep Quality, Questionnaire) [CMT = Not Established] Non-randomized study (Shift workers without SWD diagnosis)

| | 8hr | | | 12hr | | | Mean Difference | Mean Difference |
|--------------------|------|------|-------|------|------|-------|--------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 8.33.1 Field Study | | | | | | | | |
| Axelsson 1998 | 4.1 | 0.56 | 31 | 4 | 0.56 | 31 | 0.10 [-0.18, 0.38] | - |
| | | | | | | | | |
| | | | | | | | | -1 -0.5 0 0.5 Favours 12hr Favours 8hr |

^{*}Axelsson 1998: SEM converted to SD. Sleep Quality Index (1-poor to 5-good).

Figure S242. 8-hour Work Shift vs 12-hour Work Shift (Sleep Quality, Questionnaire) [CMT = Not Established] Non-randomized study (Shift workers without SWD diagnosis)

| | | 8hr | | | 12hr | | Mean Difference | Mean Difference |
|--------------------|------|------|-------|------|------|-------|---------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 6.35.1 Field Study | | | | | | | | 9 |
| Rosa 1989 | 5.99 | 1.33 | 53 | 6.14 | 1.71 | 67 | -0.15 [-0.69, 0.39] | |
| | | | | | | | | |
| | | | | | | | | -2 -1 0 1 2 Favours 12hr Favours 8hr |

^{*}Rosa 1989: Sleep quality (1-poor to 9-good).

Figure S243. 8-hour Work Shift vs 12-hour Work Shift (Sleep Quality, Shift work survey questionnaire) [CMT = Not Established] Non-randomized study (Shift workers without SWD diagnosis)

| | | 8hr | | | 12hr | | Mean Difference | Mean Difference |
|--------------------|------|------|-------|------|------|-------|--------------------|--------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 12.9.1 Field Study | | | | | | | | |
| Jaffe 1996 | 20.2 | 6.21 | 107 | 19.5 | 5.17 | 107 | 0.70 [-0.83, 2.23] | - 1 |
| | | | | | | | | |
| | | | | | | | | -4 -2 0 2 |
| | | | | | | | | Favours 8hr Favours 12hr |

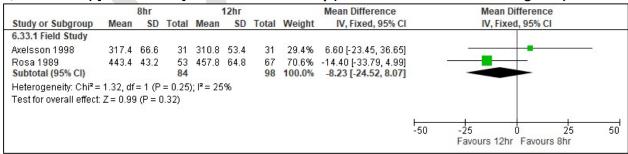
^{*}Jaffe 1996: 8hr night shift (backward rotation) vs 12hr night shift. Higher mean score= poorer sleep quality.

Figure S244. 8-hour Work Shift vs 12-hour Work Shift (Cognitive Performance, Serial Simple Reaction Time) [CMT = Not Established] Non-randomized study (Shift workers without SWD diagnosis)

| | | 8hr | | | 12hr | | Mean Difference | Mean Difference |
|--------------------|------|-------|-------|------|-------|-------|------------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 6.29.1 Field Study | | | | | | | | Y |
| Axelsson 1998 | 284 | 43.27 | 31 | 299 | 68.51 | 31 | -15.00 [-43.52, 13.52] | |
| | | | | | | | | 100 100 100 |
| | | | | | | | | -100 -50 0 50 100 Favours 8hr Favours 12hr |

^{*}Axelsson 1998: Participants worked both shift types (crossover, assumed acceptable washout period). Used end of shift; reaction time in msec; SEM converted to SD.

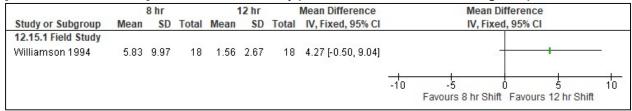
Figure S245. 8-hour Work Shift vs 12-hour Work Shift (Total Sleep Time, Karolinska Sleep Diary or Questionnaire) [CMT= 15 min] Non-randomized study (Shift workers without SWD diagnosis)



^{*}Axelsson 1998: Participants worked both shift types (crossover, assumed acceptable washout period). TST in hours converted to minutes; SEM converted to SD.

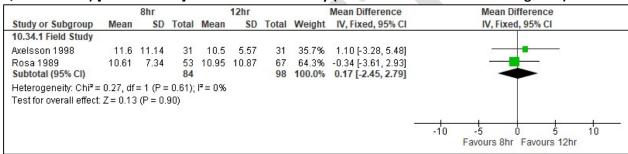
Rosa 1989: 8hr and 12hr shifts both had a rotation. TST in hours converted to minutes.

Figure S246. 8-hour Work Shift vs 12-hour Work Shift (Mental Health, General health questionnaire) [CMT = Not Established] Non-randomized study (Shift workers without SWD diagnosis)



^{*}Williamson 1994: Participants were originally on a rotating 8hr shift (day, afternoon, night) and were changed to rotating 12hr shifts (day, night). GHQ score, low score = high well-being. SD calculated from a matched t-test (of operators who participated in both 8hr and change to 12 hr shifts).

Figure S247. 8-hour Work Shift vs 12-hour Work Shift (Sleep Latency, Karolinska Sleep Diary or Questionnaire) [CMT= 20 min] Non-randomized study (Shift workers without SWD diagnosis)



^{*}Axelsson 1998: Participants worked both shift types (crossover, assumed acceptable washout period). Latency (min); SEM converted to SD.

Rosa 1989: 8hr and 12hr shifts both had a rotation.

CBT-I

Summary of Findings (GRADE)

Table S23. CBTI in adults with shiftwork disorder References: Peter 2019. Lee 2014 Jarnefelt 2019. Jarnefelt 2014

| Outcomes [Tool] | Certainty of the evidence | Absolute Difference | No of Participants (studies) | |
|--|-----------------------------------|---|------------------------------|--|
| | (GRADE) | CBT-I vs Control | | |
| Excessive sleepiness or alertness [ESS] ^a | ⊕○○○ VERY LOW ^{b,c} | The mean difference in the CBT-I group was 1.17 points lower (3.04 lower to 0.70 lower) compared to control | 33 (1 non-RCT) | |
| Sleep quality [PSQI] ^a | ⊕○○○ VERY LOW ^{b,c} | The mean difference in the CBT-I group was 1.84 points lower (3.38 lower to 0.31 lower) compared to control | 74 (2 non-RCTs) | |
| Sleep quality [SSI Sleep Disturbance] ^a | ⊕○○○ VERY LOW ^c | The mean difference in the CBT-I group was 1.8 lower (3.46 lower to 0.14 lower) compared to control | 50 (1 non-RCT) | |
| Sleep quality [GSDS: Sleep Quality] ^a | ⊕○○○ VERY LOW ^c | The mean difference in the CBT-I group was 0.89 lower (1.51 lower to 0.27 lower) compared to control | 50 (1 non-RCT) | |
| Sleep quality [Sleep diary (higher = worse)] ^a | ⊕○○○ VERY LOW ^{b,c,d} | The mean difference in the CBT-I group was 0.15 points lower (0.48 lower to 0.18 higher) compared to control | 54 (1 RCT) | |

| Sleep quality | ФООО | The mean difference in the CBT-I group was 0 (0.21 lower to | 43 |
|--------------------------------|------|---|-------------|
| [Sleep diary (lower = worse)]e | | 0.21 higher) compared to control | (1 non-RCT) |

- a. Lower values favor the intervention
- b. Imprecision due to the 95% CI crossing the CMT
- c. Imprecision due to small sample size (<200 participants)
- d. Risk of bias concerns in the randomization of participants
- e. Higher values favor the intervention
- f. Risk of bias concerns in the selection of participants
- g. Imprecision due to the 95% CI crossing the null
- h. CMT was not established by the TF

Study Characteristics

Table S24. CBT-I in adults with shiftwork disorder

| Study Citation | Study Design | Number of Participants (% Female) | Age in years | Population | Intervention (dose/intensity) | Comparator | Duration of Follow-up |
|-------------------|-----------------|---|-----------------|---|---|---------------|--------------------------|
| Jarnefelt 2014 | non-RCT | 59 (50) | 43.5 ± 8.4 | Shift workers without SWD diagnosis | CBT-I | Baseline | 24 months |
| Jarnefelt 2019 | RCT | 83 (75) | 45 | SWD | Group-base CBT-I self-help-based CBT-I | sleep hygiene | 6 months |
| Lee 2014 | non-RCT | 21 (95) | 45.5 ± 12.5 | SWD | Sleep Enhancement Training System for Shift Workers | Baseline | 4 weeks |
| Peter 2019 | non-RCT | 33 (77) | 44.7 ± 10.2 | SWD | online CBT-I face-to- face outpatient treatment | Baseline | 4 weeks |

Critical Outcomes

Figure S248. CBT-I vs pre-CBT-I (Excessive sleepiness, ESS) [CMT = 2 pts] Non-randomized study (SWD)

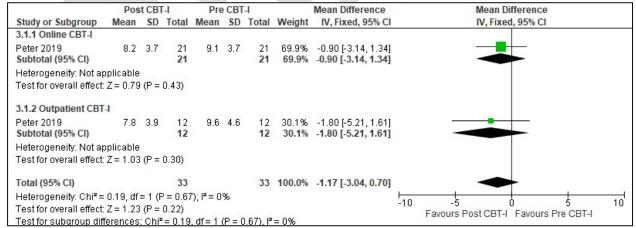
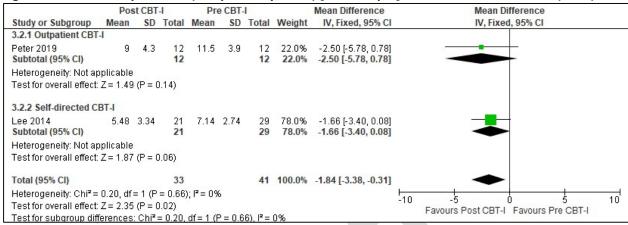


Figure S249. CBT-I vs pre-CBT-I (Sleep Quality, PSQI) [CMT = 3 pts] Non-randomized studies (SWD)



^{*}Lee 2014: Data used from timepoints T2 (post control) compared to T3 (post intervention)

Figure S250. CBT-I vs pre-CBT-I (Sleep Quality, SSI sleep disturbance) [CMT = Not Established] Non-randomized study (SWD)

| | Pos | t CB1 | Γ -I | Pre | CBT | -1 | Mean Difference | Mean Difference | | | | |
|-------------------|------|-------|-------------|------|-----|-------|----------------------|-----------------|--------------------|-----------|----------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed | 1, 95% CI | | |
| 1.3.1 Field Study | | | | | | | | | | K. | | |
| Lee 2014 | 17.3 | 3 | 21 | 19.1 | 2.9 | 29 | -1.80 [-3.46, -0.14] | 19 | - | | | |
| | | | | | | | | | 7 | | | |
| | | | | | | | | -4 | -2 | Ó | 2 | 4 |
| | | | | | | | | | Favours Post CBT-I | Favours P | re CBT-I | |

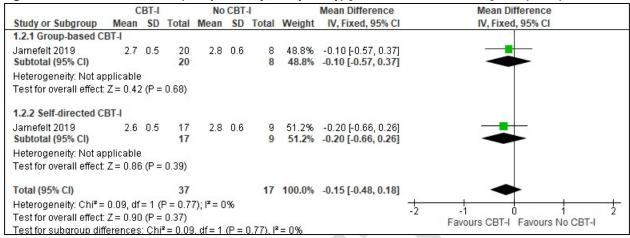
^{*}Lee 2014: Data used from timepoints T2 (post control) compared to T3 (post intervention).

Figure S251. CBT-I vs pre-CBT-I (Sleep Quality, GSDS: Sleep Quality) [CMT = Not Established] Non-randomized study (SWD)

| Post CBT-I udy or Subgroup Mean SD Tot | | -1 | Pre | e CBT- | | Mean Difference | Mean Difference | | |
|---|------|-------|---------------|--------------------|-----------------------|-----------------------------|---|--|--|
| Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | | |
| | | | | | | | | | |
| 2.41 | 1.04 | 21 | 3.3 | 1.18 | 29 | -0.89 [-1.51, -0.27] | | | |
| | | | | | | + | | | |
| | | | | | | -4 | -2 0 2 | | |
| | Mean | | Mean SD Total | Mean SD Total Mean | Mean SD Total Mean SD | Mean SD Total Mean SD Total | Mean SD Total Mean SD Total IV, Fixed, 95% CI 2.41 1.04 21 3.3 1.18 29 -0.89 [-1.51, -0.27] +- +- +- +- +- +- | Mean SD Total IV, Fixed, 95% CI IV, Fixed, 95% CI 2.41 1.04 21 3.3 1.18 29 -0.89 [-1.51, -0.27] ———————————————————————————————————— | |

^{*}Lee 2014: Data used from timepoints T2 (post control) compared to T3 (post intervention).

Figure S252. CBT-I vs Control (Sleep Quality, Sleep diary) [CMT = Not Established] RCT (SWD)



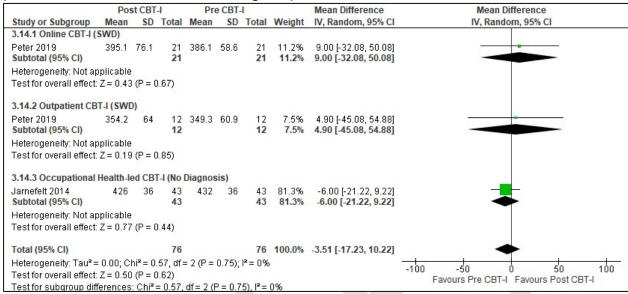
^{*}Jarnefelt 2019: Measurements taken from T2 (timepoint following the intervention), Restedness after sleep period 1(good)–5(poor). 3-arm study, control participants split (total n=17) to not double count.

Figure S253. CBT-I vs pre-CBT-I (Sleep Quality, Sleep diary) [CMT = Not Established] Non-randomized study (Shift workers without SWD diagnosis)

| | Pos | t CB1 | Γ-Ι | Pre CBT-I Mean Difference | | | | | Mean Difference | |
|-------------------|------|-------|-------|---------------------------|-----|-------|--------------------|----|--|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 95% CI | |
| 2.1.1 Field Study | | | | | | | | | 9 | |
| Jarnefelt 2014 | 3.2 | 0.5 | 43 | 3.2 | 0.5 | 43 | 0.00 [-0.21, 0.21] | | - | |
| | | | | | | | | 4 | | - |
| | | | | | | | | -1 | -0.5 0 0.5 Favours Pre CBT-I Favours Post CBT-I | 1 |

^{*}Jarnefelt 2014: Total data analyzed, measurements from T1 (prior to CBT-I) and T2 (after CBT-I).

Figure S254. CBT-I vs pre-CBT-I (Total Sleep Time, Sleep diary) [CMT =20min] Non-randomized studies (SWD and shift workers without SWD diagnosis)



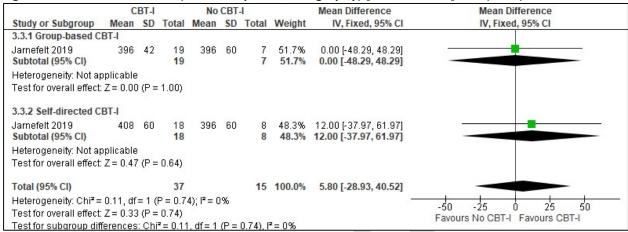
^{*}Peter 2019: Jarnefelt 2014: Total data analyzed, measurements from T1 (prior to CBT-I) and T2 (after CBT-I). TST (hours converted to minutes).

Figure S255. CBT-I vs pre-CBT-I (Total Sleep Time, Actigraphy) [CMT = 20min] Non-randomized study (SWD)

| | Pos | t CB1 | Γ -I | Pre | CBT | -1 | Mean Difference | Mean Difference |
|-------------------|------|-------|-------------|------|-----|-------|-----------------------|---------------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 3.5.1 Field Study | | | | | | | | |
| Lee 2014 | 421 | 87 | 21 | 423 | 80 | 29 | -2.00 [-49.25, 45.25] | · · · · · · · · · · · · · · · · · · · |
| | | | | | | | | |
| | | | | | | | | -100 -50 Ó 50 100 |
| | | | | | | | | Favours Pre CBT-I Favours Post CBT-I |

^{*}Lee 2014 data used from timepoints T2 (post control) compared to T3 (post intervention). Sleep during sleep periods.

Figure S256. CBT-I vs Control (Total Sleep Time, Actigraphy) [CMT = 20min] RCT (SWD)



^{*}Jarnefelt 2019: Measurements taken from T2 (timepoint following the intervention). 3-arm study, control participants split (total n=15) to not double count.

Figure S257. CBT-I vs Control (Total Sleep Time, Sleep Diary) [CMT = 20min] RCT (SWD)

| | C | BT-I | | No | CBT- | -1 | | Mean Difference | Mean Difference |
|-------------------------------------|-----------|-------|-----------------|---------------|------|----------|------------------------|--|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 3.4.1 Group-based C | BT-I | | | | | | | | |
| Jarnefelt 2019 Subtotal (95% CI) | 414 | 42 | 20 20 | 420 | 78 | 8 | 51.1% 51.1 % | | |
| Heterogeneity: Not ap | oplicable | 8 | | | | | | | |
| Test for overall effect: | Z = 0.21 | (P = | 0.84) | | | | | | |
| 3.4.2 Self-directed C | BT-I | | | | | | | | |
| Jarnefelt 2019 Subtotal (95% CI) | 444 | 60 | 17 17 | 420 | 78 | 9 | | 24.00 [-34.40, 82.40] 24.00 [-34.40, 82.40] | |
| Heterogeneity: Not ap | oplicable | 18 | | | | | | | |
| Test for overall effect: | Z = 0.81 | (P = | 0.42) | | | | | | |
| Total (95% CI) | | | 37 | | | 17 | 100.0% | 8.66 [-32.16, 49.49] | |
| Heterogeneity: Chi²= | 0.52, df | = 1 (| P = 0.4 | 7); $I^2 = 0$ | 1% | | | | -100 -50 0 50 10 |
| Test for overall effect: | Z = 0.42 | (P= | 0.68) | | | | | | -100 -50 0 50 10 Favours No CBT-I Favours CBT-I |
| Test for subgroup dif | ferences | : Chi | r = 0.52 | 2. df = 1 | (P = | 0.47), [| ² = 0% | | 1 avouis 140 CD1-1 Favouis CD1-1 |

^{*}Jarnefelt 2019: Measurements taken from T2 (timepoint following the intervention). 3-arm study, control participants split (total n=17) to not double count.

Figure S258. CBT-I vs pre-CBT-I (Mental Health, Center for Epidemiologic Studies- Depression scale) [CMT = Not Established] Non-randomized study (SWD)

| | Pos | t CB1 | Γ -I | Pre | CBT | -1 | Mean Difference | | Me | ean Differen | ce | |
|-------------------|------|-------|-------------|------|-----|-------|---------------------|-----|---------------|--------------|--------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV. | Fixed, 95% | CI | |
| 3.6.1 Field Study | | | | | | | | | | 60 | | |
| Lee 2014 | 10.4 | 8.9 | 21 | 11 | 8.5 | 29 | -0.60 [-5.51, 4.31] | | 188 T | 1 | 91 | |
| | | | | | | | | | - | | | - |
| | | | | | | | | -10 | -5 | 0 | 5 Dra ODT | 10 |
| | | | | | | | | Fa | avours Post (| BI-I Favor | Irs Pre CB1 | -1 |

^{*}Lee 2014 data used from timepoints T2 (post control) compared to T3 (post intervention).

Figure S259. CBT-I vs pre-CBT-I (Mental Health, SSI: Anxiety) [CMT = Not Established] Non-randomized study (SWD)

| Pos | t CB1 | Γ-Ι | Pre | CBT | -1 | Mean Difference | Mean Difference |
|------|-------|---------|---------------------|--------------------|-----------------------|-----------------------------|--|
| Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| | | | | | | | |
| 11.6 | 6.1 | 21 | 12.9 | 6.7 | 29 | -1.30 [-4.87, 2.27] | 1 |
| | | | | | | | |
| | | | | | | | -10 -5 0 5 1 Favours Post CBT-I Favours Pre CBT-I |
| | Mean | Mean SD | 2022430 02350 30300 | Mean SD Total Mean | Mean SD Total Mean SD | Mean SD Total Mean SD Total | Mean SD Total Mean SD Total IV, Fixed, 95% C |

^{*}Lee 2014: Data used from timepoints T2 (post control) compared to T3 (post intervention).

Figure S260. CBT-I vs pre-CBT-I (Mental Health, Beck Depression Inventory (BDI)-II) [CMT = Not Established] Non-randomized study (SWD)

| | Pos | t CB1 | Γ -I | Pr | e CBT- | I | Mean Difference | Mean Difference | |
|--------------------|------|-------|-------------|------|--------|-------|----------------------|--|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | |
| 3.11.1 Field Study | | | | | | | | | |
| Peter 2019 | 7.3 | 7.3 | 12 | 14.4 | 10.6 | 12 | -7.10 [-14.38, 0.18] | - | |
| | | | | | | | | | - |
| | | | | | | | | -20 -10 0 10 Favours Post CBT-I Favours Pre CBT-I | 20 |

^{*}Peter 2019: Pre/Post for outpatient only. Higher scores indicate worse depression.

Figure S261. CBT-I vs No CBT-I (Mental Health, Beck Depression Inventory) [CMT = Not Established] RCT (SWD)

| | C | BT-I | | No | CBT-I | | | Mean Difference | Mean Difference |
|--------------------------|----------|--------------------|---------|--------------|-------|---------|--------|---------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 1.4.1 Group-based Cl | BT-I | | | | | | | | |
| Jarnefelt 2019 | 8.5 | 5 | 20 | 7.75 | 5.25 | 10 | 48.1% | 0.75 [-3.17, 4.67] | - |
| Subtotal (95% CI) | | | 20 | | | 10 | 48.1% | 0.75 [-3.17, 4.67] | |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z = 0.37 | (P = 0 | 0.71) | | | | | | |
| 1.4.2 Self-directed Cl | BT-I | | | | | | | | |
| Jarnefelt 2019 | 6.25 | 4.25 | 19 | 7.75 | 5.25 | 10 | 51.9% | -1.50 [-5.27, 2.27] | |
| Subtotal (95% CI) | | | 19 | | | 10 | 51.9% | -1.50 [-5.27, 2.27] | |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z = 0.78 | (P = 0) | 0.44) | | | | | | |
| Total (95% CI) | | | 39 | | | 20 | 100.0% | -0.42 [-3.14, 2.30] | - |
| Heterogeneity: Chi²= | 0.66, df | = 1 (P | = 0.42) | $; I^2 = 09$ | 6 | | | | - to to to |
| Test for overall effect: | Z = 0.30 | (P = 0) | 0.76) | | | | | | -10 -5 0 5 10 Favours CBT-I Favours No CBT-I |
| Test for subgroup diff | erences | Chi ² : | = 0.66. | df = 1 (F | 0.4 | 2), 2= | 0% | | Tavouis CDT-1 Favouis No CDT-1 |

^{*}Jarnefelt 2019: Measurements taken from T2 (timepoint following the intervention). 3-arm study, control participants split (total n=20) to not double count. Higher scores indicate worse depression. Median and range data converted into Mean and SD using the formula in Hozo et al 2005 paper.

Figure S262. CBT-I vs pre-CBT-I (Mental Health, Montgomery-Åsberg Depression Rating Scale (MARDS)) [CMT = Not Established] Non-randomized study (SWD)

| | Pos | t CB1 | Γ -I | Pre | CBT | -1 | Mean Difference | | Mean Dif | ference | |
|--------------------|------|-------|-------------|------|-----|-------|------------------------|-----|--------------------|-------------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed | , 95% CI | |
| 3.12.1 Field Study | | | | | | | | | | 9 | |
| Peter 2019 | 8.2 | 6.5 | 12 | 19.2 | 5.6 | 12 | -11.00 [-15.85, -6.15] | | | | |
| | | | | | | | | _ | | 1 | - |
| | | | | | | | | -20 | -10 Ó | 10 | 20 |
| | | | | | | | | | Favours Post CBT-I | Favours Pre CBT-I | |

^{*}Peter 2019: Pre/Post for outpatient only. Higher scores indicate worse depression.

Figure S263. CBT-I vs pre-CBT-I (Mental Health, SCI-90: Global Index) [CMT = Not Established] Non-randomized study (Shift workers without a SWD diagnosis)

| | Pos | t CB | Γ-Ι | Pre | CBT | -1 | Mean Difference | Mean Difference |
|-------------------|------|------|-------|------|-----|-------|----------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 2.7.2 Field Study | | | | | | | | |
| Jarnefelt 2014 | 1.6 | 0.4 | 41 | 1.8 | 0.4 | 41 | -0.20 [-0.37, -0.03] | |
| | | | | | | | | |
| | | | | | | | | -1 -0.5 0 0.5 1 Favours Post CBT-I Favours Pre CBT-I |

^{*}Jarnefelt 2014: Total data analyzed, measurements from T1 (prior to CBT-I) and T2 (after CBT-I). Symptom Check List (SCL)-90, scale 1 (not bothered) to 5 (extremely bothered).

Figure S264. CBT-I vs pre-CBT-I (Mental Health, SCI-90: Depression Index) [CMT = Not Established] Non-randomized study (Shift workers without a SWD diagnosis)

| | Pos | t CB1 | [- | Pre | CBT | -1 | Mean Difference | | | Mean D | ifference | | |
|-------------------|------|-------|-------------|------|-----|-------|---------------------|-----|--------|-----------|-----------|--------|------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | | IV, Fixe | d, 95% CI | | |
| 2.8.3 Field Study | | | | | | | | | | | 100 | | |
| Jarnefelt 2014 | 1.9 | 0.7 | 41 | 2.1 | 0.7 | 41 | -0.20 [-0.50, 0.10] | | 10 | - | | | |
| | | | | | | | | - | 77 | | | 11 | |
| | | | | | | | 8. | -1 | -0. | 5 | 0 1 | 0.5 | 1 |
| | | | | | | | | Fav | ours P | ost CBT-I | Favours | Pre CE | BT-I |

^{*}Jarnefelt 2014: Total data analyzed, measurements from T1 (prior to CBT-I) and T2 (after CBT-I). Symptom Check List (SCL)-90, scale 1 (not bothered) to 5 (extremely bothered).

