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## Appendix A: PRIO-harms Checklist

| Section/Topic (Sub-)item # | Checklist item                                                                 | Reported on page |
|----------------------------|--------------------------------------------------------------------------------|-----------------|
| **TITLE**                  |                                                                                  |                 |
| 1. Title                   | Specifying the study design with terms such as “overview of (systematic) reviews,” “umbrella review,” “(systematic) review of systematic reviews,” or “(systematic) meta-review” in the title of the OoSRs. | 1               |
| 1b                         | Mention “safety” or harms related terms, or the adverse event(s) of interest in the title of the OoSRs. | 1               |
| **ABSTRACT**               |                                                                                  |                 |
| 2. Structured-like summary | Provide a structured-like abstract, as applicable: background, objective, data sources, selection criteria, data extraction, review appraisal, data synthesis methods, results, limitations, conclusions. | 3-4             |
| 2b                         | Report the main findings of analysis of harms undertaken in the OoSRs or/and in the included SRs. | 3-4             |
| **INTRODUCTION**           |                                                                                  |                 |
| 3a                         | Specify the rationale and the scope (wide or narrow agendas) for the overview in the context of an existing body of knowledge on the topic. | 5-6             |
| 3b                         | Provide a balanced presentation of potential benefits and harms of the intervention(s). | 5-6             |
| 3c                         | Define which events are considered harms according to previous literature and provide a clear rationale for the specific harms included in the OoSRs. | N/A             |
| 4. Objectives (PICOS)      | Provide an explicit statement of research question(s) that specifies PICOS:       | 6               |
| 4a                         | Participants [y] Interventions [y] Comparators [y] Outcomes [y] Study design [y] |                 |
| **METHODS**                |                                                                                  |                 |
| 5a                         | Indicate clearly if a protocol exists or not.                                   | 6               |
| 5b                         | If registered, provide the name of the registry (such as a valid Web address, PROSPERO). | 6               |
| 6a                         | Specify inclusion and exclusion criteria for study design, participants, interventions and comparators in detail. | 7               |
| 6b                         | List (and define whenever it is necessary) the outcomes for which data were recorded, ideally include prioritization of main and additional outcomes. | 7               |
| Section/Topic                      | (Sub-)item # | Checklist item                                                                                                                                                                                                 | Reported on page # |
|-----------------------------------|--------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|
| interest                          | 6c           | Include adverse events as (primary or secondary) outcome of interest. Define them and grade their severity (such as mild, moderate, severe, fatal; severity could also be described in the appendix), if appropriate. | 7-8               |
|                                   | 6d<sup>b</sup> | Specify report characteristics (such as language restrictions, publication status, and years considered) used as criteria for eligibility for the OoSRs (see also item 7). | 8                 |
| 7. Information sources            | 7a           | Search at least two electronic bases.                                                                                                                                                                         | 8                 |
|                                   | 7b           | Search supplementary sources (e.g. hand-searching, reference lists, related reviews and guidelines, protocol registries, conference abstracts, and other gray literature). | 8                 |
|                                   | 7c           | Report the date last searched and/or dates of coverage for each database.                                                                                                                                       | 8                 |
| 8. Search strategy<sup>c</sup>    | 8a           | Specify full electronic search strategy (algorithm) for at least one database including any limits used (e.g. language and date restrictions—see also subitems 6d and 7c) such that it could be repeated. | Appendix B        |
|                                   | 8b           | Present any additional search process (e.g. algorithm or filter for adverse events, searches in pertinent websites) specifically to identify adverse events that have been investigated. | Appendix B        |
| 9. Data management & selection    | 9a<sup>d</sup> | Describe the software that was used to manage records and data throughout the OoSRs.                                                                                                                          | 9                 |
| process                           | 9b           | Define what is a SR and provide the process for selecting SRs and its relevant details (screening the title and abstract or full text by at least two reviewers, selection by multiple independent investigators and resolving disagreements by consensus). | 9                 |