Figure S265. CBT-I vs pre-CBT-I (Mental Health, SCI-90: Anxiety Index) [CMT = Not Established] Non-randomized study (Shift workers without a SWD diagnosis)

| | Pos | t CBT | [- | Pre | CBT | -1 | Mean Difference | N | Mean Dif | ference | | |
|-------------------|------|-------|-------------|------|-----|-------|---------------------|-------------------------|-----------|-----------|----------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | r | V, Fixed, | 95% CI | | |
| 2.9.4 Field Study | | | | | | | | | | 100 | | |
| Jarnefelt 2014 | 1.5 | 0.5 | 41 | 1.6 | 0.4 | 41 | -0.10 [-0.30, 0.10] | | + | | | |
| | | | | | | | | 1 1- | | | <u> </u> | + |
| | | | | | | | | -1 -0.5 Favours Post | t CBT-I | Favours F | | 1 |

^{*}Jarnefelt 2014: Total data analyzed, measurements from T1 (prior to CBT-I) and T2 (after CBT-I). Symptom Check List (SCL)-90, scale 1 (not bothered) to 5 (extremely bothered).

Figure S266. CBT-I vs pre-CBT-I (Circadian Alignment, Actigraphy) [CMT = Not Established] Non-randomized study (SWD)

| | Pos | t CBT | -1 | Pre | CBT | -1 | Mean Difference | | Me | an Differe | nce | |
|--------------------|------|-------|-------|------|-----|-------|---------------------|-----|---------------|------------|--------------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, | Fixed, 95% | CI | |
| 3.16.1 Field Study | | | | | | | | | | 9 | | |
| Lee 2014 | 68.3 | 8.46 | 21 | 68.5 | 6.6 | 29 | -0.20 [-4.54, 4.14] | | 201 | + | | |
| | | | | | | | | 4 | - | | | |
| | | | | | | | | -10 | -5 | Ó | 5 | 10 |
| | | | | | | | | F | avours Post C | BT-I Favo | ours Pre CB1 | Г-I |

^{*}Lee 2014: Data used from timepoints T2 (post control) compared to T3 (post intervention). Mesor, defined as the 24-hr adjusted mean activity level fitted to a cosinusoidal wave form, with higher values indicating more activity.

Figure S267. CBT-I vs pre-CBT-I (Quality of Life, WHO-5) [CMT = Not Established] Non-randomized study (SWD)

| | Pos | t CB1 | Γ -I | Pre | CBT | -1 | Mean Difference | Mean Difference |
|--------------------|------|-------|-------------|------|-----|-------|-------------------|--------------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 3.13.1 Field Study | | | | | | | | |
| Peter 2019 | 13.9 | 4.2 | 21 | 10.9 | 3.8 | 21 | 3.00 [0.58, 5.42] | |
| | | | | | | | | |
| | | | | | | | | -10 -5 0 5 10 |
| | | | | | | | | Favours Pre CBT-I Favours Post CBT-I |

^{*}Peter 2019: Pre/post online CBT only. WHO-5 lower score is worse.

Figure S268. CBT-I vs No CBT-I (Quality of Life, RAND-PCS) [CMT = Not Established] RCT (SWD)

| U | | | • | | - , | ~ * | | - 7 6 - | |
|-----------------------------------|----------|----------|--------|-------------|----------|------------|--------|----------------------|---|
| | 11) | CBT-I | | N | o CBT-I | | | Mean Difference | Mean Difference |
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 1.5.1 Group-based Cl | BT-I | | | | | | | | |
| Jarnefelt 2019 | 74.55 | 15.3 | 20 | 73.93 | 15.93 | 10 | 48.2% | 0.62 [-11.32, 12.56] | |
| Subtotal (95% CI) | | | 20 | | | 10 | 48.2% | 0.62 [-11.32, 12.56] | |
| Heterogeneity: Not ap | plicable | 16 | | | | | | | |
| Test for overall effect: | Z = 0.10 | P = 0 | 92) | | | | | | |
| 1.5.2 Self-directed Cl | BT-I | | | | | | | | |
| Jarnefelt 2019 | 78.78 | 13.13 | 19 | 73.93 | 15.93 | 10 | 51.8% | 4.85 [-6.65, 16.35] | · · · · · · · · · · · · · · · · · · · |
| Subtotal (95% CI) | | | 19 | | | 10 | 51.8% | 4.85 [-6.65, 16.35] | |
| Heterogeneity: Not ap | plicable | 10 | | | | | | | |
| Test for overall effect: | Z = 0.83 | P = 0 | 41) | | | | | | |
| Total (95% CI) | | | 39 | | | 20 | 100.0% | 2.81 [-5.47, 11.10] | |
| Heterogeneity: Chi ² = | 0.25, df | = 1 (P = | 0.62); | $I^2 = 0\%$ | | | | | -20 -10 0 10 20 |
| Test for overall effect: | Z = 0.67 | P = 0. | 51) | | | | | | -20 -10 0 10 20 Favours No CBT-I Favours CBT-I |
| Test for subgroup diff | erences | : Chi²= | 0.25.0 | f=1 (P | = 0.62). | $I^2 = 09$ | 6 | | FAVOUIS IND CDI-L FAVOUIS CBI-L |

^{*}Jarnefelt 2019: Measurements taken from T2 (timepoint following the intervention). 3-arm study, control participants split (total n=20) to not double count. Median and range data converted into Mean and SD using the formula in Hozo et al 2005 paper.

Figure S269. CBT-I vs pre-CBT-I (Quality of Life, RAND-PCS) [CMT = Not Established] Non-randomized study (Shift workers without a SWD diagnosis)

| | Post CBT-I | | | Pre CBT-I | | | Mean Difference | Mean Difference |
|-------------------|------------|------|-------|-----------|------|-------|---------------------|--------------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 2.3.1 Field Study | | | | | | | | |
| Jarnefelt 2014 | 79.1 | 16.5 | 41 | 80 | 18.2 | 41 | -0.90 [-8.42, 6.62] | |
| | | | | | | | | |
| | | | | | | | | -20 -10 Ó 10 20 |
| | | | | | | | | Favours Pre CBT-I Favours Post CBT-I |

^{*}Jarnefelt 2014: Total data analyzed, measurements from T1 (prior to CBT-I) and T2 (after CBT-I). RAND-PCS (physical component) higher score is better.

Figure S270. CBT-I vs No CBT-I (WASO, Sleep Diary) [CMT = 20 min] RCT (SWD)

| | | CBT-I | | N | o CBT-I | 1 | | Mean Difference | Mean Difference | |
|-------------------------------------|----------|----------------------|-----------------|-------------|----------|------------|--------|--|---|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI | |
| 1.9.1 Group-based Cl | BT-I | | | | | | | | | |
| Jarnefelt 2019 Subtotal (95% CI) | 33.6 | 21.2 | 20 20 | 37.75 | 25.95 | 8 | | -4.15 [-24.39, 16.09] -4.15 [-24.39, 16.09] | | |
| Heterogeneity: Not ap | plicable | | | | | | | | | |
| Test for overall effect: | Z = 0.40 | (P = 0. | 69) | | | | | | | |
| 1.9.2 Self-directed Cl | BT-I | | | | | | | | | |
| Jarnefelt 2019 | 27.13 | 15.98 | 17 | 37.75 | 25.95 | 9 | 54.3% | -10.62 [-29.20, 7.96] | - | |
| Subtotal (95% CI) | | | 17 | | | 9 | 54.3% | -10.62 [-29.20, 7.96] | | |
| Heterogeneity: Not ap | plicable | | | | | | | | | |
| Test for overall effect: | Z = 1.12 | (P = 0. | 26) | | | | | | | |
| Total (95% CI) | | | 37 | | | 17 | 100.0% | -7.66 [-21.35, 6.02] | - | |
| Heterogeneity: Chi ² = | 0.21, df | = 1 (P = | 0.64); | $I^2 = 0\%$ | | | | | -50 -25 0 25 | ار |
| Test for overall effect: | Z = 1.10 | (P = 0. | 27) | | | | | | -50 -25 0 25 Favours CBT-I Favours No CBT- | 5 |
| Test for subgroup diff | erences | : Chi ^z = | 0.21, d | f=1 (P | = 0.64), | $I^2 = 09$ | 6 | | Tavouis CB1-1 Favouis No CB1- | 1 |

^{*}Jarnefelt 2019: Measurements taken from T2 (timepoint following the intervention). 3-arm study, control participants split (total n=17) to not double count. Median and range data converted into Mean and SD

Figure S271. CBT-I vs No CBT-I (WASO, Actigraphy) [CMT = 20 min] RCT (SWD)

| | | CBT-I | | N | o CBT-I | | | Mean Difference | Mean Difference |
|-------------------------|-----------|----------------------|---------|-------------|----------|------------|--------|---------------------|----------------------------------|
| Study or Subgroup | Mean | Mean SD | | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 1.11.1 Group-based | CBT-I | | | | | | | | 8) |
| Jarnefelt 2019 | 45.75 | 13.8 | 19 | 43.23 | 10.29 | 7 | 48.7% | 2.52 [-7.31, 12.35] | |
| Subtotal (95% CI) | | | 19 | | | 7 | 48.7% | 2.52 [-7.31, 12.35] | |
| Heterogeneity: Not ap | oplicable | | | | | | | | |
| Test for overall effect | Z = 0.50 | P = 0 | 62) | | | | | | |
| 1.11.2 Self-directed | CBT-I | | | | | | | | |
| Jarnefelt 2019 | 55.25 | 13.85 | 18 | 43.23 | 10.29 | 8 | 51.3% | 12.02 [2.44, 21.60] | - |
| Subtotal (95% CI) | | | 18 | | | 8 | 51.3% | 12.02 [2.44, 21.60] | |
| Heterogeneity: Not ap | oplicable | | | | | | | | |
| Test for overall effect | Z = 2.46 | P = 0. | 01) | | | | | | |
| Total (95% CI) | | | 37 | | | 15 | 100.0% | 7.39 [0.53, 14.25] | |
| Heterogeneity: Chi²= | 1.84, df | = 1 (P = | 0.17); | $I^2 = 469$ | 6 | | | | -20 -10 0 10 20 |
| Test for overall effect | Z = 2.11 | (P = 0. | 03) | | | | | | Favours CBT-I Favours No CBT-I |
| Test for subgroup dif | ferences | : Chi ² = | 1.84. d | f=1 (P | = 0.17). | $I^2 = 45$ | 7% | | 1 avouis ODI-1 Pavouis IVO CDI-1 |

^{*}Jarnefelt 2019: Measurements taken from T2 (timepoint following the intervention). 3-arm study, control participants split (total n=15) to not double count. Median and range data converted into Mean and SD

Figure S272. CBT-I vs pre-CBT-I (Wake After Sleep Onset, Sleep Diary) [CMT = 20 min] Non-randomized study (Shift workers without a SWD diagnosis)

| | Pos | Pre CBT-I | | | Mean Difference | Mean Difference | | | |
|-------------------|------|-----------|-------|------|-----------------|-----------------|----------------------|-----------------------------------|------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | |
| 2.4.1 Field Study | | | | | | | | | |
| Jarnefelt 2014 | 32.4 | 24.6 | 43 | 33.4 | 20 | 43 | -1.00 [-10.48, 8.48] | | |
| | | | | | | | | | - 1 |
| | | | | | | | | -20 -10 0 10 | 20 |
| | | | | | | | | Favours Post CBT-I Favours Pre CB | IT-I |

^{*}Jarnefelt 2014: No diagnosis. Total data analyzed, measurements from T1 (prior to CBT-I) and T2 (after CBT-I).

Figure S273. CBT-I vs pre-CBT-I (Sleep Latency, PSQI: sleep onset latency) [CMT = 20 min] Non-randomized study (SWD)

| | Post CBT-I | | | Pro | e CBT- | I | Mean Difference | Mean Difference |
|-------------------|------------|------|-------|------|--------|-------|---------------------|--------------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 3.8.1 Field Study | | | | | | | | |
| Lee 2014 | 0.85 | 0.67 | 21 | 0.95 | 0.76 | 29 | -0.10 [-0.50, 0.30] | |
| | | | | | | | | <u> </u> |
| | | | | | | | | Favours Post CBT-I Favours Pre CBT-I |

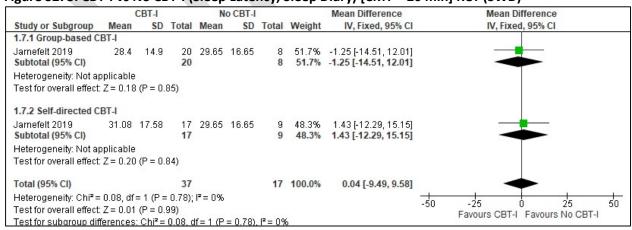
^{*}Lee 2014: Data used from timepoints T2 (post control) compared to T3 (post intervention).

Figure S274. CBT-I vs pre-CBT-I (Sleep Latency, GSDS: sleep onset latency) [CMT = 20 min] Non-randomized study (SWD)

| | Post CBT-I | | | | | I | Mean Difference | | Mean Difference | | | |
|-------------------|------------|------|-------|------|------|-------|----------------------|----|--|---|--|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Random, 95% CI | | IV, Random, 95% CI | | | |
| 3.9.1 Field Study | | | | | | | | | [8] | | | |
| Lee 2014 | 1.24 | 1.09 | 21 | 2.29 | 1.82 | 29 | -1.05 [-1.86, -0.24] | | | | | |
| | | | | | | | | _ | | - | | |
| | | | | | | | | -4 | -2 0 2 Favours Post CBT-I Favours Pre CBT-I | 4 | | |

^{*}Lee 2014: Data used from timepoints T2 (post control) compared to T3 (post intervention).

Figure S275. CBT-I vs No CBT-I (Sleep Latency, Sleep Diary) [CMT = 20 min] RCT (SWD)



^{*}Jarnefelt 2019: Measurements taken from T2 (timepoint following the intervention). 3-arm study, control participants split (total n=17) to not double count. Median and range data converted into Mean and SD using the formula in Hozo et al 2005 paper.

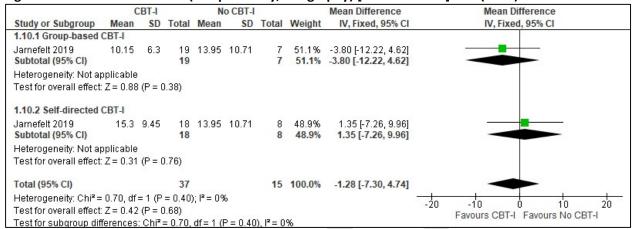


Figure S276. CBT-I vs No CBT-I (Sleep Latency, Actigraphy) [CMT = 20 min] RCT (SWD)

Figure S277. CBT-I vs pre-CBT-I (Sleep Latency, Sleep Diary) [CMT = 20 min] Non-randomized study (Shift workers without a SWD diagnosis)

| | Post CBT-I | | | | e CBT- | | Mean Difference | Mean Difference |
|-------------------|------------|------|-------|------|--------|-------|---------------------|--------------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 2.5.1 Field Study | | | | | | | | |
| Jarnefelt 2014 | 22.2 | 12.3 | 43 | 23.2 | 12.7 | 43 | -1.00 [-6.28, 4.28] | |
| | | | | | | | | |
| | | | | | | | | -20 -10 0 10 2 |
| | | | | | | | | Favours Post CBT-I Favours Pre CBT-I |

^{*}Jarnefelt 2014: Total data analyzed, measurements from T1 (prior to CBT-I) and T2 (after CBT-I).

Figure S278. CBT-I vs pre-CBT-I (Sleep Efficiency, PSQI: sleep efficiency) [CMT = Not Established] Non-randomized study (SWD)

| | Post CBT-I | | | Pre CBT-I | | | Mean Difference | | Mean Difference | | |
|--------------------|------------|------|-------|-----------|------|-------|---------------------|----|-------------------------|---------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Random, 95% CI | | IV, Random, 95% CI | | |
| 3.10.1 Field Study | | | | | | | | | | | |
| Lee 2014 | 0.56 | 0.92 | 21 | 1.06 | 1.21 | 29 | -0.50 [-1.09, 0.09] | | | | |
| | | | | | | | | | 9 | T. | - |
| | | | | | | | | -2 | -i Ó | 1 | 2 |
| | | | | | | | | | Favours Post CBT-I Favo | urs Pre CBT-I | |

^{*}Lee 2014: Data used from timepoints T2 (post control) compared to T3 (post intervention).

^{*}Jarnefelt 2019: Measurements taken from T2 (timepoint following the intervention). 3-arm study, control participants split (total n=15) to not double count. Median and range data converted into Mean and SD using the formula in Hozo et al 2005 paper.

Figure S279. CBT-I vs pre-CBT-I (Sleep Efficiency, Sleep Diary) [CMT = 10%] Non-randomized study (SWD)

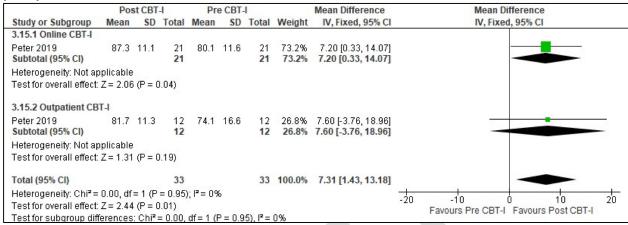
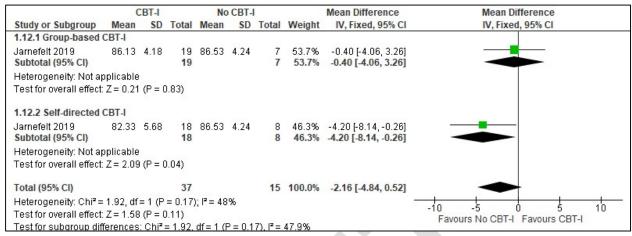


Figure S280. CBT-I vs No CBT-I (Sleep Efficiency, Sleep Diary) [CMT = 10%] RCT (SWD)

| | (| CBT-I | | No | CBT- | | | Mean Difference | Mean Difference |
|-------------------------|-----------|----------|---------|-----------------------|---------|-------------|--------|--------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 1.8.1 Group-based C | BT-I | | | | | | | | |
| Jarnefelt 2019 | 87.75 | 5.7 | 20 | 86.33 | 7.23 | 8 | 46.5% | 1.42 [-4.18, 7.02] | - |
| Subtotal (95% CI) | | | 20 | | | 8 | 46.5% | 1.42 [-4.18, 7.02] | |
| Heterogeneity: Not ap | pplicable | 18 | | | | | | | |
| Test for overall effect | Z = 0.50 | (P = 0 | 0.62) | | | | | | |
| 1.8.2 Self-directed C | BT-I | | | | | | | | |
| Jarnefelt 2019 | 90.43 | 4.68 | 17 | 86.33 | 7.23 | 9 | 53.5% | 4.10 [-1.12, 9.32] | - |
| Subtotal (95% CI) | | | 17 | | | 9 | 53.5% | 4.10 [-1.12, 9.32] | |
| Heterogeneity: Not a | pplicable | 18 | | | | | | | |
| Test for overall effect | Z= 1.54 | P = 0 | 0.12) | | | | | | |
| Total (95% CI) | | | 37 | | | 17 | 100.0% | 2.85 [-0.97, 6.67] | |
| Heterogeneity: Chi²= | 0.47, df | = 1 (P | = 0.49 | $ \mathbf{r} = 09$ | 6 | | | | -10 -5 0 5 10 |
| Test for overall effect | Z = 1.46 | 6 (P = 0 | 0.14) | Č. | | | | | -10 -5 0 5 10 Favours No CBT-I Favours CBT-I |
| Test for subgroup dif | ferences | : Chi²: | = 0.47. | df = 1 (H) | 0 = 0.4 | 9), $ ^2 =$ | 0% | | FAVOUIS NO CBI-L FAVOUIS CBI-L |

^{*}Jarnefelt 2019: Measurements taken from T2 (timepoint following the intervention). 3-arm study, control participants split (total n=17) to not double count. Median and range data converted into Mean and SD using the formula in Hozo et al 2005 paper.

Figure S281. CBT-I vs No CBT-I (Sleep Efficiency, Actigraphy) [CMT = 10%] RCT (SWD)



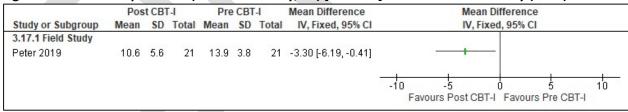
^{*}Jarnefelt 2019: Measurements taken from T2 (timepoint following the intervention). 3-arm study, control participants split (total n=15) to not double count. Median and range data converted into Mean and SD using the formula in Hozo et al 2005 paper.

Figure S282. CBT-I vs pre-CBT-I (Sleep Efficiency, Sleep Diary) [CMT = 10%] Non-randomized study (Shift workers without a SWD diagnosis)

| | Pos | Pre | CBT | -1 | Mean Difference | | Mean Difference | ce | | | |
|-------------------|------|-----|-------|------|-----------------|-------|--------------------|-----|---------------------------------|---------------------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 95% CI | | |
| 2.6.1 Field Study | | | | | | | | | (4) | | |
| Jarnefelt 2014 | 88.5 | 6.2 | 43 | 88.3 | 4.8 | 43 | 0.20 [-2.14, 2.54] | | - | | |
| | | | | | | | | + | | | _ |
| | | | | | | | | -10 | -5 Ó | 5 ura Baat CDT I | 10 |
| | | | | | | | | -10 | -5 0 Favours Pre CBT-l Favou | 5 Irs Post CBT | T-I |

^{*}Jarnefelt 2014: Total data analyzed, measurements from T1 (prior to CBT-I) and T2 (after CBT-I).

Figure S283. CBT-I vs pre-CBT-I (Disease Severity, ISI) [CMT = 8] Non-randomized study (SWD)



^{*}Peter 2019: Pre/post online CBT only, lower score is better. ISI= insomnia severity index.

Melatonin for daytime sleep

Summary of Findings (GRADE)

Table S25. Melatonin for daytime sleep in adults with shiftwork disorder

References: Aeschbach 2009, Folkard 1993, James 1998, Cavallo 2005, Gilbert 1999, Mishima 1997, Sharkey 2001, Smith 2005, Sharkey 2002, Jockovich 2000

| Outcomes [Tool] | Certainty of the evidence (GRADE) | Absolute Difference Melatonin for daytime sleep vs Control | No of Participants (studies) |
|--|-------------------------------------|---|------------------------------|
| Excessive sleepiness or alertness [KSS] | ⊕○○○ VERY LOW ^{a,b,c,d} | The mean difference in the melatonin group was 0.56 points more (0.45 fewer to 1.56 more) compared to control | 16 (1 RCT) |
| Excessive sleepiness or alertness [VAS-alertness] | ⊕○○○ VERY LOW ^{c,e} | The mean difference in the melatonin group was 11.9 higher (0.58 lower to 24.38 higher) compared to control | 14 (1 RCT) |
| Excessive sleepiness or alertness [Subjective reporting] | ⊕○○○ VERY LOW ^{c,d} | The risk ratio in the melatonin group was 0.81 (0.02 to 1.44) with an absolute risk of 3.7 fewer per 1,000 (19 fewer to 8.5 more) compared to control | |
| Excessive sleepiness or alertness [MSLT] | ⊕○○○ VERY LOW ^{a,c,e} | The mean difference in the melatonin group was 0.53 minutes higher (-2.16 fewer to 3.22 more) compared to control | 42 (1 RCT) |
| Excessive sleepiness or alertness [VAS-Alertness] | ⊕○○○ VERY LOW ^{c,d} | The mean difference in the melatonin group was 0.5 cm lower (1.38 lower to 0.38 higher) compared to control | 44 (1 RCT) |
| Excessive sleepiness or alertness [SSS] | ⊕○○○ VERY LOW ^{a,c,e} | The mean difference in the melatonin group was 0.19 points fewer (1.05 fewer to 0.67 more) compared to control | 14 (1 RCT) |
| Cognitive performance [PVT lapses] | ⊕○○○ VERY LOW ^{a,c} | The mean difference in the melatonin group was 0.4 lapses fewer (0.04 fewer to 0.72 more) compared to control | 58 (2 RCTs) |
| Cognitive performance [Conner's Continuous Performance Test] | ⊕○○○ VERY LOW ^{c,d,f} | The evidence (1 RCT) is very uncertain about the effect of naps and caffeine on cognitive performance (measured by multiple domains of the Connor's Continuous Performance Test). | 90 (1 RCT) |
| Adverse Event [Headache] | ⊕○○○ VERY LOW ^{c,d,f} | The risk ratio in the melatonin group was 0.82 (0.51 to 1.30) with an absolute risk of 11 fewer per 1,000 (30 fewer to 18.4 more) compared to control | 58 (1 RCT) |
| Adverse Event [Abdominal pain] | ⊕○○○ VERY LOW ^{c,d,f} | The risk ratio in the melatonin group was 1.85 (0.48 to 7.03) with an absolute risk of 8.2 more per 1,000 (5 fewer to 58.4 more) compared to control | 58 (1 RCT) |
| Adverse Event [Nausea] | ⊕○○○ VERY LOW ^{c,d,f} | The risk ratio in the melatonin group was 2.21 (0.75 to 6.56) with an absolute risk of 15.6 more per 1,000 (3.2 fewer to 71.7 more) compared to control | 58 (1 RCT) |
| Adverse Event [Vomiting] | ⊕○○○ VERY LOW ^{c,d,f} | The risk ratio in the melatonin group was 9.93 (0.56 to 176.60) with an absolute risk of 0.0 fewer per 1,000 (0 fewer to 0 fewer) compared to control | 58 (1 RCT) |
| Adverse Event [Dizziness] | ⊕○○○ VERY LOW ^{c,d,f} | The risk ratio in the melatonin group was 1.11 (0.07 to 16.88) with an absolute risk of 0.4 fewer per 1,000 (3 fewer to 51.2 more) compared to control | 58 (1 RCT) |
| Sleep quality [VAS-sleep quality] | ⊕○○○ VERY LOW ^{c,g} | The mean difference in the melatonin group was 10.6 cm higher (2.51 higher to 18.69 higher) compared to control | 14 (1 RCT) |

- a. Indirectness is due to the fact that participants included in the studies are healthy individuals. The effect in adults with SWD may be different
- b. Timepoints not within 2300- end of shift.
- c. Imprecision due to small sample size (<200 participants)
- d. Confidence interval crosses the line of no effect
- e. Confidence interval crosses the clinical significance threshold
- f. Bias in reported data, pooled between subject and within subject data
- g. Incomplete outcome data

Study Characteristics

Table S26. Melatonin for daytime sleep in adults with shiftwork disorder

| Study Citation | Study Design | Number of Participants (% Female) | Age (years) | Population | Intervention (dose) | Comparator | Time of Intervention Delivery | Duration of Follow-up |
|-------------------|-------------------|---|----------------|---|---|---------------|---|--------------------------|
| Aeschbach 2009 | RCT, crossover | 8 (50) | 27.8 ± 3.6 | Healthy participants | melatonin (2.1 mg patch) | Placebo patch | 1 hour before daytime sleep opportunity | 1 day |
| Cavallo 2005 | RCT, crossover | 45 (64) | 28.6 ± 1.9 | Shift workers without SWD diagnosis | melatonin (3 mg) | Placebo | before bedtime in the morning after night shift | 1 night |
| Folkard 1993 | RCT, crossover | 17 (12) | 29 ± 7 | Shift workers without SWD diagnosis | Melatonin (5 mg) | Placebo | before day sleeps between the night shifts at 06:42 h ± 7.6 min | 28 days |
| Gilbert 1999 | RCT, crossover | 20 (35) | 23.5 ± 0.4 | Healthy participants | Melatonin (5 mg) | Placebo | 14:00 | 1 night |
| James 1998 | RCT, crossover | 22 (23) | 29 ± 8 | Shift workers without SWD diagnosis | Melatonin (6 mg) | Placebo | 30 minutes before each consecutive day sleep | 4 nights |
| Jockovich 2000 | RCT, crossover | 19 (21) | 28.4 | Shift workers without SWD diagnosis | Melatonin (1 mg) | Placebo | 30-60 minutes before daytime sleep session | 3 days |
| Mishima 1997 | RCT, crossover | 6 (0) | 22.5 ± 1.9 | Healthy participants | Melatonin (3 or 9 mg) | Placebo | 9:30 | 1 day |
| Sharkey 2001 | RCT, crossover | 21 (43) | 27.0 ± 5.0 | Healthy participants | Melatonin (1.8 mg sustained release) | Placebo | 30 min before bedtime | 6 days |
| Sharkey 2002 | RCT | 32 (41) | 24.2 ± 4.8 | Healthy participants | Melatonin (0.5 or 3 mg) | Placebo | 30 min before bedtime | 8 days |
| Smith 2005 | RCT | 67 (52) | 23.9 ± 6.2 | Healthy participants | melatonin (1.8 mg sustained release) | placebo | bright light during the night shifts | 5 nights |

Critical Outcomes

Figure S284. Melatonin vs Control (Excessive Sleepiness, KSS) [CMT=1 point] RCT (Healthy participants)

| | Me | latoni | n | PI | acebo | | Mean Difference | | Mea | an Differe | ence | |
|-----------------------|---------|--------|-------|------|-------|-------|--------------------|-------------|-----|------------|------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, | Fixed, 95 | % CI | |
| 14.10.1 Lab Study (2. | 1 mg pa | itch) | | | | | | | | 16 | | |
| Aeschbach 2009 | 3.72 | 0.79 | 8 | 3.27 | 0.74 | 8 | 0.45 [-0.30, 1.20] | | | - | 100 | |
| | | | | | | | - | | | \perp | Ţ | - ! |

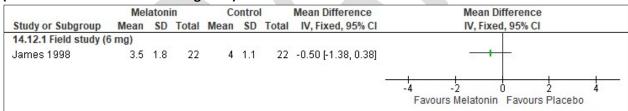
^{*}Aeschbach 2009: KSS data extracted from graph; SEM converted to SD.

Figure S285. Melatonin vs placebo (Excessive Sleepiness, VAS-Alertness) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)

| Ex | perimenta | I | | Placebo | | Mean Difference | Mean Difference |
|------|---------------|---------|-------|--------------------------|-----------------------------|--------------------------------------|---|
| Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| mg) | | | | | | | f |
| 66.1 | 12.1705 | 7 | 54.2 | 11.6413 | 7 | 11.90 [-0.58, 24.38] | - |
| | | | | | | | |
| | | | | | | | -20 -10 0 10 20 Favours Placebo Favours Melatonin |
| | Mean 5 mg) | Mean SD | 5 mg) | Mean SD Total Mean 5 mg) | Mean SD Total Mean SD 5 mg) | Mean SD Total Mean SD Total 5 mg) | Mean SD Total Mean SD Total IV, Fixed, 95% CI 5 mg) |

^{*}Folkard 1993: data extracted from the figure, pooled from 22:00-6:00, SEM converted to SD

Figure S286. Melatonin vs placebo (Excessive Sleepiness, VAS-Alertness) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)



^{*}James 1998: mean and SD calculated from median and IQR

Figure S287. Melatonin vs placebo (Excessive Sleepiness, Subjective Report of Adverse Events) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)

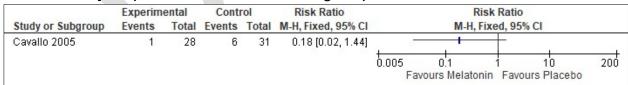


Figure S288. Melatonin vs placebo (Excessive Sleepiness, MSLT) [CMT = 1 min] RCT (Healthy participants)

| | Expe | rimen | tal | Pla | acebo | | Mean Difference | | Mean Diff | ference | |
|-----------------------|---------|-------|-------|------|-------|-------|--------------------|-----|-------------------|-----------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, | 95% CI | |
| 10.14.4 Lab Study (1. | 8 mg SF | ?) | | | | | | | 1 | | |
| Sharkey 2001 | 5.94 | 4.54 | 21 | 5.41 | 4.35 | 21 | 0.53 [-2.16, 3.22] | | <u> </u> | | |
| | | | | | | | | | | | |
| | | | | | | | | -10 | -5 Ó | 5 | 1 |
| | | | | | | | | | Favours Melatonin | Favours Placebo | |

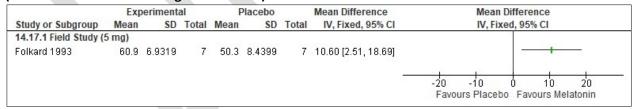
Figure S289. Melatonin vs placebo (Excessive Sleepiness, SSS) [CMT = 1 pt] RCT (Healthy participants)

| | Me | latoni | n | Pla | cebo |) | Mean Difference | | N | lean Di | fference | | |
|-----------------------|---------|--------|-------|------|------|-------|---------------------|----|-------------|----------|----------|---------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | I | V, Fixed | , 95% CI | | |
| 14.15.1 Lab Study (1. | 8 mg SF | () | | | | | | | | 18 | | | |
| Sharkey 2001 | 3.23 | 1.09 | 21 | 3.42 | 1.7 | 21 | -0.19 [-1.05, 0.67] | | | - | 100 | | |
| | | | | | | | | -1 | i i | | | 77 | - 6 |
| | | | | | | | | -2 | -1 | Ċ | | 1 | 2 |
| | | | | | | | | | Favours Mel | atonin | Favours | Placebo | |

Figure S290. Melatonin vs placebo (Sleep Quality, Movement Minutes) [CMT = Not Established] RCT (Healthy participants)

| Mean SD | T / 1 D/ F: 1 0 FW 01 | |
|-------------|-------------------------|---|
| Micali 3D | Total IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| | | |
| 43.65 16.84 | 18 -1.54 [-11.12, 8.04] | |
| | + | |
| | -20 |) -10 0 10 2 Favours Melatonin Favours Placebo |
| 3 | 3 43.65 16.84 | 3 43.65 16.84 18 -1.54 [-11.12, 8.04] -1.20 |

Figure S291. Melatonin vs placebo (Sleep Quality, VAS-sleep quality) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)



^{*}Folkard 1993: SEM converted to SD, 5 mg taken prior to each of the 6 successive day sleeps taken between the night shifts at $06:42 \text{ h} \pm 7.6 \text{ min}$

Figure S292. Melatonin vs Control (Cognitive Performance, PVT lapses) [CMT= 1 lapse] RCT (Healthy participants)

| | Me | latonii | n | PI | acebo | | | Mean Difference | Mean Difference |
|-----------------------------------|----------|----------------------|---------|----------------|---------|-------------|--------|---------------------|-------------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 14.18.1 Lab Study (2 | .1 mg pa | tch) | | | | | | | · · |
| Aeschbach 2009 | 1.31 | 1.13 | 8 | 1.31 | 1.61 | 8 | 31.0% | 0.00 [-1.36, 1.36] | - + - |
| Subtotal (95% CI) | | | 8 | | | 8 | 31.0% | 0.00 [-1.36, 1.36] | |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z = 0.00 | (P = 1 | .00) | | | | | | |
| 14.18.2 Lab Study (1 | .8 mg SF | R) | | | | | | | |
| Sharkey 2001 | 2.28 | 1.51 | 21 | 2.34 | 1.51 | 21 | 69.0% | -0.06 [-0.97, 0.85] | |
| Subtotal (95% CI) | | | 21 | | | 21 | 69.0% | -0.06 [-0.97, 0.85] | - |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z = 0.13 | (P = 0) | 0.90) | | | | | | |
| Total (95% CI) | | | 29 | | | 29 | 100.0% | -0.04 [-0.80, 0.72] | • |
| Heterogeneity: Chi ² = | 0.01, df | = 1 (P | = 0.94) | $ ^2 = 09$ | 6 | | | | + + + |
| Test for overall effect: | Z = 0.11 | (P = 0 | 0.91) | | | | | | Favours Melatonin Favours Placebo |
| Test for subgroup diff | ferences | : Chi ² : | = 0.01. | df = 1 (F | P = 0.9 | 4), $ ^2 =$ | 0% | | I avours meratorini Pavours Placebo |

^{*}Aeschbach 2009: 2.1 mg melatonin patch was placed on participants at 0800 (an hour prior to their daytime sleep). Crossover-study, acceptable washout period. 2100 timepoint used, data extracted from graph; SEM converted to SD.

Figure S293. Melatonin vs Control (Cognitive Performance, Conner's Continuous Performance Test (reaction time)) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

| | Expe | rimen | tal | Pla | cebo | 0 | Mean Difference | Me | an Difference | ce | |
|------------------------|-------|-------|-------|-------|------|-------|-----------------------|---------------|---------------|-------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, | Fixed, 95% (| CI | |
| 14.15.1 Field Study (3 | 3 mg) | | | | | | | | 11 | | |
| Cavallo 2005 | 333 | 59.8 | 45 | 339.3 | 65 | 45 | -6.30 [-32.11, 19.51] | 102 | - | | |
| | | | | | | | | | | | |
| | | | | | | | | -100 -50 | Ó | 50 | 10 |
| | | | | | | | | Favours Melat | onin Favou | irs Placebo | |

^{*}Cavallo 2005: 3 mg melatonin or placebo were given in the morning of the days of night work

Figure S294. Melatonin vs Control (Cognitive Performance, Conner's Continuous Performance Test (Hit reaction time block change)) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

| | Exp | erimenta | tl | P | lacebo | | Mean Difference | Mean Difference |
|------------------------|--------|----------|-------|--------|--------|-------|--------------------|-----------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 14.69.1 Field Study (3 | 3 mg) | | | | | | | V |
| Cavallo 2005 | 0.0025 | 0.0285 | 45 | 0.0016 | 0.0259 | 45 | 0.00 [-0.01, 0.01] | |
| | | | | | | | | -0.05 -0.025 0 0.025 0.0 |
| | | | | | | | | Favours Melatonin Favours Placebo |

^{*}Cavallo 2005: 3 mg melatonin or placebo were given in the morning of the days of night work

Figure S295. Melatonin vs Control (Cognitive Performance, Conner's Continuous Performance Test (Attentiveness)) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

| Exper | imen | tal | Pla | acebo |) | Mean Difference | Mean Difference |
|-------|-------------|----------------|------|--------------------------|-----------------------------|--------------------------------------|---|
| Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 3 mg) | | | | | | | 9 |
| 3.6 | 1 | 45 | 3.5 | 1.1 | 45 | 0.10 [-0.33, 0.53] | - 1 |
| | | | | | | | |
| | | | | | | | -2 -1 0 1 Favours Melatonin Favours Placebo |
| | Mean mg) | Mean SD mg) | mg) | Mean SD Total Mean B mg) | Mean SD Total Mean SD B mg) | Mean SD Total Mean SD Total 8 mg) | Mean SD Total Mean SD Total IV, Fixed, 95% CI 8 mg) |

^{*}Cavallo 2005: 3 mg melatonin or placebo were given in the morning of the days of night work

Figure S296. Melatonin vs Control (Cognitive Performance, Conner's Continuous Performance Test (Risk Taking)) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

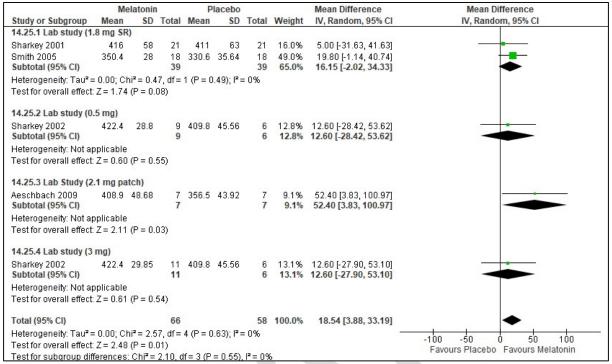
| | Expe | rimen | ital | Pla | acebo |) | Mean Difference | | Me | an Differe | nce | |
|-----------------------|-------|-------|-------|------|-------|-------|--------------------|-----|-------------|------------|-------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, | Fixed, 95% | CI | |
| 14.71.1 Field Study (| 3 mg) | | | | | | | | | | | |
| Cavallo 2005 | 0.3 | 1.6 | 45 | 0.3 | 1.6 | 45 | 0.00 [-0.66, 0.66] | | 25 | | 700 | |
| | | | | | | | | - 1 | - 1 | | | - |
| | | | | | | | | -2 | -1 | Ò | 1 | 2 |
| | | | | | | | | Fa | vours Melat | onin Favo | ours Placel | 00 |

^{*}Cavallo 2005: 3 mg melatonin or placebo were given in the morning of the days of night work

Figure S297. Melatonin vs Control (Cognitive Performance, Conner's Continuous Performance Test (No. of commission errors)) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

| | Expe | rimen | tal | Pla | cebo |) | Mean Difference | Mean Difference |
|------------------------|-------|-------|-------|------|------|-------|--------------------|-----------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 14.74.1 Field Study (3 | 3 mg) | | | | | | | 1 |
| Cavallo 2005 | 10.5 | 7.4 | 45 | 10.3 | 8 | 45 | 0.20 [-2.98, 3.38] | |
| | | | | | | | | |
| | | | | | | | | -10 -5 0 5 1 |
| | | | | | | | | Favours Melatonin Favours Placebo |

Figure S298. Melatonin vs placebo (Total Sleep Time, PSG) [CMT = 15 min] RCT (Healthy participants)

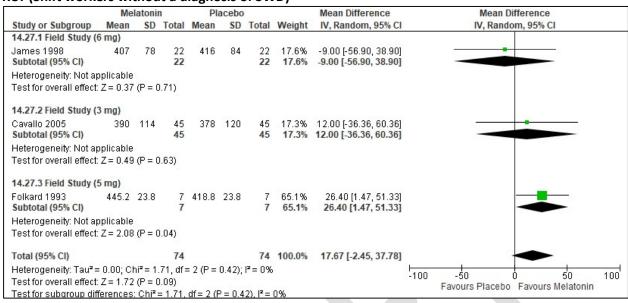


^{*}Aeschbach 2009: 2.1 mg melatonin patch was placed on participants at 0800 (an hour prior to their daytime sleep, 0900-1700, following lab shiftwork). Crossover-study, acceptable washout period. SEM converted to SD. Satomura 2001: medication administered at 13:30 h

Figure S299. Melatonin vs placebo (Total Sleep Time, Sleep Diary or questionnaire) [CMT = 15 min] RCT (Healthy participants)

| | N | Melatonin | | | Placebo | | | Mean Difference | Mean Difference |
|---|----------|--------------------------|----------|----------|---------------------|----------|----------------|--|--------------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| 14.26.1 Lab Studies | (1.8 mg | SR) | | | | | | | V |
| Sharkey 2001 | 425 | 49 | 21 | 421 | 52 | 21 | 18.4% | 4.00 [-26.56, 34.56] | |
| Smith 2005 Subtotal (95% CI) | 399 | 20.3647 | 18 39 | 388.8 | 35.6382 | 18 39 | 47.9% 66.4% | | |
| Heterogeneity: Tau² = Test for overall effect: | | | | P = 0.7 | 4); I² = 0% | | | | |
| 14.26.2 Lab Study (0 | .5 mg) | | | | | | | | |
| Sharkey 2002 Subtotal (95% CI) | 456 | 16.2 | 9 | 420 | 38.212 | 6 | 16.5% 16.5% | | |
| Heterogeneity: Not ap Fest for overall effect: | | |) | | | | | | |
| 14.26.3 Lab Study (3 | .0 mg) | | | | | | | | |
| Sharkey 2002 Subtotal (95% CI) | 444 | 13.9298 | 11 11 | 420 | 38.212 | 6 | | 24.00 [-7.66, 55.66] 24.00 [-7.66, 55.66] | |
| Heterogeneity: Not ap Test for overall effect: | | |) | | | | | | |
| Total (95% CI) | | | 59 | | | 51 | 100.0% | 15.67 [2.55, 28.80] | • |
| Heterogeneity: Tau² = | 0.00; C | hi² = 2.66, | df = 3 (| P = 0.4 | 5); I² = 0% | | | | -100 -50 0 50 10 |
| Test for overall effect: | Z = 2.34 | 4 (P = 0.02) |) | | | | | | Favours Placebo Favours Melatonin |
| Test for subgroup diff | erences | : Chi ² = 2.5 | 55, df= | 2(P = 1) | 0.28), $I^2 = 2$ | 21.5% | | | 1 atomo 1 lacebo 1 avours melatorini |

Figure S300. Melatonin vs placebo (Total Sleep Time, Sleep Diary or questionnaire) [CMT = 15 min] RCT (Shift workers without a diagnosis of SWD)



^{*}Folkard 1993: hours converted into minutes; SEM converted to SD; 5 mg taken prior to each of the 6 successive day sleeps taken between the night shifts at 06:42 h ± 7.6 min

Cavallo 2005: hours converted to minutes, data from morning treatment days was used, 3 mg melatonin or placebo were given in the morning of the days of night work

Figure S301. Melatonin vs Placebo (Mental Health, POMS (tension/anxiety)) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

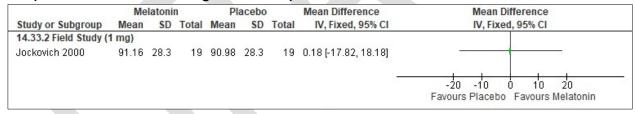


Figure S302. Melatonin vs Placebo (Mental Health, POMS (depression)) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

| IV, Fixed, 95% CI |
|--|
| |
| |
| |
| |
| -5 0 5 Favours Melatonin Favours Placebo |
| |

Figure S303. Melatonin vs Placebo (Mental Health, POMS (anger)) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

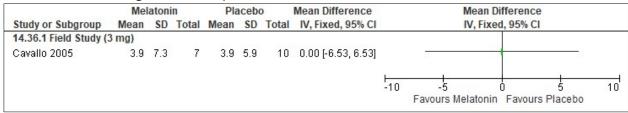
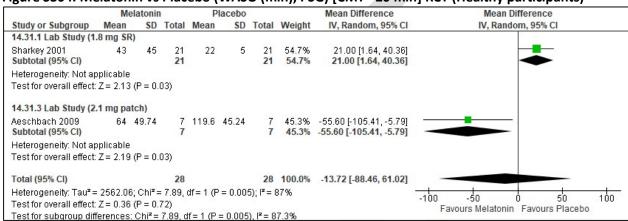


Figure S304. Melatonin vs Placebo (WASO (min), PSG) [CMT= 20 min] RCT (Healthy participants)



^{*}Aeschbach 2009: 2.1 mg melatonin patch was placed on participants at 0800 (an hour prior to their daytime sleep, 0900-1700, following lab shiftwork). Crossover-study, acceptable washout period. SEM converted to SD.

Figure S305. Melatonin vs Placebo (Sleep Latency (min), PSG) [CMT= 20 min] RCT (Shift workers without a diagnosis of SWD)

| Study or Subgroup | Melatonin | | | Placebo | | | Mean Difference | | Mean Difference | | |
|------------------------|-----------|-----|-------|---------|-----|-------|--------------------|-----|----------------------------------|------|--|
| | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 95% CI | | |
| 14.29.2 Field Study (1 | mg) | | | | | | | | | | |
| Jockovich 2000 | 7.59 | 5.7 | 19 | 6.8 | 5.7 | 19 | 0.79 [-2.83, 4.41] | | - | | |
| | | | | | | | | | | 5017 | |
| | | | | | | | | -20 | -10 0 10 | 2 | |
| | | | | | | | | | Favours Melatonin Favours Placeb | 0 | |

^{*}Jockovich 2000: SD calculated from p value, administered 30 to 60 minutes prior to their anticipated daytime sleep session

Figure S306. Melatonin vs Placebo (Sleep Latency (min), PSG) [CMT= 20 min] RCT (Healthy participants)

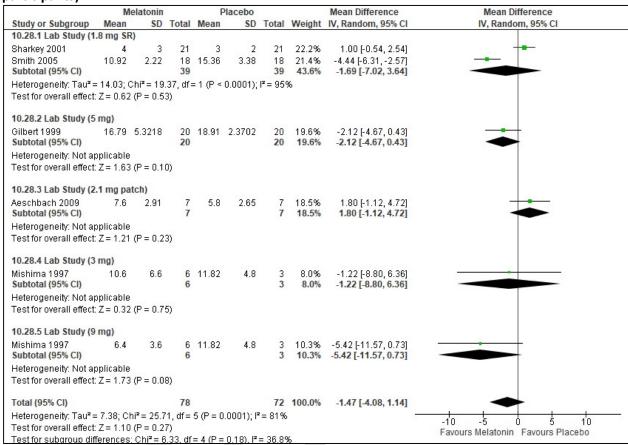


Figure S307. Melatonin vs Placebo (Sleep Latency (min), Sleep diary) [CMT= 20 min] RCT (Shift workers without a diagnosis of SWD)

| Melatonin | | | Pla | acebo | 0 | Mean Difference | Mean Difference |
|-----------|---------------|------------------|------------------------|-----------------------------|-----------------------------|--------------------------------------|--|
| Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 5 mg) | | | | | | | |
| 4.5 | 4.95 | 7 | 5.55 | 1.8 | 7 | -1.05 [-4.95, 2.85] | · · · · · · · · · · · · · · · · · · · |
| | | | | | | | |
| | | | | | | | -50 -25 0 25 5 Favours Melatonin Favours Placebo |
| | Mean 5 mg) | Mean SD 5 mg) | Mean SD Total 5 mg) | Mean SD Total Mean 5 mg) | Mean SD Total Mean SD 5 mg) | Mean SD Total Mean SD Total 5 mg) | Mean SD Total Mean SD Total IV, Fixed, 95% Co 5 mg) |

^{*}Folkard 1993: SEM converted to SD; 5 mg taken prior to each of the 6 successive day sleeps taken between the night shifts at $06:42h \pm 7.6$ min

Figure S308. Melatonin vs Placebo (Sleep Efficiency (%), PSG) [CMT= 10%] RCT (Shift workers without a diagnosis of SWD)

| | Melatonin | | | Placebo | | | Mean Difference | Mean Difference | | |
|------------------------|-----------|------|-------|---------|------|-------|----------------------|-----------------------------------|--|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | | |
| 14.33.2 Field Study (* | 1 mg) | | | | | | | 7 | | |
| Jockovich 2000 | 91.16 | 28.3 | 19 | 90.98 | 28.3 | 19 | 0.18 [-17.82, 18.18] | - | | |
| | | | | | | | 100 | -20 -10 0 10 20 | | |
| | | | | | | | | Favours Placebo Favours Melatonin | | |

^{*}Jockovich 2000: SD calculated from p value, 5 mg taken prior to each of the 6 successive day sleeps taken between the night shifts at $06:42 \text{ h} \pm 7.6 \text{ min}$

Figure S309. Melatonin vs Placebo (Sleep Efficiency (%), PSG) [CMT= 10%] RCT (Healthy participants)

| | Me | latonin | 1 | PI | acebo | | | Mean Difference | Mean Difference |
|--|-----------|--------------------|-----------------|--------|--------|--------------|--------|---------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| 14.32.1 Lab Study (1. | .8 mg SR |) | | | | | | | l' |
| Sharkey 2001 | 86.6 | 2 | 21 | 85.4 | 13 | 21 | 59.8% | 1.20 [-4.43, 6.83] | - |
| Subtotal (95% CI) | | | 21 | | | 21 | 59.8% | 1.20 [-4.43, 6.83] | • |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z = 0.42 | (P = 0. | 68) | | | | | | |
| 14.32.3 Lab Study (2 | .1 mg pat | tch) | | | | | | | |
| Aeschbach 2009 | 85.2 | 10.05 | 7 | 74.3 | 9.26 | 7 | 40.2% | 10.90 [0.78, 21.02] | - |
| Subtotal (95% CI) | | | 7 | | | 7 | 40.2% | 10.90 [0.78, 21.02] | |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z= 2.11 | (P = 0. | 03) | | | | | | |
| Total (95% CI) | | | 28 | | | 28 | 100.0% | 5.10 [-4.22, 14.42] | - |
| Heterogeneity: Tau²= | 29.59; C | SE | -20 -10 0 10 20 | | | | | | |
| Test for overall effect: $Z = 1.07$ (P = 0.28) | | | | | | | | | -20 -10 0 10 20 Favours Placebo Favours Melatonin |
| Test for subgroup diff | ferences: | Chi ² = | 2.69, d | f=1 (P | = 0.10 |), $ ^2 = 6$ | 2.9% | | avours i lacebo il avours ineratorini |

^{*}Aeschbach 2009: 2.1 mg melatonin patch was placed on participants at 0800 (an hour prior to their daytime sleep, 0900-1700, following lab shiftwork). Crossover-study, acceptable washout period. SEM converted to SD.

Figure S310. Melatonin vs Control (Adverse Events, headache) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

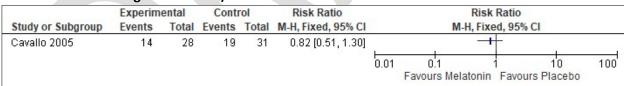


Figure S311. Melatonin vs Control (Adverse Events, Abdominal Pain) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

| | Experim | Conti | rol | Risk Ratio | Risk Ratio | | | | |
|-------------------|---------|-------|------------------|------------|--------------------|------|-------------------|--|-----|
| Study or Subgroup | Events | Total | tal Events Total | | M-H, Fixed, 95% CI | | M-H, Fix | ed, 95% CI | |
| Cavallo 2005 | 5 | 28 | 3 | 31 | 1.85 [0.48, 7.03] | | | | |
| | | | | | | 0.01 | 0.1 | 1 10 | 100 |
| | | | | | | | Favours Melatonin | Favours Placebo | |

Figure S312. Melatonin vs Control (Adverse Events, Vomiting) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

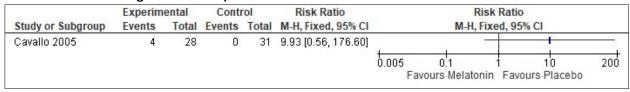


Figure S313. Melatonin vs Control (Adverse Events, Nausea) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

| | Experim | ental | | | Control | | Control | | Control | | Risk Ratio | Risk Ratio | | | | |
|-------------------|---------|-------|--------|-------|--------------------|-------------------|-----------------|-----|---------|--|------------|------------|--|--|--|--|
| Study or Subgroup | Events | Total | Events | Total | M-H, Fixed, 95% CI | M-H, Fixe | ed, 95% CI | | | | | | | | | |
| Cavallo 2005 | 8 | 28 | 4 | 31 | 2.21 [0.75, 6.56] | | . | | | | | | | | | |
| | | | | | | 0.01 0.1 | 1 10 | 100 | | | | | | | | |
| | | | | | | Favours Melatonin | Favours Placebo | | | | | | | | | |

Figure S314. Melatonin vs Control (Adverse Events, Dizziness) [CMT = Not Established] RCT (Shift workers without a diagnosis of SWD)

| | Experimental | | Contr | ol | ol Risk Ratio | | Risk Ratio | | | |
|-------------------|--------------|-------|--------|-------|--------------------|-------|----------------|-----------------|-----|--|
| Study or Subgroup | Events | Total | Events | Total | M-H, Fixed, 95% CI | | M-H, Fixe | ed, 95% CI | | |
| Cavallo 2005 | 1 | 28 | 1 | 31 | 1.11 [0.07, 16.88] | · · | - | | 9.4 | |
| | | | | | | 0.005 | 0.1 | 1 10 | 200 | |
| | | | | | | Fav | ours Melatonin | Favours Placebo | | |

Melatonin for transition from daytime to nighttime sleep following the night shift Summary of Findings (GRADE)

Table S27. Melatonin for transitioning from day to night sleeping in adults with shiftwork disorder

References: Sadeghniiat- Haghighi 2008, Sadeghniiat-Haghighi 2016, Farahmand 2018 Outcomes **Certainty of the Absolute Difference No of Participants** [Tool] evidence (studies) (GRADE) Melatonin for recovery from night shift vs Control Sleep quality The mean difference in the melatonin group was **0.11 lower** 172 $\Theta\ThetaOO$ [Questionnaire] (0.32 lower to 0.1 higher) compared to control (1 RCT) LOW^{a,b} Total sleep time $\Theta\ThetaOO$ The mean difference in the melatonin group was 20.1 172 minutes more (4.88 more to 35.32 more) compared to [Sleep diary] LOW^{a,c} (1 RCT) control **Total sleep time** The mean difference in the melatonin group was 18 minutes 56 $\Theta\ThetaOO$ [Actigraphy] more (12.49 fewer to 48.49 more) compared to control (1 RCT) LOW^{a,c} Mental health $\Theta\ThetaOO$ The mean difference in the melatonin group was 1.25 higher 48 [POMS] LOWa,b (24.15 lower to 26.65 higher) compared to control (1 RCT) WASO The mean difference in the melatonin group was 5.4 56 $\Theta\ThetaOO$ minutes fewer (19.85 fewer to 9.05 more) compared to [Actigraphy] (1 RCT) LOW^{a,b} control

| Sleep latency | ⊕⊕⊕○ | The mean difference in the melatonin group was 28.2 minutes fewer (35.62 fewer to 20.78 fewer) compared to control | 172 |
|------------------|--------------------|---|---------|
| [Sleep diary] | MODERATEª | | (1 RCT) |
| Sleep latency | ⊕⊕⊖⊖ | The mean difference in the melatonin group was 6.6 minutes fewer (11.47 fewer to 1.73 fewer) compared to control | 56 |
| [Actigraphy] | LOW ^{a,b} | | (1 RCT) |
| Sleep efficiency | ⊕⊕⊖⊖ | The mean difference in the melatonin group was 2.96 percent higher (0.84 lower to 6.76 higher) compared to control | 56 |
| [actigraphy] | LOW ^{a,b} | | (1 RCT) |

- a. Imprecision due to small sample size (<200 participants)
- b. Confidence interval crosses the line of no effect
- c. Confidence interval crosses the CMT

Table S28. Melatonin for transitioning from day to night sleeping in adults with shiftwork disorder

| Study Design | Number of Participants (% Female) | Age (years) | Population | Intervention (dose) | Comparator | Time of Intervention Delivery | of Follow- up |
|----------------|-----------------------------------|--|---|--|---|---|---|
| | | | Shift workers without SWD | | | about 1 hour before habitual nighttime | |
| RCT. Crossover | 24 (42) | 31.21±5.23 | diagnosis | melatonin (3 mg) | Placebo | sleep | 4 nights |
| | | | Shift workers without SWD | | | 30 min before night time sleep following | |
| RCT, crossover | 86 (80) | 30.5 ± 5.2 | diagnosis | Melatonin (5 mg) | Placebo | shift work | 1 night |
| DCT oroganian | 50 (0) | 22.0 8 | Shift workers without SWD | Malatania (2 ma) | Dlacaka | 30 min before night time sleep following | 3 days |
| | RCT. Crossover | RCT. Crossover 24 (42) RCT, crossover 86 (80) | Study Design (% Female) (years) RCT. Crossover 24 (42) 31.21±5.23 RCT, crossover 86 (80) 30.5 ± 5.2 | Study Design (% Female) (years) Population Shift workers without SWD diagnosis Shift workers without SWD diagnosis Shift workers without SWD diagnosis Shift workers without SWD diagnosis | Study Design (% Female) (years) Population (dose) Shift workers without SWD diagnosis melatonin (3 mg) Shift workers without SWD diagnosis Melatonin (5 mg) Shift workers without SWD diagnosis Melatonin (5 mg) | Study Design (% Female) (years) Population (dose) Comparator Shift workers without SWD diagnosis melatonin (3 mg) Placebo RCT. Crossover 24 (42) 31.21±5.23 diagnosis melatonin (3 mg) Placebo Shift workers without SWD diagnosis Melatonin (5 mg) Placebo Shift workers without SWD | Study Design (% Female) (years) Population (dose) Comparator Delivery about 1 hour before habitual nighttime sleep RCT. Crossover 24 (42) 31.21±5.23 diagnosis melatonin (3 mg) Placebo sleep Shift workers without SWD RCT, crossover 86 (80) 30.5 ± 5.2 diagnosis Melatonin (5 mg) Placebo shift work Shift workers without SWD Shift workers without SWD Shift workers without SWD Shift workers without SWD Shift workers without SWD |

Critical Outcomes

Figure S315. Sleep Promoting Medication (Melatonin) vs Control (Sleep quality, questionnaire) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)

| • | | | | | | | <u> </u> | |
|---------------------------|-----------|------|-------|------|---------------------------------|----|---------------------|-----------------------------------|
| | Melatonin | | | PI | acebo | | Mean Difference | Mean Difference |
| Study or Subgroup | Mean | SD | Total | Mean | Mean SD Total IV, Fixed, 95% CI | | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 14.5.1 Field Study (5 mg) | | | | | | | | |
| Sadeghniiat-Haghighi 2008 | 2.58 | 0.76 | 86 | 2.69 | 0.67 | 86 | -0.11 [-0.32, 0.10] | |
| | | | | | | | | |
| | | | | | | | | -2 -1 0 1 2 |
| | | | | | | | | Favours Melatonin Favours Placebo |

^{*}Sadeghniiat- Haghighi 2008: 5 mg Melatonin tablet, 30 min prior to bedtime (on the first night after shift work) (crossover-study, acceptable washout period). Sleep quality questionnaire (1= very satisfied, 5= very unsatisfied)

Important Outcomes

Figure S316. Melatonin vs placebo (Total Sleep Time, Sleep Diary or questionnaire) [CMT = 15 min] RCT (Shift workers without SWD diagnosis)

| | Me | n | Placebo | | | Mean Difference | Mean Difference | |
|----------------------------|---------------------|------|---------|------------|------|-----------------|---------------------|---|
| Study or Subgroup | or Subgroup Mean SD | | Total | Mean SD To | | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 14.51.1 Field Study (5 mg) | | | | | | | | |
| Sadeghniiat-Haghighi 2008 | 392.1 | 52.4 | 86 | 372 | 49.4 | 86 | 20.10 [4.88, 35.32] | - |
| | | | | | | | | |
| | | | | | | | | -50 -25 0 25 5 Favours Placebo Favours Melatonin |

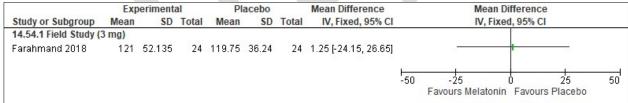
^{*}Sadeghniiat- Haghighi 2008: 5 mg Melatonin tablet, 30 min prior to bedtime (on the first night after shift work); questionnaire. Crossover-study, acceptable washout period.

Figure S317. Melatonin vs placebo (Total Sleep Time, Actigraphy) [CMT = 15 min] RCT (Shift workers without SWD diagnosis)

| | Melatonin | | | Placebo | | | Mean Difference | Mean Difference | | | | | |
|----------------------------|-----------|------|------|---------|------|------|-----------------------|-----------------------------------|------|----|-------|-------------------|-------------------|
| Study or Subgroup | Mean | Mean | Mean | Mean | Mean | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 14.67.2 Field Study (3 mg) | | | | | | | | | | | | | |
| Sadeghniiat-Haghighi 2016 | 354 | 58.2 | 28 | 336 | 58.2 | 28 | 18.00 [-12.49, 48.49] | - | | | | | |
| | | | | | | | | -50 -25 0 25 5 | | | | | |
| | | | | | | | | Favours Placebo Favours Melatonin | | | | | |

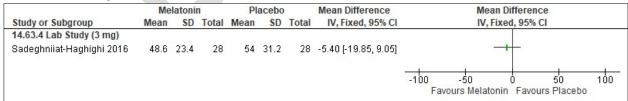
^{*}Sadeghniiat-Haghighi 2016: hours converted to minutes, used average of the three days, 3 mg of melatonin or placebo was administered 30 minutes before usual sleep time

Figure S318. Melatonin vs Placebo (Mental Health, POMS) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)



^{*}Farahmand 2018: POMS pooled for night 1 and 2, 3 mg tablets taken one hour before their night-time sleep at their first and second nights off

Figure S319. Melatonin vs Placebo (WASO (min), Actigraphy) [CMT= 20 min] RCT (Shift workers without SWD diagnosis)



^{*}Sadeghniiat-Haghighi 2016: hours converted to minutes, 3 mg of melatonin or placebo was administered 30 minutes before usual sleep time

Figure S320. Melatonin vs Placebo (Sleep Latency (min), Questionnaire) [CMT= 20 min] RCT (Shift workers without SWD diagnosis)

| | Me | latonii | n | Placebo | | | Mean Difference | Mean D | Mean Difference | | |
|----------------------------|------|---------|-------|---------|------|-------|-------------------------|------------------------------|-------------------------|----|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixe | d, 95% CI | | |
| 14.52.1 Field Study (5 mg) | | | | | | | | | | | |
| Sadeghniiat-Haghighi 2008 | 21.5 | 17.7 | 86 | 49.7 | 30.3 | 86 | -28.20 [-35.62, -20.78] | | | | |
| | | | | | | | | t. J. | <u> </u> | | |
| | | | | | | | | -50 -25 Favours Melatonin | 0 25 Favours Placebo | 50 | |

^{*}Sadeghniiat- Haghighi 2008: 5 mg Melatonin tablet, 30 min prior to bedtime (on the first night after shift work). All participants used in both arms (crossover-study, acceptable washout period). Measured by sleep onset latency.

Figure S321. Melatonin vs Placebo (Sleep Latency (min), Actigraphy) [CMT= 20 min] RCT (Shift workers without SWD diagnosis)

| | Melatonin | | | Placebo | | | Mean Difference | Mean Difference | | | |
|----------------------------|-----------|----|-------|---------|-------|-------|-----------------------|---|----|--|--|
| Study or Subgroup | Mean | SD | Total | Mean | an SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | | | |
| 14.68.4 Field Study (3 mg) | | | | | | | | | | | |
| Sadeghniiat-Haghighi 2016 | 12 | 9 | 28 | 18.6 | 9.6 | 28 | -6.60 [-11.47, -1.73] | | | | |
| | | | | | | | | | 1 | | |
| | | | | | | | | -20 -10 0 10 Favours Melatonin Favours Placebo | 20 | | |

^{*}Sadeghniiat-Haghighi 2016: hours converted to minutes, used average of the three days, 3 mg of melatonin or placebo was administered 30 minutes before usual sleep time

Figure S322. Melatonin vs Placebo (Sleep Efficiency (%), PSG) [CMT= 10%] RCT (Shift workers without SWD diagnosis)

| | Mel | n | Placebo | | | Mean Difference | Mean Difference | | |
|----------------------------|----------------|----|---------|-----------|----|--------------------|--------------------|-----------------------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Random, 95% CI | IV, Random, 95% CI | |
| 14.66.4 Field Study (3 mg) | | | | | | | | * | |
| Sadeghniiat-Haghighi 2016 | 016 85.5 6.3 2 | | 28 | 82.54 8.1 | 28 | 2.96 [-0.84, 6.76] | + | | |
| | | | | | | | | -20 -10 0 10 20 | |
| | | | | | | | | Favours Placebo Favours Melatonin | |

Melatonin for naps prior to the first night shift

Summary of Findings (GRADE)

Table S29. Melatonin for daytime sleep prior to the first night shift in adults with shiftwork disorder

References: Hughes 1997, Satomura 2001, Dijk 1995, Dollins 1994

| Outcomes [Tool] | Certainty of the evidence (GRADE) | Absolute Difference Melatonin vs Control | No of Participants (studies) |
|--------------------|---|---|------------------------------|
| Total sleep time | ⊕○○○ | The mean difference in the melatonin group was 15.7 minutes more (6.06 more to 25.34 more) compared to control | 76 |
| [PSG] | VERY LOW ^{a,b,c} | | (3 RCTs) |
| WASO | ⊕○○○ | The mean difference in the melatonin group was 20.04 minutes fewer (29.69 fewer to 10.43 fewer) compared to control | 60 |
| [PSG] | VERY LOW ^{a,b,c} | | (2 RCTs) |

| Sleep latency | ⊕⊕⊜⊝ | The mean difference in the melatonin group was 1.97 minutes fewer (2.55 fewer to 1.39 fewer) compared to control | 56 |
|-------------------------------|-----------------------------|--|----------------|
| [PSG] | LOW ^{a,b} | | (3 RCTs) |
| Sleep latency [Sleep test] | LOWa,b | The mean difference in the melatonin group was 9.52 minutes lower (12.36 lower to 6.68 lower) compared to control | 100 (1 RCT) |
| Sleep latency | ⊕⊕⊜⊝ | The mean difference in the melatonin group was 10.76 minutes fewer (13.55 fewer to 7.96 fewer) compared to control | 100 |
| [Sleep diary] | LOW ^{a,b} | | (1 RCT) |
| Sleep efficiency | ⊕○○○ | The mean difference in the melatonin group was 7.22 percent higher (1.68 lower to 16.12 higher) compared to control | 44 |
| [PSG] | VERY LOW ^{a,b,c,d} | | (2 RCTs) |

- a. Indirectness is due to the fact that participants included in the studies are healthy individuals. The effect in adults with SWD may be different.
- b. Imprecision due to small sample size (<200 participants)
- c. Imprecision due to the 95% CI crossing the CMT
- d. Imprecision due to the 95% CI crossing the null

Table S30. Melatonin for daytime sleep prior to the first night shift in adults with shiftwork disorder

| Study Citation | Study Design | Number of Participants (% Female) | Age in years | Population | Intervention (dose) | Comparator | Time of Intervention Delivery | Duration of Follow-up |
|-------------------|----------------|---|------------------|--------------|------------------------|------------|-------------------------------------|--------------------------|
| Dijk | | | | | | | 12:30 (30 min before nap | |
| 1995 | | | | Healthy | Melatonin (5 | | from 13:00- | |
| 1,,,, | RCT, crossover | 8 (0) | 22.4 | participants | mg) | Placebo | 17:00) | 1 night |
| | | | | | |) | 11:45 (1h 45 | |
| Dollins | | | | | Melatonin (0.1, | | min before a | |
| 1994 | | | | Healthy | 0.3, 1, or 10 | | sleep onset | |
| | RCT, crossover | 20(0) | 23.05 ± 4.22 | participants | mg) | Placebo | test at 13:30) | 5 nights |
| | | | | | | | 10:00 (2h | |
| Hughes | | | | | | | before nap | |
| 1997 | | | | Healthy | Melatonin (1, | | from 12:00- | |
| | RCT, crossover | 8 (0) | 18-30 | participants | 10, or 40 mg) | placebo | 16:00) | 1 day |
| | | | | | | | 13:30 (30 min | |
| Satomura | | | | | | | before nap | |
| 2001 | | | | Healthy | Melatonin (1, | | from 14:00 h | |
| | RCT, crossover | 7(0) | 23.7 ± 1.7 | participants | 3, or 6 mg) | Placebo | to 17:00) | 1 day |

Critical Outcomes

None

Important Outcomes

Figure S323. Melatonin vs placebo (Total Sleep Time, PSG) [CMT = 15 min] RCT (Healthy participants)

| | Mel | atonin | | Pla | cebo | | | Mean Difference | Mean Difference |
|------------------------------------|------------------|-------------|----------------|-------------|----------------------|--------------|----------------|---|-----------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| 14.69.1 Lab Study (1 | mg) | | | | | | | | |
| Hughes 1997 | 219.62 | 23.5 | 8 | 203.91 | 14.2 | 3 | 12.8% | 15.71 [-7.17, 38.59] | • |
| Satomura 2001 Subtotal (95% CI) | 160.7 | 22.6 | 7 15 | 138.9 | 29.2 | 2 5 | 4.4% 17.2% | 21.80 [-21.99, 65.59] 17.02 [-3.26, 37.29] | • |
| Heterogeneity: Tau ² = | 0.00; Ch | $i^2 = 0.0$ | 6, df= | 1 (P = 0.3) | 31); l² = | = 0% | | | |
| Test for overall effect: | Z=1.64 | (P = 0.1 | 10) | | | | | | |
| 14.69.4 Lab Study (3 | mg) | | | | | | | | |
| Satomura 2001 Subtotal (95% CI) | 166.9 | 10 | 7 | 138.9 | 29.2 | 2 2 | | 28.00 [-13.14, 69.14] 28.00 [-13.14, 69.14] | |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z=1.33 | (P = 0.1 | 18) | | | | | | |
| 14.69.5 Lab Study (5 | mg) | | | | | | | | |
| Dijk 1995 Subtotal (95% CI) | 227.3 | 5.9 | 8 | 223.3 | 8.2 | 8 | 36.8% 36.8% | 4.00 [-3.00, 11.00] 4.00 [-3.00, 11.00] | * |
| Heterogeneity: Not ap | | (D = 0 : | 267 | | | | | | |
| rest for overall effect. | Z= 1.12 | (P = 0 | 20) | | | | | | |
| 14.69.6 Lab Study (6 | mg) | | | | | | | | |
| Satomura 2001 Subtotal (95% CI) | 169.6 | 6.7 | 7 | 138.9 | 29.2 | 3 | 7.0% 7.0% | 30.70 [-2.71, 64.11] 30.70 [-2.71, 64.11] | |
| Heterogeneity: Not as | nlicable | | , | | | 3 | 1.070 | 30.70 [-2.71, 04.11] | |
| Test for overall effect: | | (P = 0.1 | 07) | | | | | | |
| 14.69.7 Lab Study (1 | 0 mg) | | | | | | | | |
| Hughes 1997 Subtotal (95% CI) | 226.5 | 8.7 | 8 | 203.91 | 14.2 | 3 | 18.7% 18.7% | 22.59 [5.43, 39.75] 22.59 [5.43, 39.75] | • |
| Heterogeneity: Not as | pplicable | | | | | | | | |
| Test for overall effect: | | (P = 0.1 | 010) | | | | | | |
| 14.69.8 Lab Study (4 | 0 mg) | | | | | | | | |
| Hughes 1997 Subtotal (95% CI) | 226.7 | 5.1 | 8 | 203.91 | 14.2 | 2 2 | 15.4% 15.4% | 22.79 [2.80, 42.78] 22.79 [2.80, 42.78] | • |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z= 2.23 | (P = 0.1 | 03) | | | | | | |
| Total (95% CI) | 42 EMPL 18 | 1712 FF | 53 | 0.000 PA | | | 100.0% | 15.70 [6.06, 25.34] | • |
| Heterogeneity: Tau ² = | | | | : 6 (P = 0 | .16); l ^a | = 35% | | | -100 -50 0 50 10 |
| Test for overall effect: | | , | | 6 - E (D | 0.40 | 12 - 45 | 201 | | Favours Placebo Favours Melatonin |
| Test for subgroup diff | <u>rerences:</u> | Uni*= | <u>9.13, d</u> | I = 5 (P = | U.TU), | $1^{2} = 45$ | .2% | | |

^{*}Hughes 1997: SEM converted to SD

Figure S324. Melatonin vs Placebo (WASO (min), PSG) [CMT= 20 min] RCT (Healthy participants)

| | N | Melatonin | | | Placebo | | | Mean Difference | Mean Difference |
|--|---|-----------------|----------|----------|---------------------|-------|--------|-------------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| 14.71.1 Lab Study (1 | mg) | | | | | | | | |
| Hughes 1997 | 15.53 | 23.5325 | 8 | 29.59 | 13.1809 | 3 | 19.0% | -14.06 [-36.16, 8.04] | |
| Satomura 2001 | 14 | 23.2 | 7 | 25.3 | 31.9 | 2 | 4.1% | -11.30 [-58.73, 36.13] | |
| Subtotal (95% CI) | | | 15 | | | 5 | 23.1% | -13.57 [-33.60, 6.46] | • |
| Heterogeneity: Tau ² : | = 0.00; CI | hi² = 0.01, | df = 1 (| P = 0.93 | 2); $I^2 = 0\%$ | | | | |
| Test for overall effect | : Z= 1.33 | (P = 0.18) |) | | | | | | |
| 14.71.4 Lab Study (3 | mg) | | | | | | | | |
| Satomura 2001 | 6.7 | 4.3 | 8 | 25.3 | 31.9 | 3 | | -18.60 [-54.82, 17.62] | |
| Subtotal (95% CI) | | | 8 | | | 3 | 7.1% | -18.60 [-54.82, 17.62] | |
| Heterogeneity: Not a | | | | | | | | | |
| Test for overall effect | : Z = 1.01 | (P = 0.31) |) | | | | | | |
| 14.71.5 Lab Study (6 | mg) | | | | | | | | |
| Satomura 2001 | 7.9 | 5.5 | 8 | 25.3 | 31.9 | 2 | | -17.40 [-61.77, 26.97] | |
| Subtotal (95% CI) | | | 8 | | | 2 | 4.7% | -17.40 [-61.77, 26.97] | |
| Heterogeneity: Not ap Test for overall effect | | | Ý. | | | | | | |
| | | | | | | | | | |
| 14.71.6 Lab Study (1 | 100000000000000000000000000000000000000 | | | | | | | | 0.651 |
| Hughes 1997 | 7.38 | 8.4399 | | 29.59 | 13.1809 | 2 | | -22.21 [-41.52, -2.90] | |
| Subtotal (95% CI) | | | 7 | | | 2 | 24.9% | -22.21 [-41.52, -2.90] | - |
| Heterogeneity: Not a | | | | | | | | | |
| Test for overall effect | : Z= 2.25 | P = 0.02 |) | | | | | | |
| 14.71.7 Lab Study (4 | 70.00 | | | | | | | | |
| Hughes 1997 | 6.57 | 3.7834 | 7 | 29.59 | 13.1809 | 3 | 40.3% | -23.02 [-38.20, -7.84] | <u> </u> |
| Subtotal (95% CI) | | | 7 | | | 3 | 40.3% | -23.02 [-38.20, -7.84] | - |
| Heterogeneity: Not a | | | 200 | | | | | | |
| Test for overall effect | :∠= 2.97 | (P = 0.00) | 3) | | | | | | |
| Total (95% CI) | | | 45 | | | 15 | 100.0% | -20.06 [-29.69, -10.43] | • |
| Heterogeneity: Tau ² : | = 0.00; CI | hi² = 0.63, | df = 5 (| P = 0.99 | 9); I² = 0% | | | | -100 -50 0 50 10 |
| Test for overall effect | | | | | | | | | Favours Melatonin Favours Placebo |
| Test for subaroup dif | ferences | $: Chi^2 = 0.6$ | 62. df= | 4 (P = 1 | 0.96), $I^2 = 0$ | 1% | | | i avodis ilielatolilli Favodis Flacebo |

^{*}Hughes 1997: SEM converted to SD

Figure S325. Melatonin vs Placebo (Sleep Latency (min), PSG) [CMT= 20 min] RCT (Healthy participants)

| | Me | latonin | 1 | PI | acebo | | | Mean Difference | Mean Difference |
|--|---|---------|---------------|--------|---------|---------|----------------------|--|-----------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| 14.72.1 Lab Study (1 | mg) | | | | | | | | |
| Hughes 1997 | 2.94 | 0.35 | 8 | 4.83 | 0.85 | 3 | 34.1% | -1.89 [-2.88, -0.90] | - |
| Satomura 2001 Subtotal (95% CI) | 6.1 | 2.3 | 7 15 | 12 | 5.3 | 2 5 | 0.6% 34.7% | -5.90 [-13.44, 1.64] - 2.08 [- 3.76 , - 0.41] | • |
| Heterogeneity: Tau² = Test for overall effect: | | | | 1 (P = | 0.30); | l² = 6% | | | |
| 14.72.5 Lab Study (3 | mg) | | | | | | | | |
| Satomura 2001 Subtotal (95% CI) | 4.5 | 1.7 | 7 7 | 12 | 5.3 | 2 | | -7.50 [-14.95, -0.05] - 7.50 [-14.95, -0.05] | |
| Heterogeneity: Not ap Test for overall effect: | | | .05) | | | | | | |
| 14.72.6 Lab Study (5 | mg) | | | | | | | | |
| Dijk 1995 Subtotal (95% CI) | 3 | 1.98 | 8 | 4.3 | 2.3 | 8 | 7.6% 7.6 % | -1.30 [-3.40, 0.80] - 1.30 [- 3.40 , 0.80] | • |
| Heterogeneity: Not ap Test for overall effect: | • | | .23) | | | | | | |
| 14.72.7 Lab Study (6 | mg) | | | | | | | | |
| Satomura 2001 Subtotal (95% CI) | 7.7 | 2.9 | 7 | 12 | 5.3 | 3 | 0.8% | -4.30 [-10.67, 2.07] -4.30 [-10.67, 2.07] | |
| Heterogeneity: Not ap Test for overall effect: | • | | .19) | | | | | | |
| 14.72.8 Lab Study (10 | mg) | | | | | | | | |
| Hughes 1997 Subtotal (95% CI) | 2.63 | 0.4 | 8 | 4.83 | 0.85 | 3 | 33.5% 33.5% | -2.20 [-3.20, -1.20] -2.20 [-3.20, -1.20] | * |
| Heterogeneity: Not ap Test for overall effect: | • | | .0001) | | | | | | |
| 14.72.9 Lab Study (40 | mg) | | | | | | | | |
| Hughes 1997 Subtotal (95% CI) | 3.19 | 0.42 | 8 | 4.83 | 0.85 | 2 | 22.8% 22.8% | -1.64 [-2.85, -0.43] -1.64 [-2.85, -0.43] | * |
| Heterogeneity: Not ap | • | | 2012-00-00 | | | | | | |
| Test for overall effect: | Z = 2.65 | (P = 0 | .008) | | | | | | |
| Total (95% CI) | | | 53 | | | 23 | 100.0% | -1.97 [-2.55, -1.39] | • |
| Heterogeneity: Tau ² = | | | | | 0.60); | l² = 0% | | | -20 -10 0 10 : |
| Test for overall effect: Test for subgroup diff | | • | | | 9 = 0.6 | 2). I²= | N% | | Favours Melatonin Favours Placebo |

^{*}Hughes 1997: SEM converted to SD

Figure S326. Melatonin vs Placebo (Sleep Latency (min), sleep test) [CMT= 20 min] RCT (Healthy participants)

| | M | lelatonin | | F | Placebo | | | Mean Difference | Mean Difference |
|-----------------------------------|----------|------------------------|-----------------|-----------|----------------|--------|--------|------------------------|---------------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| 14.78.1 Lab study (0. | .1 mg) | | | | | | | | |
| Dollins 1994 Subtotal (95% CI) | 9.61 | 8.2287 | 20 20 | 17.06 | 5.4336 | 5 5 | | | • |
| Heterogeneity: Not ap | plicable | 10 | | | | | | | |
| Test for overall effect: | Z = 2.44 | (P = 0.0 | 1) | | | | | | |
| 14.78.2 Lab study (0. | .3 mg) | | | | | | | | |
| Dollins 1994 | 8.03 | 7.1554 | 20 | 17.06 | 5.4336 | 5 | 24.8% | -9.03 [-14.73, -3.33] | - |
| Subtotal (95% CI) | | | 20 | | | 5 | 24.8% | -9.03 [-14.73, -3.33] | • |
| Heterogeneity: Not ap | plicable | 1 | | | | | | | |
| Test for overall effect: | Z = 3.10 |) (P = 0.0 | 02) | | | | | | |
| 14.78.3 Lab Study (1 | mg) | | | | | | | | |
| Dollins 1994 | 6.04 | 7.379 | | 17.06 | 5.4336 | | | -11.02 [-16.78, -5.26] | |
| Subtotal (95% CI) | | | 20 | | | 5 | 24.3% | -11.02 [-16.78, -5.26] | • |
| Heterogeneity: Not as | plicable | | | | | | | | |
| Test for overall effect: | Z = 3.75 | 5 (P = 0.0 | 002) | | | | | | |
| 14.78.4 Lab Study (1 | 0 mg) | | | | | | | | |
| Dollins 1994 | 6.74 | 5.5454 | | 17.06 | 5.4336 | | | -10.32 [-15.67, -4.97] | - |
| Subtotal (95% CI) | | | 20 | | | 5 | 28.2% | -10.32 [-15.67, -4.97] | • |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z = 3.78 | 3 (P = 0.0 | 002) | | | | | | |
| Total (95% CI) | | | 80 | | | 20 | 100.0% | -9.52 [-12.36, -6.68] | • |
| Heterogeneity: Tau ² = | 0.00; C | $hi^2 = 0.84$ | l, $df = 3$ | (P = 0.3) | $84); I^2 = 0$ | % | | · · | -20 -10 0 10 20 |
| Test for overall effect: | Z = 6.57 | (P < 0.0 | 0001) | | | | | | Favours Melatonin Favours Placebo |
| Test for subgroup diff | ferences | : Chi ² = 0 |).84, df | = 3 (P = | 0.84), 12 | = 0% | | | 1 avouro moraconini 1 avouro 1 idoebo |

^{*}Dollins 1994: SEM converted to SD

Figure S327. Melatonin vs Placebo (Sleep Latency (min), self-report) [CMT= 20 min] RCT (Healthy participants)

| | M | lelatonin | | F | Placebo | | | Mean Difference | Mean Difference |
|-----------------------------------|-----------|---------------|-----------------|-----------|-------------------|--------|----------------|--|---------------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| 14.79.1 Lab study (0. | .1 mg) | | | | | | | | |
| Dollins 1994 Subtotal (95% CI) | 12.95 | 9.2573 | 20 20 | 20.55 | 4.9864 | 5 5 | 22.0% 22.0% | -7.60 [-13.56, -1.64] - 7.60 [- 13.56 , - 1.64] | • |
| Heterogeneity: Not ap | plicable | 10 | | | | | | | |
| Test for overall effect: | Z = 2.50 | P = 0.0 | 1) | | | | | | |
| 14.79.2 Lab study (0. | .3 mg) | | | | | | | | |
| Dollins 1994 | 9.95 | 7.5579 | 20 | 20.55 | 4.9864 | 5 | 26.0% | -10.60 [-16.08, -5.12] | - |
| Subtotal (95% CI) | | | 20 | | | 5 | 26.0% | -10.60 [-16.08, -5.12] | • |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z = 3.79 | 9 (P = 0.0 | 002) | | | | | | |
| 14.79.3 Lab Study (1 | mg) | | | | | | | | |
| Dollins 1994 | 7.28 | 5.9479 | 20 | 20.55 | 4.9864 | 5 | | -13.27 [-18.36, -8.18] | ± |
| Subtotal (95% CI) | | | 20 | | | 5 | 30.1% | -13.27 [-18.36, -8.18] | • |
| Heterogeneity: Not ap | • | | | | | | | | |
| Test for overall effect: | Z= 5.11 | (P < 0.0 | 0001) | | | | | | |
| 14.79.4 Lab Study (1 | 0 mg) | | | | | | | | |
| Dollins 1994 | 9.9 | 9.2573 | 20 | 20.55 | 4.9864 | 5 | 22.0% | -10.65 [-16.61, -4.69] | |
| Subtotal (95% CI) | | | 20 | | | 5 | 22.0% | -10.65 [-16.61, -4.69] | • |
| Heterogeneity: Not ap | oplicable | | | | | | | | |
| Test for overall effect: | Z = 3.50 |) (P = 0.0 | 005) | | | | | | |
| Total (95% CI) | | | 80 | | | 20 | 100.0% | -10.76 [-13.55, -7.96] | • |
| Heterogeneity: Tau ² = | 0.00; C | $hi^2 = 2.02$ | df = 3 | (P = 0.5) | $57); I^2 = 0$ | % | | | -20 -10 0 10 20 |
| Test for overall effect: | Z = 7.55 | 6 (P < 0.0 | 0001) | | | | | | Favours Melatonin Favours Placebo |
| Test for subgroup diff | ferences | $: Chi^2 = 2$ | .02, df | = 3 (P = | 0.57), I^2 : | = 0% | | | 1 Ground Michaelmin 1 Ground 1 Iacebo |

^{*}Dollins 1994: SEM converted to SD

Favours Placebo Favours Melatonin

Melatonin Placebo Mean Difference Mean Difference SD Total Mean SD Total Weight IV, Random, 95% CI IV, Random, 95% CI Study or Subgroup Mean 14.74.1 Lab Study (1 mg) Satomura 2001 89.3 12.5 77.1 16.1 2 11.2% 12.20 [-11.96, 36.36] Subtotal (95% CI) 2 11.2% 12.20 [-11.96, 36.36] Heterogeneity: Not applicable Test for overall effect: Z = 0.99 (P = 0.32) 14.74.5 Lab Study (3 mg) Satomura 2001 2 12.4% 15.70 [-6.98, 38.38] 92.8 5.5 77.1 16.1 Subtotal (95% CI) 12.4% 15.70 [-6.98, 38.38] Heterogeneity: Not applicable Test for overall effect: Z = 1.36 (P = 0.17) 14.74.8 Lab Study (5 mg) Diik 1995 95.1 2.8 93.4 3.1 59.4% 1.70 [-1.19, 4.59] Subtotal (95% CI) 59.4% 1.70 [-1.19, 4.59] Heterogeneity: Not applicable Test for overall effect: Z = 1.15 (P = 0.25) 14.74.9 Lab Study (6 mg) Satomura 2001 94.1 3.6 77.1 16.1 17.1% 17.00 [-1.41, 35.41] Subtotal (95% CI) 17.1% 17.00 [-1.41, 35.41] Heterogeneity: Not applicable Test for overall effect: Z = 1.81 (P = 0.07) Total (95% CI) 15 100.0% 7.22 [-1.68, 16.12] Heterogeneity: Tau² = 32.53; Chi² = 4.59, df = 3 (P = 0.20); I² = 35% -50 50 -25 25 Test for overall effect: Z = 1.59 (P = 0.11)

Figure S328. Melatonin vs Placebo (Sleep Efficiency (%), PSG) [CMT= 10%] RCT (Healthy participants)

Ramelteon

Summary of Findings (GRADE)

Table S31. Ramelteon in adults with shiftwork disorder

Test for subgroup differences: Chi² = 4.59, df = 3 (P = 0.20), I^2 = 34.7%

| References: Markwald 2010 | | | |
|---|-----------------------------------|--|---------------------------------|
| Outcomes [Tool] | Certainty of the evidence (GRADE) | Absolute Difference Ramelteon vs Control | No of Participants (studies) |
| Excessive sleepiness or alertness [Percent wakefulness] | ⊕⊕⊖⊖ LOW ^{a,b,c} | The mean difference in the ramelteon group was 16.2 percent lower (31.95 lower to 0.45 lower) compared to control | 28 (1 RCT) |
| Total sleep time | ⊕⊕⊜⊖ | The mean difference in the ramelteon group was 43.2 minutes higher (5.05 higher to 81.35 higher) compared to control | 28 |
| [EEG] | LOW ^{a,b,d} | | (1 RCT) |
| Total sleep time | ⊕⊕⊜⊜ | The mean difference in the ramelteon group was 76 minutes higher (25.75 higher to 126.25 higher) compared to control | 28 |
| [Sleep log] | LOW ^{a,b} | | (1 RCT) |
| WASO | ⊕⊕⊖⊖ | The mean difference in the melatonin group was 36.50 minutes lower (72.54 lower to 0.46 lower) compared to control | 28 |
| [EEG] | LOW ^{a,b,d} | | (1 RCT) |
| Sleep latency | ⊕⊕⊖⊖ | The mean difference in the melatonin group was 1.6 minutes lower (4.66 lower to 1.46 higher) compared to control | 28 |
| [EEG] | LOW ^{a,b,d} | | (1 RCT) |

- a. Indirectness is due to the fact that participants included in the studies are healthy individuals. The effect in adults with SWD may be different
- b. Imprecision due to small sample size (<200 participants)
- c. Wide confidence intervals
- d. Confidence interval crosses the CMT

Table S32. Ramelteon in adults with shiftwork disorder

| Study Citation | Study Design | Number of Participants (% Female) | Age in years | Population | Intervention (dose) | Comparator | Time of Intervention Delivery | Duration of Follow- up |
|----------------|----------------|---|-----------------|----------------------|---------------------|------------|--|---------------------------------|
| Markwald 2010 | RCT, crossover | 14 (36) | 23.2 ± 4.2 | Healthy participants | Ramelteon (8 mg) | Placebo | 2 h prior to a 4-h daytime sleep opportunity. | 1 day |

Critical Outcomes

None

Important Outcomes

Figure S329. Sleep Promoting medication (Ramelteon) vs Placebo (Total Sleep Time, EEG) [CMT= 15 min] RCT (Healthy participants)

| | Experimental | | Pla | acebo | | Mean Difference | | Mean Difference | | | | |
|-------------------|--------------|------|-------|-------|------|-----------------|---------------------|-----------------|-------------|-----------|-----------------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV | Fixed, 95 | % CI | |
| Markwald 2010 | 193.9 | 40.4 | 14 | 150.7 | 60.6 | 14 | 43.20 [5.05, 81.35] | | 10 | | | |
| | | | | | | | | -100 | -50 | o o | 50 | 100 |
| | | | | | | | | | Favours Pla | cebo Fa | vours Ramelteor | n |

^{*} Markwald 2010: SEM converted to SD

Figure S330. Sleep Promoting medication (Ramelteon) vs Placebo (Total Sleep Time, Subjective Sleep Log) [CMT= 15 min] RCT (Healthy participants)

| | Experimental Placebo | | | | | | Mean Difference | | Mea | n Difference |
|-------------------|----------------------|------|-------|-------|------|-------|---------------------------------------|-------|-----------|-----------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, F | ixed, 95% CI |
| Markwald 2010 | 177.5 | 76.7 | 14 | 101.5 | 57.6 | 14 | 76.00 [25.75, 126.25] | 9.3 | 9.4 | |
| | | | | | | | · · · · · · · · · · · · · · · · · · · | -100 | -50 | 0 50 100 |
| | | | | | | | | Favou | urs Place | ebo Favours Ramelteon |

^{*} Markwald 2010: SEM converted to SD

Figure S331. Sleep Promoting medication (Ramelteon) vs Placebo (WASO, EEG) [CMT=20 min] RCT (Healthy participants)

| | | | Pla | acebo | | Mean Difference | Mean Difference | | | |
|-------------------|------|------|-------|-------|------|-----------------|------------------------|--|--|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | | |
| Markwald 2010 | 45.7 | 35.9 | 14 | 82.2 | 58.7 | 14 | -36.50 [-72.54, -0.46] | - t | | |
| | | | | | | | a a a a a a | -100 -50 0 50 100 Favours Ramelteon Favours Placebo | | |

^{*} Markwald 2010: SEM converted to SD

Figure S332. Sleep Promoting Medication (Ramelteon) vs Control (Wakefulness during sleep opportunity, Percent Wakefulness) [CMT=10%] RCT (Healthy participants)

| | Expe | erimen | tal | Pla | acebo | | Mean Difference | | | Mean Di | fference | |
|-------------------|------|--------|-------|------|-------|-------|------------------------|------|------------|------------|-----------------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | | IV, Fixed | I, 95% CI | |
| Markwald 2010 | 21 | 16.1 | 14 | 37.2 | 25.4 | 14 | -16.20 [-31.95, -0.45] | | - | - | | |
| | | | | | | | | -100 | -50 | annyte e i | 50 | 100 |
| | | | | | | | | | Favours Ra | amelteon | Favours Placebo | |

^{*}Markwald 2010: SEM converted to SD, % wakefulness is expressed relative to the 240-minute sleep opportunity recording time (RT)

Figure S333. Sleep Promoting medication (Ramelteon) vs Placebo (Sleep Latency, PSG) [CMT= 20 min] RCT (Healthy participants)

| | Exp | erimenta | al | Pla | acebo | | Mean Difference | | Mean D | ifference | |
|-------------------|------|----------|-------|------|-------|-------|---------------------|-----|-------------------|-----------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixe | d, 95% CI | |
| Markwald 2010 | 6.5 | 3.7417 | 14 | 8.1 | 4.49 | 14 | -1.60 [-4.66, 1.46] | | | _ | |
| | | | | | | | | -10 | -5 | 0 5 | 10 |
| | | | | | | | | | Favours Ramelteon | Favours Placebo | |

^{*} Markwald 2010: SEM converted to SD

Suvorexant

Summary of Findings (GRADE)

Table S33. Suvorexant in adults with shiftwork disorder

| References: Zeitzer 2020 | | | |
|--|-----------------------------------|---|------------------------------|
| Outcomes [Tool] | Certainty of the evidence (GRADE) | Absolute Difference Suvorexant vs Control | No of Participants (studies) |
| Sleep Quality [Subjective sleep quality score] | ⊕⊕⊕⊜ MODERATEª | The mean difference in the suvorexant group was 0.97 points higher (0.27 higher to 1.67 higher) compared to control | 22 (1 RCT) |
| Total Sleep Time [Actigraphy] | ⊕⊕⊕○ MODERATE ^a | The mean difference in the suvorexant group was 201.6 minutes higher (139.96 higher to 263.24 higher) compared to control | 22 (1 RCT) |
| Total Sleep Time [Subjective Report] | ⊕⊕⊕⊜ MODERATEª | The mean difference in the suvorexant group was 172.8 minutes higher (108.36 higher to 237.24 higher) compared to control | 22 (1 RCT) |
| Sleep Latency [Subjective Report] | ⊕⊕⊜⊜ LOW ^{a,b} | The mean difference in the suvorexant group was 22.96 minutes fewer (34.21 fewer to 11.71 fewer) compared to control | 22 (1 RCT) |
| Disease Severity [CGI-S] | ⊕⊕⊜⊝ LOW ^{a,b} | The mean difference in the suvorexant group was 1.9 points lower (3.4 lower to 0.4 lower) compared to control | 22 (1 RCT) |

- a. Imprecision due to small sample size (<200 participants)
- b. Confidence intervals cross the critical significance threshold

Table S34. Suvorexant in adults with shiftwork disorder

| Study Citation | Study Design | Number of Participants (% Female) | Age in years | Population | Intervention (dose) | Comparator | Time of Intervention Delivery | Duration of Follow- up |
|-------------------|-----------------|---|-----------------|---|-------------------------|------------|--|---------------------------|
| Zeitzer 2020 | RCT | 13 (42) | 37.7 (11.1) | Shift workers without SWD diagnosis | Suvorexant 10 or 20 mg) | Placebo | before each daytime sleep episode | 3 weeks |

Critical Outcomes

Figure S334. Sleep Promoting Medication (Suvorexant) vs Control (Sleep Quality, Subjective Sleep Quality Score) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)

| | Expe | erimen | tal | PI | acebo | | - 1 | Mean Difference | Mean Dit | ference |
|-----------------------------------|----------|----------------------|---------|----------------|---------|-------------|--------|--------------------|------------------|--------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed | , 95% CI |
| 14.47.1 10 mg | | | | | | | | | | |
| Zeitzer 2020 | 0.4 | 0.48 | 11 | 0.09 | 0.5 | 11 | 74.6% | 0.31 [-0.10, 0.72] | - | |
| Subtotal (95% CI) | | | 11 | | | 11 | 74.6% | 0.31 [-0.10, 0.72] | + | • |
| Heterogeneity: Not ap | plicable | | | | | | | | | |
| Test for overall effect: | Z = 1.48 | (P = 0 | 0.14) | | | | | | | |
| 14.47.2 20 mg | | | | | | | | | | |
| Zeitzer 2020 | 0.75 | 0.85 | 11 | -0.22 | 0.83 | 11 | 25.4% | 0.97 [0.27, 1.67] | | - |
| Subtotal (95% CI) | | | 11 | | | 11 | 25.4% | 0.97 [0.27, 1.67] | | • |
| Heterogeneity: Not ap | plicable | | | | | | | | | |
| Test for overall effect: | Z = 2.71 | (P = 0) |).007) | | | | | | | |
| Total (95% CI) | | | 22 | | | 22 | 100.0% | 0.48 [0.12, 0.83] | <i>y</i> | * |
| Heterogeneity: Chi ² = | 2.53, df | = 1 (P | = 0.11) | $ ^2 = 61$ | % | | | | 1, 1 | |
| Test for overall effect: | Z = 2.65 | (P = 0) | (800.0 | | | | | | -4 -2 L | Favours Suvorexant |
| Test for subgroup dif | ferences | : Chi ² : | = 2.53, | df = 1 (F | P = 0.1 | 1), $I^2 =$ | 60.5% | | l'avours Control | ravours Suvorexam |

^{*} Zeitzer 2020, Subjective sleep quality score: 5-point Likert-like scale (with 1 indicating very poor and 5, very good), change from baseline data presented, data extracted from graph

Important Outcomes

Figure S335. Sleep Promoting medication (Suvorexant) vs Placebo (Total Sleep Time, Actigraphy) [CMT= 15 min] RCT (Shift workers without SWD diagnosis)

| _ | • | | | | | | | • | |
|-----------------------------------|----------|---------|---------|--------------------|---------|---------|--------|-------------------------|--|
| | Expe | erimen | ital | PI | acebo | | | Mean Difference | Mean Difference |
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 14.50.1 10 mg | | | | | | | | | |
| Zeitzer 2020 | 108.6 | 96.6 | 11 | -35.4 | 69.6 | 11 | 43.4% | 144.00 [73.64, 214.36] | |
| Subtotal (95% CI) | | | 11 | | | 11 | 43.4% | 144.00 [73.64, 214.36] | |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z = 4.01 | (P < 0 |).0001) | | | | | | |
| 14.50.2 20 mg | | | | | | | | | |
| Zeitzer 2020 | 143.4 | 64.2 | 11 | -58.2 | 82.2 | 11 | 56.6% | 201.60 [139.96, 263.24] | |
| Subtotal (95% CI) | | | 11 | | | 11 | 56.6% | 201.60 [139.96, 263.24] | • |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z= 6.41 | (P < 0 | 0.00001 |) | | | | | |
| Total (95% CI) | | | 22 | | | 22 | 100.0% | 176.59 [130.23, 222.95] | • |
| Heterogeneity: Chi ² = | 1.46, df | = 1 (P | = 0.23) | $ \cdot ^2 = 31$ | % | | | | |
| Test for overall effect: | Z = 7.47 | '(P < 0 | 0.00001 |) | | | | | -200 -100 0 100 200 Favours Control Favours Suvorexant |
| Test for subgroup diff | erences | : Chi²: | = 1.46. | df = 1 (F | 0 = 0.2 | 3), I²= | 31.3% | | ravours Control Favours Suvorexant |

^{*}Zeitzer 2020, One participant in the suvorexant and 1 participant in the placebo treatment groups were excluded from actigraphy-based sleep analyses owing to data loss, data converted from hours to minutes, change from baseline data presented, data extracted from graph

Figure S336. Sleep Promoting medication (Suvorexant) vs Placebo (Total Sleep Time, Sleep Log) [CMT= 15 min] RCT (Shift workers without SWD diagnosis)

| | Expe | eriment | tal | PI | acebo | | | Mean Difference | Mean Difference |
|---|----------|----------|----------|------|-------|----------|------------------------|--|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 14.49.1 10 mg | | | | | | | | | 1 |
| Zeitzer 2020 Subtotal (95% CI) | 69 | 106.2 | 11 11 | -45 | 135 | 11 11 | 28.7% 28.7% | 114.00 [12.49, 215.51] 114.00 [12.49, 215.51] | |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z = 2.20 | (P = 0. | 03) | | | | | | |
| 14.49.2 20 mg | | | | | | | | | |
| Zeitzer 2020 Subtotal (95% CI) | 133.8 | 52.8 | 11 11 | -39 | 95.4 | 11 11 | 71.3% 71.3 % | 172.80 [108.36, 237.24] 172.80 [108.36, 237.24] | - |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z= 5.26 | (P < 0. | 00001) | | | | | | |
| Total (95% CI) | | | 22 | | | 22 | 100.0% | 155.91 [101.51, 210.31] | • |
| Heterogeneity: Chi ² = Test for overall effect: Test for subgroup diff | Z = 5.62 | (P < 0.1 | 00001) | | | \ IZ _ O | ov | ® | -200 -100 0 100 200 Favours Control Favours Suvorexant |

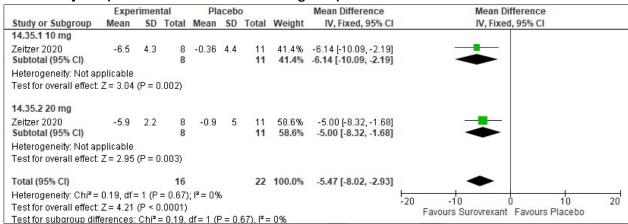
^{*}Zeitzer 2010, data converted from hours to minutes, change from baseline data presented, data extracted from graph

Figure S337. Sleep Promoting medication (Suvorexant) vs Placebo (Disease Severity, CGI-S) [CMT= 1 point] RCT (Shift workers without SWD diagnosis)

| | Expe | rimen | tal | Pla | cebo |) | | Mean Difference | Mean Difference |
|-------------------------|-----------|--------------------|---------|---------------|--------|-----------------------|--------|----------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 14.34.1 10 mg | | | | | | | | | |
| Zeitzer 2020 | 3.4 | 0.9 | 8 | 3.6 | 0.8 | 11 | 78.5% | -0.20 [-0.98, 0.58] | - |
| Subtotal (95% CI) | | | 8 | | | 11 | 78.5% | -0.20 [-0.98, 0.58] | • |
| Heterogeneity: Not ap | pplicable | | | | | | | | |
| Test for overall effect | Z = 0.50 | (P = 0) | 1.62) | | | | | | |
| 14.34.2 20 mg | | | | | | | | | |
| Zeitzer 2020 | 2.1 | 1.6 | 8 | 4 | 1.7 | 11 | 21.5% | -1.90 [-3.40, -0.40] | - |
| Subtotal (95% CI) | | | 8 | | | 11 | 21.5% | -1.90 [-3.40, -0.40] | • |
| Heterogeneity: Not ap | pplicable | | | | | | | | |
| Test for overall effect | Z = 2.49 | (P = 0 | 0.01) | | | | | | |
| Total (95% CI) | | | 16 | | | 22 | 100.0% | -0.57 [-1.26, 0.13] | • |
| Heterogeneity: Chi²= | 3.89, df= | = 1 (P | = 0.05) | $ 1^2 = 74 $ | % | | | | 140 1 |
| Test for overall effect | Z = 1.60 | (P = 0 |).11) | | | | | | -10 -5 0 5 Favours Surovrexant Favours Placebo |
| Test for subaroup dif | ferences: | Chi ² : | = 3.89. | df = 1 (F | 0 = 0. | 05), l ^z = | 74.3% | | ravours suroviexant Favours Flacebo |

^{*}Zeitzer 2020, SD calculated from median and IQR

Figure S338. Sleep Promoting medication (Suvorexant) vs Placebo (Mental Health, CES-D) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)



^{*}Zeitzer 2020, data reported as change score

Figure S339. Sleep Promoting medication (Suvorexant) vs Placebo (Sleep Latency, Patient reported sleep logs) [CMT= 20 min] RCT (Shift workers without SWD diagnosis)

| | Expe | eriment | al | P | lacebo | | | Mean Difference | Mean Difference | |
|-----------------------------------|-----------|--------------------|----------|--------------------|----------|--------------|--------|-------------------------|---|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI | |
| 14.48.1 10 mg | | | | | | | | | 4 | |
| Zeitzer 2020 | -17.71 | 28.93 | 11 | -7.63 | 19.41 | 11 | 23.0% | -10.08 [-30.67, 10.51] | | |
| Subtotal (95% CI) | | | 11 | | | 11 | 23.0% | -10.08 [-30.67, 10.51] | | |
| Heterogeneity: Not ap | plicable | | | | | | | | | |
| Test for overall effect: | Z = 0.96 | (P = 0.3) | 34) | | | | | | | |
| 14.48.2 20 mg | | | | | | | | | | |
| Zeitzer 2020 | -24.8 | 18.67 | 11 | -1.84 | 3.73 | 11 | 77.0% | -22.96 [-34.21, -11.71] | | |
| Subtotal (95% CI) | | | 11 | | | 11 | 77.0% | -22.96 [-34.21, -11.71] | - | |
| Heterogeneity: Not ap | plicable | | | | | | | | | |
| Test for overall effect: | Z = 4.00 | (P < 0.0 | 0001) | | | | | | | |
| Total (95% CI) | | | 22 | | | 22 | 100.0% | -20.00 [-29.87, -10.12] | • | |
| Heterogeneity: Chi ² = | 1.16, df= | = 1 (P = | 0.28); | ² = 14% | | | | | 1 | _ |
| Test for overall effect: | Z = 3.97 | (P < 0.0 | 0001) | | | | | | -50 -25 0 25 Favours Suvorexant Favours Control | 5 |
| Test for subgroup diff | ferences: | Chi ² = | 1.16. dt | = 1 (P = | = 0.28). | $I^2 = 13$. | 6% | | FAVOUIS SUVUIEXAIIL FAVOUIS COIIIIOI | |

^{*}Zeitzer 2010, data converted from hours to minutes, change from baseline data presented, data extracted from graph

Triazolam

Summary of Findings (GRADE)

Table S35. Triazolam in adults with shiftwork disorder

References: Seidel 1986, Stomura 2001, Walsh 1991, Walsh 1998

| Outcomes [Tool] | Certainty of the evidence (GRADE) | Absolute Difference Ramelteon vs Control | No of Participants (studies) |
|-----------------------------|-----------------------------------|---|---------------------------------|
| Excessive Sleepiness [MSLT] | ⊕⊕⊕⊜ MODERATEª | The mean difference in the triazolam group was 1.01 minutes more (0.44 more to 1.58 more) compared to control | 240 (4 RCTs) |
| Excessive Sleepiness [RTSW] | ⊕○○○ VERY LOW ^{a,b,c} | The mean difference in the triazolam group was 1.19 minutes more (4.82 fewer to 7.21 more) compared to control | 12 (1 RCT) |

| Sleep Quality | ФООО | The mean difference in the triazolam group was 0.8 points | 12 |
|----------------------------|-----------------|---|---------|
| [Subjective Questionnaire] | VERY LOWa,b,c,d | more (0.24 fewer to 1.84 more) compared to control | (1 RCT) |

- a. Indirectness is due to the fact that participants included in the studies are healthy individuals. The effect in adults with SWD may be different
- b. Imprecision due to small sample size (<200 participants)
- c. Confidence intervals cross the line of no effect
- d. Lack of blinding of participants and personnel

Table S36. Triazolam in adults with shiftwork disorder

| Study Citation | Study Design | Number of Participants (% Female) | Age in years | Population | Intervention (dose/) | Comparator | Time of Intervention Delivery | Duratio n of Follow- up |
|-------------------|-------------------|---|----------------------------------|----------------------|----------------------------|------------|--|----------------------------------|
| Satomura 2001 | RCT, crossover | 7 (0) | 23.7 ± 1.7 | Healthy participants | Triazolam (0.125 mg) | Placebo | 13:30 | 1 day |
| Seidel 1986 | RCT, crossover | 48 | 24.3 ± 3.4 to 26.6 ± 4.6 | Healthy participants | Triazolam (0.25 or 0.5 mg) | Placebo | 30 minutes before bedtime | 2 days |
| Walsh 1988 | RCT, crossover | 18 (56) | 23.2 | Healthy participants | Triazolam (0.25 -0.5 mg) | Placebo | 30 min prior to sleep periods 1 through 4 during one tour | 6 nights |
| Walsh 1991 | RCT, crossover | 15 (73) | 41.1 | Healthy participants | Triazolam (0.25 mg) | Placebo | before the first sleep period of both tours | 2 weeks |

Critical Outcomes

Figure S340. Sleep Promoting Medication (Triazolam) vs Control (Excessive Sleepiness, MLST) [CMT= 1 minute] RCT (Healthy participants)

| | Tria | azolan | n | PI | acebo | | | Mean Difference | Mean Difference |
|---|-----------------|----------------------|-----------------|-----------|---------|---------------------|----------------|--|---------------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| 14.3.1 0.25 mg Triaz | olam | | | | | | | | |
| Seidel 1986 Subtotal (95% CI) | 9.9 | 1.9 | 48 48 | 9.5 | 3.2 | 48 48 | 29.0% 29.0% | 0.40 [-0.65, 1.45] 0.40 [-0.65, 1.45] | * |
| Heterogeneity: Not ap | oplicable | | | | | | | | |
| Test for overall effect: | Z = 0.74 | P = 0 | 0.46) | | | | | | |
| 14.3.2 0.5 mg Triazo | lam | | | | | | | | |
| Seidel 1986 | 12.1 | 4.8 | 48 | 10.3 | 3.6 | 48 | 11.1% | 1.80 [0.10, 3.50] | |
| Walsh 1991 Subtotal (95% CI) | 9.68 | 4.82 | 6 54 | 8.248 | 4.28 | 6 54 | 1.2% 12.3% | 1.43 [-3.73, 6.59] 1.76 [0.15, 3.38] | • |
| Heterogeneity: Tau ² = Test for overall effect: | | | | = 1 (P = | 0.89); | l² = 0% | | | |
| 14.3.3 0.25 mg- 0.5 r | | | , | | | | | | |
| Walsh 1988 | _ | 1.25 | 18 | 10.45 | 1 | 18 | 58.7% | 1.15 [0.41, 1.89] | - |
| Subtotal (95% CI) | | 1.20 | 18 | 10.40 | | 18 | 58.7% | 1.15 [0.41, 1.89] | • |
| Heterogeneity: Not as | oplicable | 10 | | | | | | | |
| Test for overall effect | Z = 3.05 | 6 (P = 0 | 0.002) | | | | | | |
| Total (95% CI) | | | 120 | | | 120 | 100.0% | 1.01 [0.44, 1.58] | ◆ |
| Heterogeneity: Tau² = | = 0.00; C | hi² = 2. | .29, df= | = 3 (P = | 0.52); | l ² = 0% | | | -10 -5 0 5 1 |
| Test for overall effect: | Z = 3.49 | P = 0 | 0.0005) | | | | | | Favours Placebo Favours Triazolam |
| Test for subgroup dif | <u>ferences</u> | : Chi ² : | = 2.27. | df = 2 (l | P = 0.3 | 2), $ z = 1$ | 11.8% | | vaiv i ideas i i arvaiv i iliazoidiii |

*Walsh 1988-averaged across Sleep periods 1-4, 0.5 mg Triazolam (listed in the Walsh 1991 paper); Walsh 1991- MSLT averaged across the nights, participants received 0.25 mg on night one, dose was increased for subsequent nights if TST was <7 hours

Figure S341. Sleep Promoting Medication (Triazolam) vs Control (Excessive Sleepiness, RTSW) [CMT= 2 minutes] RCT (Healthy participants)

| | Tria | zolam | 1 | Pla | cebo |) | Mean Difference | | Mean Di | fference | | |
|------------------------|-----------|-------|-------|-------|------|-------|--------------------|-----|-----------------|-----------|----------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed | , 95% CI | | |
| 14.4.1 0.25 mg - 0.5 i | mg Triazo | lam | | | | | | | | 8 | | |
| Walsh 1991 | 13.304 | 5.12 | 6 | 12.11 | 5.5 | 6 | 1.19 [-4.82, 7.21] | | - | 1 | | |
| | | | | | | | | | Ti . | | 13 | |
| | | | | | | | | -10 | -5 (|) | 5 | 10 |
| | | | | | | | | | Favours Placebo | Favours T | riazolam | |

^{*} Walsh 1991- RTSW averaged across the nights, participants received 0.25 mg on night one, dose was increased for subsequent nights if TST was <7 hours

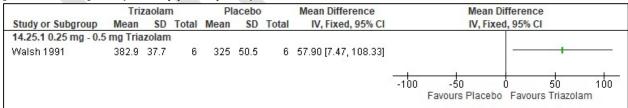
Figure S342. Sleep Promoting Medication (Triazolam) vs Control (Sleep Quality, Subjective Questionnaire) [CMT = Not Established] RCT (Healthy participants)

| Study or Subgroup Mean SD Total IV, Fixed, 95% CI IV, Fixed, 95% CI 14.6.1 0.25 mg - 0.5 mg Triazolam Walsh 1991 5.2 0.7 6 4.4 1.1 6 0.80 [-0.24, 1.84] ———————————————————————————————————— | | Tria | zolar | n | Pla | cebo |) | Mean Difference | | Mean Dif | ference | |
|--|------------------------|----------|-------|-------|------|------|-------|--------------------|----|----------------|-----------|----------|
| | Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed | , 95% CI | |
| Walsh 1991 5.2 0.7 6 4.4 1.1 6 0.80 [-0.24, 1.84] | 14.6.1 0.25 mg - 0.5 r | ng Triaz | olam | | | | | | | | | |
| | Walsh 1991 | 5.2 | 0.7 | 6 | 4.4 | 1.1 | 6 | 0.80 [-0.24, 1.84] | | - | - | |
| | | | | | | | | | | | - 1 | - |
| | | | | | | | | | Fa | avours Placebo | Favours T | riazolam |

^{*}Walsh 1991, 2 = extremely bad; 7 = extremely good, participants received 0.25 mg on night one, dose was increased for subsequent nights if TST was <7 hours

Important Outcomes

Figure S343. Sleep Promoting medication (Triazolam) vs Placebo (Total Sleep Time, Subjective Report) [CMT= 15 min] RCT (Healthy participants)



^{*}Walsh 1991, participants received 0.25 mg on night one, dose was increased for subsequent nights if TST was <7 hours

Figure S344. Sleep Promoting medication (Triazolam) vs Placebo (Total Sleep Time, PSG) [CMT=15 min] RCT (Healthy participants)

| | Tria | zolam | ľ | PI | acebo | | | Mean Difference | Mean Difference |
|------------------------------------|------------|--------------------|-----------------|-------------|--------|-----------------|------------------------|--|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 14.24.1 0.125 mg Tria | azolam | | | | | | | | |
| Satomura 2001 Subtotal (95% CI) | 170.7 | 7.3 | 7 7 | 138.9 | 29.2 | 7 7 | 77.3% 77.3 % | 31.80 [9.50, 54.10] 31.80 [9.50, 54.10] | - |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z = 2.80 (| P = 0. | 005) | | | | | | |
| 14.24.2 0.5 mg Triazo | olam | | | | | | | | |
| Walsh 1988 Subtotal (95% CI) | 448.01 | 53.6 | 18 18 | 398.4 | 71 | 18 18 | 22.7% 22.7% | 49.61 [8.51, 90.71] 49.61 [8.51, 90.71] | |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | | P = 0. | 02) | | | | | | |
| Total (95% CI) | | | 25 | | | 25 | 100.0% | 35.85 [16.25, 55.45] | • |
| Heterogeneity: Chi ² = | 0.56, df= | 1 (P= | 0.46); | $I^2 = 0\%$ | | | | | 100 20 10 |
| Test for overall effect: | Z = 3.59 (| P = 0. | 0003) | | | | | | -100 -50 0 50 10 Favours Placebo Favours Triazolam |
| Test for subgroup diff | erences: | Chi ² = | 0.56, d | f=1 (P | = 0.46 |), $I^2 = 0$ | % | | Favours Flacebo Favours Illazoralli |

^{*}Walsh 1988-averaged across Sleep periods 1-4, participants received 0.5 mg Triazolam; Satomura 2001, 0.125 mg Triazolam

Figure S345. Sleep Promoting medication (Triazolam) vs Placebo (WASO, PSG) [CMT= 20 min] RCT (Healthy participants)

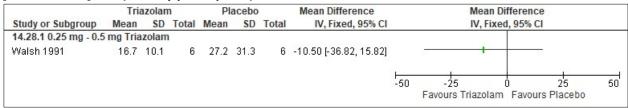
| | Tria | zola | m | PI | acebo | | Mean Difference | Mean Di | | ence | |
|----------------------|--------|------|-------|------|-------|-------|-----------------------|-------------------|------------------------|---------------------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 95 | % CI | |
| 14.29.1 0.125 mg Tri | azolam | | | | | | | | 1 | | |
| Satomura 2001 | 5.7 | 5.3 | 6 | 25.3 | 31.9 | 6 | -19.60 [-45.47, 6.27] | | - | | |
| | | | | | | | | 1 | | | |
| | | | | | | | | -100 -5 Favour | i0 Ö s Triazolam Fa | 50 vours Placebo | 100 |

Figure S346. Sleep Promoting medication (Triazolam) vs Placebo (Sleep Latency, PSG) [CMT= 20 min] RCT (Healthy participants)

| Tria | zolar | n | Pla | cebo | 0 | Mean Difference | Mean Difference |
|--------|----------------|-------------------|--------|---------------------------|------------------------------|------------------------------------|---|
| Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| azolam | | | | | | | |
| 4.8 | 1.8 | 7 | 12 | 5.3 | 7 | -7.20 [-11.35, -3.05] | - |
| | | | | | | _ | |
| | | | | | | | -20 -10 0 10 20 Favours Triazolam Favours Placebo |
| | Mean azolam | Mean SD azolam | azolam | Mean SD Total Mean azolam | Mean SD Total Mean SD azolam | Mean SD Total Mean SD Total azolam | Mean SD Total Mean SD Total IV, Fixed, 95% CI azolam |

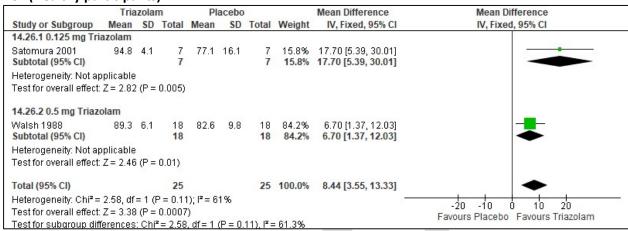
^{*}Satomura 2001, 0.125 mg Triazolam

Figure S347. Sleep Promoting medication (Triazolam) vs Placebo (Sleep Latency, Subjective Report) [CMT= 20 min] RCT (Healthy participants)



^{*}Walsh 1991, participants received 0.25 mg on night one, dose was increased for subsequent nights if TST was <7 hours

Figure S348. Sleep Promoting medication (Triazolam) vs Placebo (Sleep Efficiency, PSG) [CMT= 10%] RCT (Healthy participants)



^{*}Walsh 1988: averaged across Sleep periods 1-4, participants received 0.5 mg Triazolam; Satomura 2001, 0.125 mg Triazolam

Bright light during the night shift

Summary of Findings (GRADE)

Table S37. Phase shift bright light in adults with shiftwork disorder

References: Bjorvatn 2007, Bjorvatn 1999, Horowitz 2001, Campbell 1995, Costa 1995, Rizza 2022, Smith 2008, Dawson 1991

| Outcomes [Tool] | Certainty of the evidence (GRADE) | Absolute Difference Bright light vs Control | No of Participants (studies) |
|---|-------------------------------------|--|-----------------------------------|
| Excessive Sleepiness [KSS] | ⊕○○○ VERY LOW ^{a,b,c} | The mean difference in the bright light group was 0.32 points fewer (1 fewer to 0.35 more) compared to control | 34 (1 RCT) |
| Excessive Sleepiness [KSS] | ⊕○○○ VERY LOW ^{a,b,c} | The mean difference in the bright light group was 0.62 points fewer (1.71 fewer to 0.46 more) compared to control | 14 (1 non-randomized study) |
| Excessive Sleepiness [VAS, Alertness] | ⊕○○○ VERY LOW ^{a,b,c,d} | The mean difference in the bright light group was 5.51 higher (7.33 lower to 18.35 higher) compared to control | 27 (1 RCT) |
| Excessive Sleepiness [RTSW] | ⊕○○○ VERY LOW ^{b,c,d} | The mean difference in the bright light group was 2.25 minutes more (0.28 fewer to 4.79 more) compared to control | 51 (2 RCTs) |
| Excessive Sleepiness [Fatigue Ratings] | ⊕○○○ VERY LOW ^{b,c} | The mean difference in the bright light group was 0.9 higher (3.14 lower to 4.94 higher) compared to control | 30 (1 non-randomised study) |
| Sleep Quality [VAS-sleep quality] | ⊕○○○ VERY LOW ^{a,b,c} | The mean difference in the bright light group was 0 (0.49 lower to 0.49 higher) compared to control | 34 (1 RCT) |
| Sleep Quality [VAS-sleep quality] | ⊕○○○ VERY LOWa,b,c | The mean difference in the bright light group was 0 (0.31 lower to 0.31 higher) compared to control | 14 (1 non-randomised study) |
| Sleep Quality [PSQI (number of participants with score 1-4)] | ⊕○○○ VERY LOW ^{a,b,c} | The risk ratio in the bright light group was 1.04 (0.22 to 5.01) with an absolute risk of 9 more per 1,000 (173 fewer to 891 more) compared to control | 22 (1 RCT) |
| Sleep Quality [PSQI (number of participants with score 5-21)] | ⊕○○○ VERY LOW ^{a,b,c} | The risk ratio in the bright light group was 1.15 (0.67 to 2.00) with an absolute risk of 100 more per 1,000 (220 fewer to 667 more) compared to control | 22 (1 RCT) |

| Cognitive Performance [SALT (% Correct)] | ⊕○○○ VERY LOW ^{b,c,d} | The mean difference in the bright light group was 0.81 percent lower (7.41 lower to 5.79 higher) compared to control | 26 (1 RCT) |
|--|-----------------------------------|---|---------------|
| Cognitive Performance | ФООО | The mean difference in the bright light group was 0.52 lower | 26 |
| [SALT (Time to respond)] | VERY LOW ^{b,c,d} | (2.03 lower to 0.99 higher) compared to control | (1 RCT) |
| Cognitive Performance | ФООО | The mean difference in the bright light group was 21.21 | 24 |
| [ANAM (Reaction time)] | VERY LOWa,b,c,d | lower (48.83 lower to 6.41 higher) compared to control | (1 RCT) |
| Cognitive Performance | $\Theta\ThetaOO$ | The mean difference in the bright light group was 10.4 lower | 34 |
| [Karolinska sleep diary] | LOW ^b | (18.12 lower to 2.68 lower) compared to control | (1 RCT) |

- a. Risk of bias concerns due to lack of blinding
- b. Imprecision due to small sample size (<200 participants)
- c. Certainty in evidence lowered because of a small number of events leading to wide confidence intervals.
- d. Indirectness is due to the fact that participants included in the studies are healthy individuals. The effect in adults with SWD may be different.

Table S38. Phase shift bright light in adults with shiftwork disorder

| Study Citation | Study Design | Number of Participants (% Female) | Age (years) | Population | Interventio n (intensity) | Comparator | Time of Intervention Delivery | Duration of Follow- up |
|-------------------|-----------------------|---|-----------------------|---|---|---|---|------------------------------|
| Bjorvatn 1999 | non-RCT | 7 (0) | 38.9 (range 29–47) | Shift workers without SWD diagnosis | Bright light (10,000 lux) | Normal light (20-700 lux) | 30 min between 14:00 -15:30 during the first day at home | 1 day |
| Bjorvatn 2007 | RCT, crossover | 17 (6) | 29–55 | Shift workers without SWD diagnosis | Bright light (10,000 lux) Melatonin (3 mg) | Ambient Light (200-300 lux) Placebo | 30 minutes of bright light between 00:00- 05:00; Melatonin or placebo given 1 hour before bedtime | 1 week |
| Campbell 1995 | RCT | 26 (27) | 49.1 ± 6.4 | Healthy participants | Bright light (>4,000 lux) Bright light (1,000 lux) | dim light (<100 lux) | 4-hour pulse of bright light from 24:00 to 04:00 on night shift one Exposure lasted for duration of the night shift on night shifts two and three | 3 nights |
| Costa 1995 | non-RCT, crossover | 15 (100) | 23.4 (range 21-29) | Shift workers without SWD diagnosis | Bright Light (2350 lux) | normal light (100 lux) | 4 x 20min during the night shift (before work and every 2hrs while working) | 2 nights |
| Crowley 2003 | RCT | 67 (52) | 23.9 ± 6.2 | Healthy participants | Bright light (~5000 lux) | room light (~150 lux) | bright light during the night shifts | 5 nights |

| Dawson 1991 | RCT | 13 (46) | 21.2 ± 3.1 | Healthy participants | bright light (6,000 lux) | normal ambient room illumination (150-200 lux) | 24:00-04:00 on the first night shift | 1 night |
|------------------|---------|---------|--|---|--------------------------------------|---|--|----------|
| Dawson 1995 | RCT | 36 | 23.6 ± 3.9 | Healthy participants | Bright light (4,000-7,000 lux) | dim red light (50 lux) | 24:00 -04:00 | 3 nights |
| Dumont 2009 | RCT | 38 (61) | 20 to 35 | Healthy participants | Bright light (1800 lux) | dim indoor light (20 lux) | 08:00 to 09:00 | 7 days |
| Horowitz 2001 | RCT | 27 (74) | 26.99 ± 6.22 | Healthy participants | Bright light (2,500 lux) | room light (150 lux) | 23:00-05:00 | 3 nights |
| Rizza 2022 | RCT | 22 (59) | 40.4 ± 6.9 | Shift workers without SWD diagnosis | Bright light (10,000 lux) | control | 30 min per day between 06:00 and 09:00 h | 12 weeks |
| Smith 2008 | non-RCT | 24 (58) | 28.9 ± 5.8 (bright light) 23.7 ± 3.6 (control) | Healthy participants | ~ 4100 lux | normal room light (< 50 lux) | five 15-min intermittent bright light pulses each night shift beginning at 00:45 and ending at 05:00 | |

Critical Outcomes

Figure S349. Bright Light vs Control (Excessive Sleepiness, KSS) [CMT = 1 point] RCT (Shift workers without a SWD diagnosis)

| | Brig | ht | Control | | | Std. Mean Difference | Std. Mean Difference | | | | |
|----------------------|------|-----|---------|------|----|----------------------|----------------------|--|--|--|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | | | |
| 21.3.2 Field Studies | | | | | | | | | | | |
| Bjorvatn 2007 | 4 | 0.8 | 17 | 4.3 | 1 | 17 | -0.32 [-1.00, 0.35] | | | | |
| | | | | | | | | | | | |
| | | | | | | | | -2 -1 0 1 Favours Bright Light Favours Control | | | |

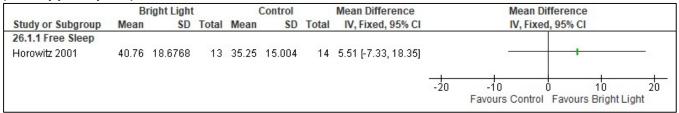
Bjorvatn 2007: Bright Light (10,000 lux for 30min/day between 24:00-0500) across a week. Ambient Light (200-300 lux). Crossover, acceptable washout period. KSS data across the week.

Figure S350. Bright Light vs Control (Excessive Sleepiness, KSS) [CMT = 1 point] non-RCT (Shift workers

| | Brig | ht Lig | ht | Control | | | Std. Mean Difference | Std. Mean Difference | | | | |
|----------------------|------|--------|-------|---------|-----|-------|----------------------|---|----------|--|--|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | | | | |
| 21.4.2 Field Studies | | | | | | | | | | | | |
| Bjorvatn 1999 | 4.7 | 0.3 | 7 | 4.9 | 0.3 | 7 | -0.62 [-1.71, 0.46] | | | | | |
| | | | | | | | | | <u> </u> | | | |
| | | | | | | | | -2 -1 0 1 Favours Bright Light Favours Control | | | | |

Bjorvatn 1999: SEM converted to SD, used on the platform data

Figure S351. Bright Light vs Control (Excessive Sleepiness, VAS- Alertness) [CMT = Not Established] RCT (Healthy participants)



^{*}Horowitz 2001: BL (~2500 lux from 2300-0500hrs, ~150 lux from 0500-0700hrs). Room Light ~105 lux for the full 8hrs. Participants were then moved to <8 lux of constant routine, in a semi-recumbent posture; VAS (for phase shifting) was measured during the first 24 hours of constant routine (higher= more alert). Data extracted from graph; SEM converted to SD.

Figure S352. Bright Light vs Control (Excessive Sleepiness, RTSW) [CMT = 2.0 min] RCT (Healthy participants)

| | Brig | Bright Light | | | Control | | | Mean Difference | Mean Difference |
|--------------------------|----------|--------------|---------|-----------------------|---------|-------|--------|--------------------|--------------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 3.2.1 Lab Studies | | | | | | | | | |
| Campbell 1995 | 15.06 | 5.99 | 13 | 12.41 | 6.53 | 13 | 27.8% | 2.65 [-2.17, 7.47] | |
| Dawson 1991 | 18.8 | 2.28 | 9 | 16.7 | 5.28 | 16 | 72.2% | 2.10 [-0.89, 5.09] | |
| Subtotal (95% CI) | | | 22 | | | 29 | 100.0% | 2.25 [-0.28, 4.79] | |
| Heterogeneity: Chi²= | 0.04, df | = 1 (P | = 0.85) | $ \mathbf{r} = 09$ | 6 | | | | |
| Test for overall effect: | Z = 1.74 | P = 0 | 0.08) | | | | | | |
| | | | | | | | | | |
| | | | | | | | | | -10 -5 0 5 10 |
| | | | | | | | | | Favours Control Favours Bright Light |

^{*}Campbell 1995: SEM converted to SD, extracted from graphs.

Dawson 1991: data extracted from Figure 4, SEM converted to SD

Figure S353. Bright Light vs Control (Excessive Sleepiness, Fatigue Ratings) [CMT = Not Established] non-randomized study (Shift workers without SWD diagnosis)

| Brig | ht Lig | ht | Co | ntro | I | Mean Difference | Mean Difference |
|------|--------|---------|--------------------------|--------------------|-----------------------|-----------------------------|---|
| Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| | | | | | | | |
| 26.1 | 5.6 | 15 | 25.2 | 5.7 | 15 | 0.90 [-3.14, 4.94] | |
| | | | | | | | + |
| | | | | | | | -10 -5 0 5 1 Favours Bright Light Favours Control |
| | Mean | Mean SD | 900000000 4000000 900000 | Mean SD Total Mean | Mean SD Total Mean SD | Mean SD Total Mean SD Total | Mean SD Total Mean SD Total IV, Fixed, 95% CI |

^{*}Costa 1995- 4 x 20min of Bright Light (2350 lux) in the break room (versus 100 lux) during Night Shift (before work and every 2hrs while working). Crossover, acceptable washout period. First night of bright light, overall fatigue (5 min to 35 max).

Figure S354. Bright Light vs Control (Sleep Quality, Sleep Diary) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)

| | Brig | ht | Control Mean Difference | | | | | Mean Difference | | | |
|--------------------|------|-----|-------------------------|------|-----|-------|--------------------|-----------------|--|---|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 95% CI | | |
| 21.8.1 Field Study | | | | | | | | | | | |
| Bjorvatn 2007 | 3.1 | 0.7 | 16 | 3.1 | 0.7 | 16 | 0.00 [-0.49, 0.49] | | | | |
| | | | | | | | | 4 | | | |
| | | | | | | | | -1 | -0.5 0 0.5 Favours Bright Light Favours Control | 1 | |

*Bjorvatn 2007: Bright Light (10,000 lux for 30min/day between 24:00-0500). Ambient Light (200-300 lux) across a week. Crossover, acceptable washout period. Higher value indicates better sleep. Sleep diary data across the week.

Figure S355. Bright Light vs Control (Sleep Quality, Sleep Diary) [CMT = Not Established] non-RCT (Shift workers without SWD diagnosis)

| | Brig | ht | Co | ontrol | I. | Mean Difference | Mean Difference | |
|--------------------|------|-----|-------|--------|-----|-----------------|--------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 21.9.1 Field Study | | | | | | | | |
| Bjorvatn 1999 | 3.4 | 0.3 | 7 | 3.4 | 0.3 | 7 | 0.00 [-0.31, 0.31] | |
| | | | | | | | | + |
| | | | | | | | | -1 -0.5 0 0.5 1 Favours Bright Light Favours Control |

^{*}Bjorvatn 1999: SEM converted to SD, at the platform data was used.

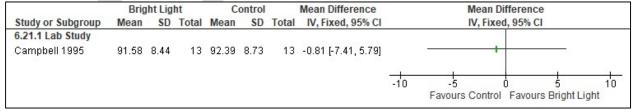
Figure S356. Bright Light vs Control (Sleep Quality, PSQI (number of participants with score 1-4)) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)

| | Experim | ental | Contr | ol | Risk Ratio | Risk Ratio |
|-------------------|---------|-------|--------|-------|--------------------|--------------------------------------|
| Study or Subgroup | Events | Total | Events | Total | M-H, Fixed, 95% CI | M-H, Fixed, 95% CI |
| RIzza 2022 | 3 | 13 | 2 | 9 | 1.04 [0.22, 5.01] | |
| | | | | | | 0.01 0.1 1 10 10 |
| | | | | | | Favours Bright Light Favours Control |

Figure S357. Bright Light vs Control (Sleep Quality, PSQI (number of participants with score 5-21)) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)

| | Experim | ental | Contr | ol | Risk Ratio | Risk Ratio | | | | | |
|-------------------|---------|-------|--------|-------|--------------------|------------------------------------|---|--|--|--|--|
| Study or Subgroup | Events | Total | Events | Total | M-H, Fixed, 95% CI | M-H, Fixed | , 95% CI | | | | |
| Rizza 2022 | 10 | 13 | 6 | 9 | 1.15 [0.67, 2.00] | | | | | | |
| | | | | | | 0.01 0.1 1 Favours Bright Light | 1 ['] 0 100 Favours Control | | | | |

Figure S358. Bright Light vs Control (Cognitive Performance, Night 3 % Correct SALT) [CMT = Not Established] RCT (Healthy participants)



^{*}Campbell 1995: BL 1000 lux, dim light <100 lux; Night 3 data was the average of timepoint during 2300-0700 (phase shift) SEM converted to SD, extracted from graphs.

Figure S359. Bright Light vs Control (Cognitive Performance, Night 3 Time to respond SALT) [CMT = Not Established] RCT (Healthy participants)

| | Bright Light | | | C | ontrol | Mean Difference | | | Mean Difference | | | | |
|-------------------|--------------|------|-------|------|--------|-----------------|---------------------|----|-----------------|---------|--------|---------|-----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV. | Fixed, | 95% CI | | |
| 6.23.1 Lab Study | | | | | | | | | | 100 | | | |
| Campbell 1995 | 5.13 | 1.55 | 13 | 5.65 | 2.31 | 13 | -0.52 [-2.03, 0.99] | | (D) | + | | | |
| | | | | | | | | | - 1 | | | 17 | - 1 |
| | | | | | | | | -4 | -2 | Ó | | 2 | 4 |
| | | | | | | | | | Favours Bright | Light F | avours | Control | |

^{*}Campbell 1995: BL 1000 lux, dim light- <100 lux; Night 3 data was the average of timepoint during 2300- 0700 (phase shift) SEM converted to SD, extracted from graphs.

Figure S360. Bright Light vs Control (Cognitive Performance, ANAM mean reaction time) [CMT = Not Established] non-RCT (Healthy participants)

| | Bri | ght Ligh | nt | Control | | | Mean Difference | Mean Difference | | | |
|-------------------|-------|----------|-------|---------|-------|-------|-----------------------|---|--|--|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | | | |
| 6.15.1 Lab Study | | | | | | | | | | | |
| Smith 2008 | 26.31 | 25.77 | 12 | 47.52 | 41.47 | 12 | -21.21 [-48.83, 6.41] | | | | |
| | | | | | | | | | | | |
| | | | | | | | | -50 -25 0 25 50 Favours Bright Light Favours Control | | | |

^{*}Smith 2008: BL ~4100 lux, dim light<50 lux, only used NS7. SEM converted SD for study, extracted from graphs. ANAM= Automated Neurophysiological Assessment Metrics.

Figure S361. Bright Light vs Control (Cognitive Performance, Karolinska sleep diary: reduced performance) [CMT = Not Established] Non-RCT (Shift workers without SWD diagnosis)

| | Exp | eriment | al | | Control | | Mean Difference | Mean Difference IV, Fixed, 95% CI | | | | |
|---------------------|------|---------|-------|------|---------|-------|------------------------|--------------------------------------|--|--|--|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | | | | |
| 26.14.1 Field Study | | | | | | | | | | | | |
| Bjorvatn 1999 | 14.5 | 9.4831 | 17 | 24.9 | 13.1939 | 17 | -10.40 [-18.12, -2.68] | | | | | |
| | | | | | | | | -20 -10 0 10 20 | | | | |
| | | | | | | | | Favours Bright Light Favours Control | | | | |

Important Outcomes

Figure S362. Bright Light vs Control (Total Sleep Time, EEG) [CMT = 15 min] RCT (Healthy participants)

| | Brig | ht Ligh | it | Co | ntrol | | Mean Difference | | Mean Di | fference | |
|-------------------|--------|---------|-------|--------|-------|-------|------------------------|------|-----------------|----------------|---------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed | I, 95% CI | |
| 6.33.1 Lab Study | | | | | | | | | | | |
| Campbell 1995 | 345.71 | 83.4 | 13 | 355.88 | 70.1 | 13 | -10.17 [-69.39, 49.05] | | + | 90 | |
| 100 | | | | | | | | | į. | 10 | |
| | | | | | | | | -100 | -50 (| 50 | 100 |
| | | | | | | | | | Favours Control | Favours Bright | t Light |

^{*}Campbell 1995: BL 1000 lux, dim light <100 lux; Night 3 data was the average of timepoint during 2300- 0700 (phase shift). Healthy.

Figure S363. Bright Light vs Control (Total Sleep Time, Actigraphy) [CMT = 15 min] RCT (Shift workers without SWD diagnosis)

| | Brigl | ht Lig | ht | Control | | | Mean Difference | Mean Difference | | | | |
|----------------------|-------|--------|-------|---------|----|-------|-----------------------|--------------------------------------|--|--|--|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | | | | |
| 21.30.1 No diagnosis | | | | | | | | | | | | |
| Bjorvatn 2007 | 419 | 63 | 15 | 403 | 60 | 15 | 16.00 [-28.03, 60.03] | | | | | |
| | | | | | | | | -100 -50 0 50 100 | | | | |
| | | | | | | | | Favours Control Favours Bright Light | | | | |

^{*}Bjorvatn 2007: Bright Light (10,000 lux for 30min/day between 24:00-0500). Ambient Light (200-300 lux). Crossover, acceptable washout period. Actigraphy data across the week. No dx

Figure S364. Bright Light vs Control (Total Sleep Time, Sleep Diary) [CMT = 15 min], RCT (Shift workers without SWD diagnosis)

| | | | | ntro | | Mean Difference | | weall bi | fference | | |
|------|-----|--------|-----------|---------------|------------------|----------------------|--|--|------------|------------|-----|
| lean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed | , 95% CI | | |
| | | | | | | | | | | | |
| 392 | 56 | 16 | 386 | 53 | 16 | 6.00 [-31.78, 43.78] | | | 1 | à | |
| | | | | | | | | | | + | - |
| | | | | | | | -100 | | Foundate I | | 100 |
| | 392 | 392 56 | 392 56 16 | 392 56 16 386 | 392 56 16 386 53 | 392 56 16 386 53 16 | 392 56 16 386 53 16 6.00 [-31.78, 43.78] | 392 56 16 386 53 16 6.00 [-31.78, 43.78] | -100 -50 (| -100 -50 0 | |

^{*}Bjorvatn 2007: Bright Light (10,000 lux for 30min/day between 24:00-0500). Ambient Light (200-300 lux). Crossover, acceptable washout period. Sleep diary data across the week., no dx

Figure S365. Bright Light vs Control (Total Sleep Time, Sleep Diary) [CMT = 15 min], non-RCTs (Shift workers without SWD diagnosis)

| | Bri | ght Ligh | nt | (| ontrol | | | Mean Difference | Mean Difference |
|-----------------------------------|----------|-----------|---------|----------------------|--------|-------|--------|-------------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 21.17.1 Field Study | | | | | | | | | |
| Bjorvatn 1999 | 449.5 | 27.78 | 7 | 442.7 | 21.96 | 7 | 71.1% | 6.80 [-19.43, 33.03] | |
| Costa 1995 | 437.4 | 75.6 | 15 | 489 | 30 | 15 | 28.9% | -51.60 [-92.76, -10.44] | |
| Subtotal (95% CI) | | | 22 | | | 22 | 100.0% | -10.07 [-32.19, 12.05] | - |
| Heterogeneity: Chi ² = | 5.50, df | = 1 (P = | 0.02); | I ² = 829 | 6 | | | | |
| Test for overall effect | Z = 0.89 | 9 (P = 0. | 37) | | | | | | |
| Total (95% CI) | | | 22 | | | 22 | 100.0% | -10.07 [-32.19, 12.05] | - |
| Heterogeneity: Chi ² = | 5.50, df | = 1 (P = | 0.02); | I ² = 829 | 6 | | | | 100 100 100 |
| Test for overall effect: | Z = 0.89 | 9 (P = 0. | 37) | | | | | | -100 -50 0 50 100 Favours Control Favours Bright Light |
| Test for subgroup dif | ferences | : Not an | plicabl | е | | | | | Favours Control Favours Bright Light |

^{*}Bjorvatn 1999: SEM converted to SD, at the platform data was used.

Figure S366. Bright Light vs Control (Total Sleep Time, PSG/EEG) [CMT=15 min], non-RCTs (healthy participants)

| | Brig | ht Ligh | nt | Din | n Light | | | Mean Difference | Mean Difference |
|-----------------------------------|-----------|---------|---------|-------------|---------|-------|--------|------------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 20.36.1 Lab Studies | | | | | | | | | ¥ |
| Campbell 1995 | 345.71 | 83.4 | 13 | 355.88 | 70.1 | 13 | 6.3% | -10.17 [-69.39, 49.05] | |
| Dawson 1991 | 439.5 | 5.3 | 6 | 464.6 | 19.9 | 7 | 93.7% | -25.10 [-40.44, -9.76] | s - |
| Subtotal (95% CI) | | | 19 | | | 20 | 100.0% | -24.16 [-39.01, -9.31] | • |
| Heterogeneity: Chi ² = | 0.23, df= | 1 (P= | 0.63); | $I^2 = 0\%$ | | | | | |
| Test for overall effect: | Z= 3.19 | (P = 0. | 001) | | | | | | |
| Total (95% CI) | | | 19 | | | 20 | 100.0% | -24.16 [-39.01, -9.31] | • |
| Heterogeneity: Chi ² = | 0.23, df= | 1 (P= | 0.63); | $I^2 = 0\%$ | | | | | 1.00 |
| Test for overall effect: | Z = 3.19 | (P = 0. | 001) | | | | | | -100 -50 0 50 100 Favours Dim Light Favours Bright Light |
| Test for subgroup dif | ferences: | Not ap | plicabl | е | | | | | ravours Dim Light Favours Bright Light |

Figure S367. Bright Light vs Control (Mental Health, HADS-anxiety) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)

| | Brig | ht Lig | ht | Co | ntro | I | Mean Difference | Mean Difference |
|--------------------|------|--------|-------|------|------|-------|--------------------|--------------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 21.1.1 Field Study | | | | | | | | |
| Bjorvatn 2007 | 3.8 | 2.8 | 16 | 3.4 | 2.5 | 16 | 0.40 [-1.44, 2.24] | - |
| | | | | | | | | |
| | | | | | | | | -10 -5 0 5 10 |
| | | | | | | | | Favours Bright Light Favours Control |

^{*}Bjorvatn 2007: Bright Light (10,000 lux for 30min/day between 24:00-0500). Ambient Light (200-300 lux). Crossover, acceptable washout period. Overall questionnaire; higher scores on HADS indicate more severe impairment.

Figure S368. Bright Light vs Control (Mental Health, HADS-depression) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)

| | Brig | ht Lig | ht | Co | ntro | I | Mean Difference | Mean Difference |
|---------------------|------|--------|-------|------|------|-------|--------------------|--------------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 21.29.1 Field Study | | | | | | | | |
| Bjorvatn 2007 | 3.5 | 2.3 | 16 | 2.9 | 2.6 | 16 | 0.60 [-1.10, 2.30] | |
| | | | | | | | | |
| | | | | | | | | -10 -5 0 5 10 |
| | | | | | | | | Favours Bright Light Favours Control |

^{*}Bjorvatn 2007: Bright Light (10,000 lux for 30min/day between 24:00-0500). Ambient Light (200-300 lux). Crossover, acceptable washout period. Overall questionnaire; higher scores on HADS indicate more severe impairment.

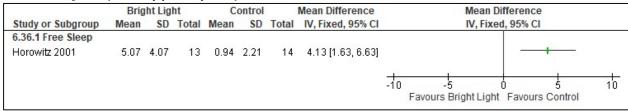
Figure S369. Bright Light vs Control (Circadian Adaptation, DLMO) [CMT = Not Established] RCT (Healthy participants)

| | Brig | ht Lig | ht | C | ontrol | | | Mean Difference | Mean Difference |
|-----------------------------------|----------|----------|----------|----------|--------|-------|--------|----------------------|--------------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 26.35.3 Lab Studies | | | | | | | | | |
| Dumont 2009 | 2.26 | 1.25 | 10 | -1.7 | 1.64 | 11 | 80.6% | 3.96 [2.72, 5.20] | - |
| Horowitz 2001 | -4.12 | 3.21 | 9 | -0.45 | 2.39 | 11 | 19.4% | -3.67 [-6.20, -1.14] | - |
| Subtotal (95% CI) | | | 19 | | | 22 | 100.0% | 2.48 [1.37, 3.59] | • |
| Heterogeneity: Chi ² = | 28.19, 0 | df = 1 (| P < 0.0 | 0001); P | = 969 | 6 | | | |
| Test for overall effect: | Z = 4.36 | 6 (P < 0 | 0.0001) | | | | | | |
| Total (95% CI) | | | 19 | | | 22 | 100.0% | 2.48 [1.37, 3.59] | • |
| Heterogeneity: Chi ² = | 28.19, 0 | df = 1 (| P < 0.0 | 0001); P | = 969 | 6 | | | -10 -5 0 5 10 |
| Test for overall effect: | Z = 4.38 | 6 (P < 0 | 0.0001) | | | | | | Favours Bright Light Favours Control |
| Test for subgroup diff | ferences | : Not a | applical | ole | | | | | Favours Bright Light Favours Control |

^{*}Horowitz 2001: BL (~2500 lux from 2300-0500hrs, ~150 lux from 0500-0700hrs). Room Light ~105 lux for the full 8hrs. Participants were then moved to <8 lux of constant routine, in a semi-recumbent posture; Phase shift of the DLMO was defined as constant routine phase minus DLMO (measured from 1700-2300) prior to the start of night shift. Data extracted from graph; SEM converted to SD.

Dumont 2009: DLMO phase shift (h), advance group vs stable group, Healthy

Figure S370. Bright Light vs Control (Circadian Adaptation, Midpoint Melatonin Secretion) [CMT = Not Established] RCT (Healthy participants)



^{*}Horowitz 2001: BL (~2500 lux from 2300-0500hrs, ~150 lux from 0500-0700hrs). Room Light ~105 lux for the full 8hrs. Participants were then moved to <8 lux of constant routine, in a semi-recumbent posture; Midpoint melatonin secretion episode was calculated for the first 24hrs of constant routine. Data (in clock hours) extracted from graph; SEM converted to SD. Healthy.

Figure S371. Bright Light vs Control (Circadian Adaptation, Core Body Temperature Phase) [CMT = Not Established] RCT (Healthy participants)

| | Brig | ht Lig | ht | C | ontrol | | | Mean Difference | Mean Difference |
|-----------------------------------|----------|----------|----------|---------------|--------|-------|--------|-------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 26.33.1 Lab Studies | | | | | | | | | |
| Campbell 1995 | 6.25 | 2.8 | 13 | 3.51 | 2.6 | 13 | 64.1% | 2.74 [0.66, 4.82] | |
| Horowitz 2001 | 6.41 | 4.22 | 13 | 2.23 | 2.99 | 14 | 35.9% | 4.18 [1.40, 6.96] | |
| Subtotal (95% CI) | | | 26 | | | 27 | 100.0% | 3.26 [1.59, 4.92] | • |
| Heterogeneity: Chi ² = | 0.66, df | = 1 (P | = 0.42 | $); I^2 = 09$ | 6 | | | | |
| Test for overall effect: | Z = 3.84 | 4 (P = 0 | 0.0001) | | | | | | |
| Total (95% CI) | | | 26 | | | 27 | 100.0% | 3.26 [1.59, 4.92] | • |
| Heterogeneity: Chi² = | 0.66, df | = 1 (P | = 0.42 | $); I^2 = 09$ | 6 | | | | -10 -5 0 5 10 |
| Test for overall effect: | Z = 3.84 | 4 (P = 0 | 0.0001) | Ĺ | | | | | -10 -5 0 5 10 Favours Control Favours Bright Light |
| Test for subgroup diff | ferences | : Not a | applical | ble | | | | | ravours Control Pavours Bright Light |

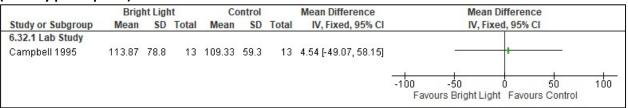
^{*}Horowitz 2001: BL (~2500 lux from 2300-0500hrs, ~150 lux from 0500-0700hrs). Room Light ~105 lux for the full 8hrs. Participants were then moved to <8 lux of constant routine, in a semi-recumbent posture. Core Body Temp phase was defined as the average nadir of the fundamental and the composite from a 2-harmonic cosine fit, by group. Data extracted from graph; SEM converted to SD.

Figure S372. Bright Light vs Control (Quality of Life, Karolinska Sleep Diary) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)

| | Bri | ight Light | t | (| Control | | Mean Difference | Mean Difference |
|-------------------|------|------------|-------|------|---------|-------|---------------------|--------------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| Bjorvatn 1999 | 3.9 | 0.2646 | 7 | 4.2 | 0.5292 | 7 | -0.30 [-0.74, 0.14] | |
| | | | | | | | | -2 -1 0 1 2 |
| | | | | | | | | Favours Bright Light Favours Control |

^{*}Bjorvatn 1999: SEM converted to SD, at the platform data was used. No Dx.

Figure S373. Bright Light vs Control (Wake After Sleep Onset (WASO), EEG) [CMT= 20 min] RCT (Healthy participants)



^{*}Campbell 1995: BL-1000 lux, dim light- <100 lux; Night 3 data was the average of timepoint during 2300- 0700 (phase shift).

^{*}Campbell 1995: BL-1000 lux, dim light- <100 lux; Net shift relative to baseline (phase shift).

Figure S374. Bright Light vs Control (Wake After Sleep Onset (WASO), Karolinska Sleep Diary) [CMT= 20 min] non-RCT (Shift workers without SWD diagnosis)

| | Br | ight Light | t | (| Control | | Mean Difference | Mean Difference |
|---------------------|------|------------|-------|------|---------|-------|--------------------|--------------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 26.32.1 Field Study | | | | | | | | |
| Bjorvatn 1999 | 3.9 | 0.2646 | 7 | 3.8 | 0.2646 | 7 | 0.10 [-0.18, 0.38] | |
| | | | | | | | | |
| | | | | | | | | -1 -0.5 Ö 0.5 |
| | | | | | | | | Favours Control Favours Bright Light |

Bjorvatn 1999: SEM converted to SD, at the platform data was used.

Figure S375. Bright Light vs Control (Sleep Latency, EEG) [CMT= 20 min] RCT (Healthy participants)

| | Brig | ht Lig | ht | Co | ontro | l | Mean Difference | Mean Difference |
|-------------------|-------|--------|-------|------|-------|-------|---------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 6.31.1 Lab Study | | | | | | | | 1 |
| Campbell 1995 | 18.92 | 11.1 | 13 | 8.54 | 5.2 | 13 | 10.38 [3.72, 17.04] | |
| | | | | | | | | -20 -10 0 10 20 |
| | | | | | | | | -20 -10 0 10 Favours Bright Light Favours Control |

^{*}Campbell 1995: BL-1000 lux, dim light- <100 lux; Night 3 data was the average of timepoint during 2300- 0700 (phase shift).

Figure S376. Bright Light vs Control (Sleep Latency, Sleep Diary) [CMT= 20 min] RCT (Shift workers without SWD diagnosis)

| | Brig | ht Lig | ht | Co | ntrol | | Mean Difference | Mean Difference |
|---------------------|------|--------|-------|------|-------|-------|----------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 21.21.1 Field Study | | | | | | | | |
| Bjorvatn 2007 | 9 | 5 | 16 | 14 | 9 | 16 | -5.00 [-10.04, 0.04] | |
| | | | | | | | 9. | |
| | | | | | | | | -20 -10 0 10 20 Favours Bright Light Favours Control |

^{*}Bjorvatn 2007: Bright Light (10,000 lux for 30min/day between 24:00-0500). Ambient Light (200-300 lux). Crossover, acceptable washout period. Sleep diary data across the week.

Figure S377. Bright Light vs Control (Sleep Latency, Sleep Diary) [CMT= 20 min] non-RCT (Shift workers without SWD diagnosis)

| Bright Lig | | ight Light | t | Control | | Mean Difference | | Mean Difference | | |
|---------------------|------|------------|-------|---------|--------|-----------------|--------------------|--------------------------------------|--|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI | | |
| 21.23.1 Field Study | | | | | | | | | | |
| Bjorvatn 1999 | 20.1 | 6.0852 | 7 | 18.9 | 5.5561 | 7 | 1.20 [-4.90, 7.30] | | | |
| | | | | | | | | | | |
| | | | | | | | | -20 -10 0 10 20 | | |
| | | | | | | | | Favours Bright Light Favours Control | | |

^{*}Bjorvatn 1999: SEM converted to SD, at the platform data was used.

Figure S378. Bright Light vs Control (Sleep Efficiency, EEG) [CMT = 10%] non-RCT (Healthy participants)

| 2i t Light |
|---------------|
| h |

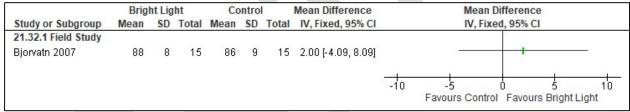
^{*}Campbell 1995: BL-1000 lux, dim light- <100 lux; Night 3 data was the average of timepoint during 2300- 0700 (phase shift).

Figure S379. Bright Light vs Control (Sleep Efficiency, Sleep Diary) [CMT = 10%] RCT (Shift workers without SWD diagnosis)

| | Bright Light | | Control Mean Difference | | | Mean Difference | | Mean Dif | fference | | |
|--------------------|--------------|----|-------------------------|------|----|-----------------|--------------------|----------|-----------------|----------------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed | , 95% CI | |
| 7.34.1 Field Study | | | | | | | | | | Ų. | |
| Bjorvatn 2007 | 86 | 9 | 16 | 86 | 6 | 16 | 0.00 [-5.30, 5.30] | | is: | 200 | |
| | | | | | | | | | | 1 | - |
| | | | | | | | | -10 | -5 Ć | 5 | 10 |
| | | | | | | | | | Favours Control | Favours Bright Light | |

^{*}Bjorvatn 2007: Bright Light (10,000 lux for 30min/day between 24:00-0500). Ambient Light (200-300 lux). Crossover, acceptable washout period. Sleep diary data across the week.

Figure S380. Bright Light vs Control (Sleep Efficiency, Actigraphy) [CMT = 10%] RCT (Shift workers without SWD diagnosis)



^{*}Bjorvatn 2007: Bright Light (10,000 lux for 30min/day between 24:00-0500). Ambient Light (200-300 lux). Crossover, acceptable washout period. Actigraphy data across the week.

Bright Light and fixed sleep timing

Summary of Findings (GRADE)

Table S39. Bright light and fixed sleep timing in adults with shiftwork disorder

| References: Horowitz 2001 | | | |
|---------------------------|---------------------------|---|------------------------------|
| Outcomes [Tool] | Certainty of the evidence | Absolute Difference | No of Participants (studies) |
| | (GRADE) | Bright light and fixed sleep timing vs Control | |
| Excessive sleepiness or | ФООО | The mean difference in the bright light and fixed sleep group | 27 |
| alertness | VERY LOW ^{a,b,c} | was 19.8 higher (5.49 lower to 34.11 higher) compared to | (1 RCT) |
| [VAS-alertness] | | control | |

| Circadian adaptation [DLMO] | ⊕⊕⊜⊝ LOW ^{a,b,c} | The mean difference in the bright light and fixed sleep group was 5.52 hours lower (7.04 lower to 4 lower) compared to control | 22 (1 RCT) |
|--|------------------------------|---|---------------|
| Circadian adaptation [Midpoint melatonin secretion | ⊕⊕○○ on] LOW a,b,c | The mean difference in the bright light and fixed sleep group was 7.31 hours higher (5.97 higher to 8.65 higher) compared to control | 22 (1 RCT) |
| Circadian adaptation [Core body temperature phase] | ⊕⊕⊜⊖ LOW ^{a,b,c} | The mean difference in the bright light and fixed sleep group was 7.19 hours higher (5.26 higher to 9.12 lower) compared to control | |

- a. Risk of bias concerns due to the lack of blinding
- b. Indirectness is due to the fact that participants included in the studies are healthy individuals. The effect in adults with SWD may be different.
- c. Imprecision due to small sample size (<200 participants)

Table S40. Bright light and fixed sleep timing in adults with shiftwork disorder

| Study Citation | Study Design | Number of Participants (% Female) | Age (years) | Population | Intervention (intensity) | Comparator | Time of Intervention Delivery | Duration of Follow-up |
|-------------------|--------------|-----------------------------------|----------------|--------------|--------------------------|------------|-------------------------------------|--------------------------|
| Horowitz | | | 26.99 ± | Healthy | Bright light | room light | | |
| 2001 | RCT | 27 (74) | 6.22 | participants | (2,500 lux) | (150 lux) | 23:00-05:00 | 3 nights |

Critical Outcomes

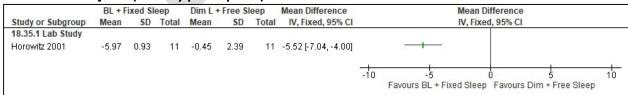
Figure S381. Bright Light + Fixed Sleep vs Dim Light + Free Sleep (Excessive Sleepiness, VAS- Alertness) [CMT = Not Established] RCT (Healthy participants)

| | BL + Fix | xed SI | eep | Dim L 4 | Free S | leep | Mean Difference Mean Difference | | | | | |
|-------------------|----------|--------|-------|---------|--------|-------|---------------------------------|-------|---------------|---------------|----------------|-------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IN | /, Fixed, 95% | CI | |
| 18.28.3 Lab Study | | | | | | | | | | | | |
| Horowitz 2001 | 55.05 | 22 | 13 | 35.25 | 15 | 14 | 19.80 [5.49, 34.11] | | | - | - | |
| | | | | | | | | | 1 | | ī. | |
| | | | | | | | - | -50 | -25 | Ó | 25 | 50 |
| | | | | | | | | Favou | rs Dim + Free | Sleep Favo | urs BL + Fixed | Sleep |

^{*}Horowitz 2001: BL (~2500 lux from 2300-0500hrs, ~150 lux from 0500-0700hrs). Room Light ~105 lux for the full 8hrs. Participants were then moved to <8 lux of constant routine, in a semi-recumbent posture; VAS (for phase shifting) was measured during the first 24 hours of constant routine (higher= more alert). Data extracted from graph; SEM converted to SD.

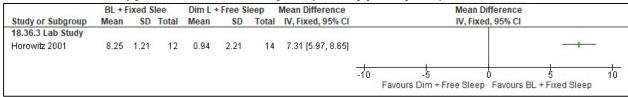
Important Outcomes

Figure S382. Bright Light + Fixed Sleep vs Dim Light + Free Sleep (Circadian Alignment, DLMO) [CMT = Not Established] RCT (Healthy participants)



^{*}Horowitz 2001: BL (~2500 lux from 2300-0500hrs, ~150 lux from 0500-0700hrs). Room Light ~105 lux for the full 8hrs. Participants were then moved to <8 lux of constant routine, in a semi-recumbent posture; Phase shift of the DLMO was defined as constant routine phase minus DLMO (measured from 1700-2300) prior to the start of night shift. Data extracted from graph; SEM converted to SD.

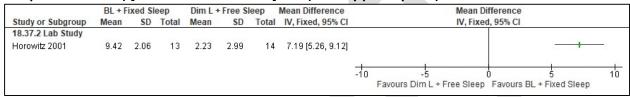
Figure S383. Bright Light + Fixed Sleep vs Dim Light + Free Sleep (Circadian Alignment, Midpoint Melatonin Secretion) [CMT = Not Established] RCT (Healthy participants)



^{*}Horowitz 2001: BL (~2500 lux from 2300-0500hrs, ~150 lux from 0500-0700hrs). Room Light ~105 lux for the full 8hrs.

Participants were then moved to <8 lux of constant routine, in a semi-recumbent posture; Midpoint melatonin secretion episode was calculated for the first 24hrs of constant routine. Data (in clock hours) extracted from graph; SEM converted to SD.

Figure S384. Bright Light + Fixed Sleep vs Dim Light + Free Sleep (Circadian Alignment, Core Body Temperature Phase) [CMT = Not Established] RCT (Healthy participants)



^{*}Horowitz 2001: BL (~2500 lux from 2300-0500hrs, ~150 lux from 0500-0700hrs). Room Light ~105 lux for the full 8hrs. Participants were then moved to <8 lux of constant routine, in a semi-recumbent posture. Core Body Temp phase was defined as the average nadir of the fundamental and the composite from a 2-harmonic cosine fit, by group. Data extracted from graph; SEM converted to SD.

Bright Light, fixed sleep timing, and reduced light-transmittance glasses Summary of Findings (GRADE)

Table S41. Bright light, fixed sleep timing, and reduced light-transmittance glasses in adults with shiftwork disorder

| References: Olson 2020, Boivin 2012, Boivin 2012, Lee 2006, Crowley 2003 | | | | | | | | | |
|--|-----------------------------------|--|-----------------------------------|--|--|--|--|--|--|
| Outcomes [Tool] | Certainty of the evidence (GRADE) | Absolute Difference Bright light, fixed sleep timing, an vs Control | No of Participants (studies) | | | | | | |
| Excessive sleepiness or alertness [KSS] | ⊕○○○ VERY LOW ^{a,b,c} | The mean difference in the bright light, fixed sleep, and glasses group was 0.39 points fewer (1.47 fewer to 0.69 more) compared to control | 66 (1 non-randomized study) | | | | | | |
| Accident risk [Number of errors] | ⊕○○○ VERY LOW ^{b,c} | The risk ratio in the bright light, fixed sleep, and glasses group was 0.38 (0.15 to 0.96) with an absolute risk of 244 fewer per 1,000 (335 fewer to 16 fewer) compared to control | 66 (1 non-randomized study) | | | | | | |
| Sleep quality [Sleep quality scale] | ⊕○○○ VERY LOW ^{b,c} | The mean difference in the bright light, fixed sleep, and glasses group was 0.41 points higher (0.27 lower to 1.09 higher) compared to control | 66 (1 non-randomized study) | | | | | | |
| Cognitive performance [PVT reaction time] | ⊕⊕⊜⊝ LOW ^{b,c} | The mean difference in the bright light, fixed sleep, and glasses group was 16.2 ms fewer (44.75 fewer to 12.35 more) compared to control | 17 (1 RCT) | | | | | | |
| Cognitive performance [PVT reaction speed] | ⊕⊕⊖⊖ LOW ^{b,c} | The mean difference in the bright light, fixed sleep, and glasses group was 0.24 1/s more (0.22 fewer to 0.7 more) compared to control | 17 (1 RCT) | | | | | | |

| Total sleep time | ⊕⊕⊜⊝ | The mean difference in the bright light, fixed sleep, and glasses group was 30 minutes higher (3.34 higher to 56.66 higher) compared to control | 17 |
|-----------------------------------|-------------------------------------|---|-----------------------------------|
| [PSG] | LOW ^{b,d} | | (1 RCT) |
| Total sleep time [Self-report] | ⊕○○○ VERY LOW ^{a,b,d} | The mean difference in the bright light, fixed sleep, and glasses group was 15 minutes higher (74.36 lower to 104.36 higher) compared to control | 66 (1 non-randomized study) |
| Total sleep time | ⊕○○○ | The mean difference in the bright light, fixed sleep, and glasses group was 117 minutes higher (54.49 higher to 179.51 higher) compared to control | 23 |
| [Sleep log] | VERY LOW ^{a,b,e} | | (1 RCT) |
| Circadian adaptation [DLMO] | ⊕○○○ VERY LOW ^{a,b,e,f} | The mean difference in the bright light, fixed sleep, and glasses group was 2.82 hours higher (1.97 higher to 3.98 lower) compared to control | 45 (2 RCTs) |

- a. Risk of bias concerns due to a lack of blinding
- b. Imprecision due to small sample size (<200 participants)
- c. Imprecision due to the 95% CI crossing the null
- d. Imprecision due to the 95% CI crossing the CMT
- e. Indirectness is due to the fact that participants included in the studies are healthy individuals. The effect in adults with SWD may be different.
- f. Crowley 2003 used only a subset of participants for the DLMO.

Table S42. Bright light, fixed sleep timing, and reduced light-transmittance glasses in adults with shiftwork disorder

| Study Citation | Study Design | Number of Participants (% Female) | Age (years) | Population | Intervention (intensity) | Comparator | Time of Intervention Delivery | Duration of Follow-up |
|----------------------------|-----------------|-----------------------------------|----------------|---|---|---|--|--------------------------|
| Boivin 2012 (police) | RCT | 17 (47) | 30.1 ± 5.2 | Shift workers without SWD diagnosis | Bright light (5,000 lux) orange-tinted goggles | no bright light or goggles | bright light used intermittently during the first 6 hours of the night shift, and goggles used from sunrise until daytime sleep | 2 nights |
| Boivin 2012 (nurses) | non-RCT | 15 (60) | 41.6 ± 8.6 | Shift workers without SWD diagnosis | Bright light (3243 ± 2274 lux) shaded goggles on the commute home | normal lighting (111 ± 97 lux) clear, ultraviolet (UV)- excluding goggles on the commute home | Bright light during the first 6 hr of each night shift and glasses worn during the commute home | 1 night |
| Crowley 2003 | RCT | 67 (52) | 23.9 ± 6.2 | Healthy participants | Bright light (~5000 lux) fixed daytime dark/sleep dark sunglasses melatonin (1.8 mg sustained release) | room light (~150 lux) normal sunglasses placebo | fixed daytime dark/sleep schedule sunglasses whenever they were outside during the day bright light during the night shifts melatonin before | 5 nights |

| | | | | | | daytime sleep at 08:30 | |
|---------------|-----------------------|---------|----------------|---|---|---|----------|
| Lee 2006 | RCT | 23 (52) | 27.3 ± 6.2 | Healthy participants | Bright light (3500 lux) and blue-blocker glasses | 5x 15 min light pulses ending at 01:00, 02:00, 03:00, 04:00, and 05:00 glasses worn after nightshift & while driving home | 25 days |
| Olson 2020 | non-RCT, crossover | 33 (76) | 32.7 ± 8.6 | Shift workers without SWD diagnosis | Bright light (~5,500 lux), sunglasses, and control fixed sleep schedule | 40 min of bright light before night shift, sunglasses worn after night shift until bedtime | 3-6 days |

Critical Outcomes

Figure S385. Bright Light + Glasses vs Dim-light + No glasses (Excessive Sleepiness, KSS) [CMT = 1pt] non-randomized study (Shift workers without SWD diagnosis)

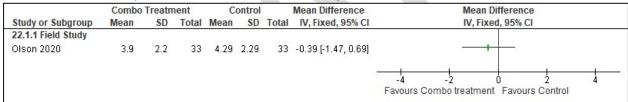


Figure S386. Bright Light + Glasses vs Dim-light + No glasses (Accident Risk, number of errors) [CMT = Not Established] non-randomized study (Shift workers without SWD diagnosis)

| | Experimental | | Conti | rol | Risk Ratio | Risk Ratio | | | | | | | |
|--------------------|--------------|-------|---------------|-------|--------------------|---|----|--|--|--|--|--|--|
| Study or Subgroup | Events | Total | Events | Total | M-H, Fixed, 95% CI | M-H, Fixed, 95% CI | | | | | | | |
| 22.4.1 Field Study | | | | | | | | | | | | | |
| Olson 2020 | 5 | 33 | 13 | 33 | 0.38 [0.15, 0.96] | - | | | | | | | |
| | | | | | | 0.01 0.1 1 10 | 10 | | | | | | |
| | | | | | | Favours Combo Treatment Favours Control | 1 | | | | | | |

Figure S387. Bright Light + Glasses vs Dim-light + No glasses (Sleep Quality, Sleep Quality Scale) [CMT = Not Established] non-randomized study (Shift workers without SWD diagnosis)

| | Experimental | | | | | | Mean Difference | | Me | ean Differen | ce | |
|--------------------|--------------|------|-------|------|------|-------|--------------------|----|------------|--------------|-----------|---------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, | Fixed, 95% | CI | |
| 22.5.1 Field Study | | | | | | | | | | | | |
| Olson 2020 | 3.92 | 1.37 | 33 | 3.51 | 1.45 | 33 | 0.41 [-0.27, 1.09] | | | - | Ti) | |
| | | | | | | | - | | | | | |
| | | | | | | | | -4 | -2 | 0 | 2 | 4 |
| | | | | | | | | | Favours Co | ontrol Favo | urs Combo | Treatme |

Figure S388. Bright Light + Glasses vs Dim-light + No glasses (Cognitive Performance, PVT mean reaction time) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)

| | Bright li | ght+sungla | sses | C | ontrol | | Mean Difference | Mean Difference |
|----------------------|-----------|------------|-------|-------|--------|-------|------------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 22.2.1 Field Study | | | | | | | | |
| Boivin 2012 (police) | 239.6 | 28.5671 | 8 | 255.8 | 31.5 | 9 | -16.20 [-44.75, 12.35] | |
| | | | | | | | | |
| | | | | | | | | -100 -50 0 50 10 |
| | | | | | | | | Favours Combo Treatment Favours Control |

^{*}Boivin 2012: night shift 7 data used, SEM converted to SD

Figure S389. Combination Treatment (Bright light + Glasses) vs Control (Dim-light + No glasses) (Cognitive Performance, PVT reaction speed) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)

| | Bright lig | ht+sungla | sses | C | ontrol | | Mean Difference | Mean Difference |
|----------------------|------------|-----------|-------|------|--------|-------|--------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 22.3.1 Field Study | | | | | | | | |
| Boivin 2012 (police) | 4.17 | 0.4243 | 8 | 3.93 | 0.54 | 9 | 0.24 [-0.22, 0.70] | - |
| | | | | | | | | |
| | | | | | | | | -2 -1 0 1 Favours Control Favours Combo Treat |

^{*}Boivin 2012: night shift 7 data used, SEM converted to SD

Important Outcomes

Figure S390. Combination Treatment (Bright light + Glasses) vs Dim-light + No Glasses (Total Sleep Time, PSG) [CMT = 15 min] RCT (Shift workers without SWD diagnosis)

| | Bright light | + sungla | sses | | Control | | Mean Difference | Mean Difference |
|----------------------|--------------|----------|-------|------|---------|-------|---------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 22.6.1 Lab Study | | | | | | | | |
| Boivin 2012 (nurses) | 426 | 24 | 9 | 396 | 31.1127 | 8 | 30.00 [3.34, 56.66] | |
| | | | | | | | | |
| | | | | | | | | -100 -50 Ó 50 100 |
| | | | | | | | | Favours Control Favours Combo Treatment |

^{*}Boivin 2012 (nurses): SEM converted to SD

Figure S391. Combination Treatment (Bright light + Glasses) vs Dim-light + No Glasses (Total Sleep Time, self-reported) [CMT = 15 min] non-randomized study (Shift workers without SWD diagnosis)

| Exp | eriment | al | (| ontrol | | Mean Difference | | Mean | Differenc | е | |
|-------|---------|---------|------------------------------|--------------------|-----------------------|-----------------------------|---|---|---|---|--|
| Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fix | ed, 95% C | 1 | |
| | | | | | | | | | 400 | | |
| 235.2 | 191.4 | 33 | 220.2 | 178.8 | 33 | 15.00 [-74.36, 104.36] | | | - | | 91 |
| | | | | | | | | | <u> </u> | | 100 |
| | | | | | | | -100 | | U Favour | | 100 o Treatment |
| | Mean | Mean SD | 1474 MATTER - MATTER TO 1244 | Mean SD Total Mean | Mean SD Total Mean SD | Mean SD Total Mean SD Total | Mean SD Total Mean SD Total IV, Fixed, 95% CI | Mean SD Total Mean SD Total IV, Fixed, 95% CI | Mean SD Total Mean SD Total IV, Fixed, 95% CI IV, Fixed 235.2 191.4 33 220.2 178.8 33 15.00 [-74.36, 104.36] ———————————————————————————————————— | Mean SD Total Mean SD Total IV, Fixed, 95% CI IV, Fixed, 95% CI 235.2 191.4 33 220.2 178.8 33 15.00 [-74.36, 104.36] -100 -50 0 | Mean SD Total Mean SD Total IV, Fixed, 95% CI IV, Fixed, 95% CI 235.2 191.4 33 220.2 178.8 33 15.00 [-74.36, 104.36] + |

Figure S392. Combination Treatment (Bright light + Glasses) vs Dim-light + No Glasses (Total Sleep Time, self-reported) [CMT = 15 min] RCT (Healthy participants)

| | Bright Li | ight + Glas | sses | C | ontrol | | Mean Difference | | Mean D | ifference | |
|---------------------|-----------|-------------|-------|-------|--------|-------|------------------------|------|-------------------|-----------------|-------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed, 95% CI | | |
| 20.14.1 Field Study | | | | | | | | | | 3 | |
| Lee 2006 | 380.4 | 69.65 | 11 | 263.4 | 83.14 | 12 | 117.00 [54.49, 179.51] | | | | 100 |
| | | | | | | | | | | | |
| | | | | | | | | -200 | -100 | 0 100 | 201 |
| | | | | | | | | | Favours Contro | Favours BL + GI | asses |

^{*}Lee 2006: Combo (bright light and blue-blocker glasses). Night shift (2300-0700). Experimental received 5x 15min BL pulses (3500 lux) 1/hr on night shift. Wore blue-blocker glasses after nightshift & while driving home. Data extracted from graph (Day sleep after 2nd night shift); SEM converted to SD. Healthy

Figure S393. Combination Treatment (Bright light + Glasses) vs Dim-light + No Glasses (Mental Health, I-PANAS-SF positive mood) [CMT = Not Established] non-randomized study (Shift workers without SWD diagnosis)

| Expe | erimen | tal | C | ontrol | | Mean Difference | Mean Difference | | | | | |
|-------|--------|---------|--------------------------|--------------------|-----------------------|-----------------------------|---|--|---|--|--|--|
| Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, Fixed | 1, 95% CI | | | |
| | | | | | | | | | | | | |
| 15.09 | 4.23 | 33 | 13.81 | 4.72 | 33 | 1.28 [-0.88, 3.44] | | 1 | | | _ | |
| | | | | | | - | - | 1 | | -1 | - 1 | |
| | | | | | | | -4 | -2 Favours Control | Eavoure (| 2 Combo T | 4 | |
| | Mean | Mean SD | 2000-000 000-000 000-000 | Mean SD Total Mean | Mean SD Total Mean SD | Mean SD Total Mean SD Total | Mean SD Total Mean SD Total IV, Fixed, 95% CI | Mean SD Total Mean SD Total IV, Fixed, 95% CI 15.09 4.23 33 13.81 4.72 33 1.28 [-0.88, 3.44] | Mean SD Total IV, Fixed, 95% CI IV, Fixed 15.09 4.23 33 13.81 4.72 33 1.28 [-0.88, 3.44] ———————————————————————————————————— | Mean SD Total Mean SD Total IV, Fixed, 95% CI IV, Fixed, 95% CI 15.09 4.23 33 13.81 4.72 33 1.28 [-0.88, 3.44] -4 -2 0 | Mean SD Total IV, Fixed, 95% CI IV, Fixed, 95% CI 15.09 4.23 33 13.81 4.72 33 1.28 [-0.88, 3.44] | |

Figure S394. Combination Treatment (Bright light + Glasses) vs Dim-light + No Glasses (Mental Health, I-PANAS-SF negative mood) [CMT = Not Established] non-randomized study (Shift workers without SWD diagnosis)

| | Experimental | | | C | ontrol | | Mean Difference | | Me | an Differenc | e | |
|---------------------|--------------|------|-------|------|--------|-------|---------------------|-----------|-------------|--------------|------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV, | Fixed, 95% (| | |
| 22.11.1 Field Study | | | | | | | | | | | | |
| Olson 2020 | 6.05 | 1.76 | 33 | 6.2 | 1.83 | 33 | -0.15 [-1.02, 0.72] | | - | | | |
| | | | | | | | | | - | | | |
| | | | | | | | | -4 | -2 | Ò | Ż | 4 |
| | | | | | | | | Favours C | ombo Treatr | nent Favou | rs Control | |

Figure S395. Bright Light + Fixed Sleep + Glasses vs Control (Circadian Alignment, DLMO in hours) [CMT= Not Established] RCT (Healthy participants)

| | Bright Lig | ht + Glas | ses | Co | ontro | l | | Mean Difference | Mean Difference |
|-----------------------------------|--------------|--------------|---------------|----------|----------|-------|--------|-------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 18.16.1 Lab Study | | | | | | | | | |
| Crowley 2003 | 7.1 | 2.1 | 12 | 2.5 | 2.5 | 10 | 19.3% | 4.60 [2.65, 6.55] | |
| Subtotal (95% CI) | | | 12 | | | 10 | 19.3% | 4.60 [2.65, 6.55] | • |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z= 4.62 (P | < 0.0000 | 1) | | | | | | |
| 18.16.2 Field Study | | | | | | | | | |
| Lee 2006 | 3.2 | 1.3 | 11 | 0.8 | 1 | 12 | 80.7% | 2.40 [1.45, 3.35] | |
| Subtotal (95% CI) | | | 11 | | | 12 | 80.7% | 2.40 [1.45, 3.35] | • |
| Heterogeneity: Not ap | plicable | | | | | | | | |
| Test for overall effect: | Z= 4.93 (P | < 0.0000 | 1) | | | | | | |
| Total (95% CI) | | | 23 | | | 22 | 100.0% | 2.82 [1.97, 3.68] | • |
| Heterogeneity: Chi ² = | 3.94, df = 1 | (P = 0.05) |); $I^2 = 75$ | 5% | | | | | |
| Test for overall effect: | Z = 6.46 (P | < 0.0000 | 1) | | | | | | -10 -5 0 5 10 Favours Control Favours BL + Glasses |
| Test for subaroup diff | erences: Ch | $i^2 = 3.94$ | df = 1.0 | P = 0.05 | i). I² = | 74.6% | 1 | | ravours Control Favours BL + Glasses |

^{*}Crowley 2003: Combo (dark sunglasses and bright light with or without melatonin). Bright light (~5000 lux, 20 min on, 40 min off, 4-5 light pulses/night), phase delay shift in hours.

Lee 2006: Combo (bright light and blue-blocker glasses). Night shift (2300-0700). Experimental received 5x 15min BL pulses (3500 lux) 1/hr on night shift. Wore blue-blocker glasses after nightshift & while driving home. Data extracted from graph (Day sleep after 2nd night shift); SEM converted to SD.

Figure S396. Bright Light vs Control (Circadian Adaptation, Plasma Melatonin (tmidpoint)) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)

| | Brig | ht Lig | ht | (| Control | | Mean Difference | Mean Difference |
|---------------------------|------|--------|-------|------|---------|-------|--------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 26.29.1 Field Study | | | | | | | | |
| Biovin 2002 (bio rhythms) | 15.1 | 7.44 | 9 | 9 | 2.7436 | 8 | 6.10 [0.88, 11.32] | 1 |
| | | | | | | | | -20 -10 0 10 20 |
| | | | | | | | | -20 -10 0 10 Favours Control Favours Bright Light |

^{*}Boivin 2002: SEM converted to SD, data following the night shifts

Figure S397. Bright Light vs Control (Circadian Adaptation, Plasma Melatonin (phase angle)) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)

| | Brig | ht Lig | ht | (| Control | | Mean Difference | | M | lean Differ | ence | |
|---------------------------|-------|--------|-------|------|---------|-------|-----------------------|-----|-----|--------------|-----------------|----|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | | IV | /, Fixed, 95 | 5% CI | |
| 21.29.1 Field Study | | | | | | | | | | 155 | | |
| Biovin 2002 (bio rhythms) | -5.54 | 2.76 | 9 | 0.62 | 7.1559 | 8 | -6.16 [-11.44, -0.88] | | - | - | | |
| | | | | | | | | -20 | -10 | | 10 | 20 |
| | | | | | | | | | | t Light Fa | vours Dim Light | 20 |

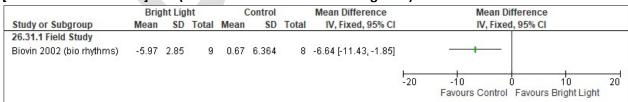
^{*}Boivin 2002: SEM converted to SD, data following the night shifts

Figure S398. Bright Light vs Control (Circadian Adaptation, Core body temperature (t_{mint})) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)

| | Brigh | ht Lig | ht | (| Control | | Mean Difference | Mean Difference |
|---------------------------|-------|--------|-------|------|---------|-------|--------------------|--------------------------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 26.32.1 Field Study | | | | | | | | |
| Biovin 2002 (bio rhythms) | 15.52 | 3 | 9 | 8.96 | 6.2225 | 8 | 6.56 [1.82, 11.30] | |
| | | | | | | | | -20 -10 0 10 20 |
| | | | | | | | | Favours Control Favours Bright Light |

^{*}Boivin 2002: SEM converted to SD, data following the night shifts

Figure S399. Bright Light vs Control (Circadian Adaptation, Core body temperature (phase angle)) [CMT = Not Established] RCT (Shift workers without SWD diagnosis)



^{*}Boivin 2002: SEM converted to SD, data following the night shifts

Figure S400. Combination Treatment (Bright light + Glasses) vs Dim-light + No Glasses (Sleep Latency, PSG) [CMT = 15 min] RCT (Shift workers without SWD diagnosis)

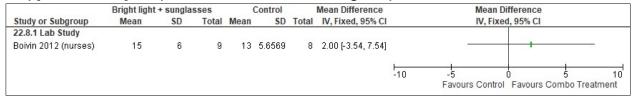


Figure S401. Combination Treatment (Bright light + Glasses) vs Dim-light + No Glasses (Sleep Latency, Self-reported) [CMT = 15 min] non-randomized study (Shift workers without SWD diagnosis)

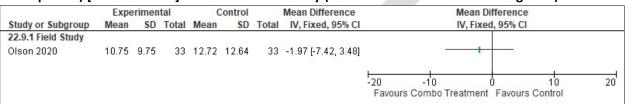


Figure S402. Combination Treatment (Bright light + Glasses) vs Dim-light + No Glasses (Sleep Efficiency, PSG) [CMT = 10%] RCT (Shift workers without SWD diagnosis)

| | Bright light | (| Control | Mean Difference | | Mean Difference | | |
|----------------------|---------------------|----|---------|-----------------|--------|-----------------|---------------------|--|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | IV, Fixed, 95% CI | IV, Fixed, 95% CI |
| 22.12.1 Lab Study | | | | | | | | 1 |
| Boivin 2012 (nurses) | 92 | 3 | 9 | 88 | 8.4853 | 8 | 4.00 [-2.20, 10.20] | 1 |
| | | | | | | | | |
| | | | | | | | | -20 -10 0 10 Favours Control Favours Combo Treatmen |