|                                   | 9c           | Report any attempt to handle overlapping (include one review among multiple potential candidates by choosing for example the most updated SR, the most methodologically rigorous SR or the SR with larger number of primary studies). | 9                 |
| 10. Additional search for         | 10           | Report additional search to identify eligible primary studies (e.g. searching in more databases or update the search) and its relevant details.                                                                | N/A               |
| primary studies                   |              |                                                                                                                                                                                                              |                   |
| 11. Data collection process       | 11a          | Describe the method of data extraction from included SRs (e.g. data collection form, extraction in duplicate and independently, resolving disagreements by consensus).                                               | 9                 |
|                                   | 11b          | Report any processes for obtaining, confirming or updating data from investigators (e.g. contact with authors of included reviews, obtain data from primary studies of included reviews).                  | N/A               |
| Section/Topic | (Sub-)item # | Checklist item | Reported on page # |
|---------------|-------------|----------------|-------------------|
| 12. Data items | 12 | List (and define whenever is necessary) the specific variables for which data were recorded (e.g. PICOS items, number of included studies and participants, dose, length of follow up, results, funding sources) and any data assumptions and simplifications made. | 9 |
| 13. Assessment of methodological quality & quality of evidence | 13a | State the evaluation of reporting or/and methodological quality (eg. using PRISMA or PRISMA-harms, AMSTAR or R-AMSTAR) of the included reviews. | 10 |
| | 13b | State the evaluation of quality for individual studies that were included in the SRs (inform whether tools such as Jadad or RoB of Cochrane were used by the included reviews) and for the additional primary studies. | N/A |
| | 13c | State the evaluation of quality of evidence (e.g. using GRADE approach). | N/A |
| | 13d | Describe the methods (e.g. piloted forms, independently, in duplicate) used for the quality assessment. | 10 |
| 14. Meta-bias(es) | 14 | Specify any planned assessment of meta-bias(es) (such as publication bias or selective reporting across studies, ROBIS tool). | N/A |
| 15. Data synthesis | 15a | Specify clearly the method (narrative, meta-analysis or network meta-analysis) of handling or synthesizing data and their details (e.g. state the principal summary measures that were extracted or calculated, how heterogeneity was assessed, what statistical approaches were used if a quantitative synthesis has been conducted). | 10 |
| | 15b | Describe the software that was used to analyze the data if a quantitative synthesis has been conducted. | N/A |
| | 15c | Report if zero events are included in the studies and how they were handled in statistical analyses, if relevant. | N/A |
| | 15d | Describe methods of any pre-specified additional analyses (such as sensitivity or subgroup analyses, meta-regression). | N/A |
| RESULTS | | | |
| 16. Review & primary study selection | 16a | Provide the details of review selection (e.g. numbers of reviews screened, retrieved, and included and excluded in the overview) and the number of the additional eligible primary studies that were included, ideally with a flow diagram of the overview process. | 10 |
| | 16b | Present a flow diagram that gives separately the number of studies focused on harms outcomes. | Figure 1 |
| | 16c | List the studies (full citation) that were excluded after reading the full text and provide reasons. | N/A |
| 17. Review & primary study characteristics | 17a | Describe characteristics of each included SR in tables (such as title or author, search date, PICOS, design and number of studies included, number and age range of participants, dose/frequency, follow up period [treatment duration], review limitations, results or conclusion) and of each additional primary study. | 10-11, Table 1-2, Appendix C |
| | 17b | For each included SR report language and publication status restrictions that have been used. | N/A |
| Section/Topic | (Sub-) item # | Checklist item | Reported on page # |
|--------------|--------------|----------------|-------------------|
| 18. Overlapping | 18 | Present or/and discuss about overlapping of studies within SRs (at least one of the following): | 12-17 |
| | | • Present measures of overlap (such as CCA). | N/A |
| | | • Provide citation matrix. | Appendix F |
| | | • Give the number of index publications or/and discuss about overlapping. | 12-17 |
| 19. Present assessment of methodological quality & quality of evidence | 19 | Present results in text or/and tables of any quality assessment (see also subitems 13a-c): | 12, Figure 2, Appendix D |
| | | • Reporting or/and methodological quality of the included SRs. | 12, Figure 2, Appendix D |
| | | • Inform for the quality of the individual studies that were included in the SRs (report results for sequence generation, allocation concealment, blinding, withdrawals, bias etc.) and for the additional included primary studies. | N/A |
| | | • Quality of evidence. | N/A |
| 20. Present meta-bias(es) | 20 | Present results of any assessment of meta-bias(es) (such as publication bias or selective reporting across studies, ROBIS assessment). | N/A |
| 21. Synthesis of results | 21a | Summarize and present the main findings of the overview for benefits and harms. If a quantitative synthesis has been conducted, present each summary measure with a confidence interval, prediction interval or a credible interval and measures of heterogeneity or inconsistency. | 13-17, Table 3, Appendix E |
| | 21b | Give results of any additional analyses (such as sensitivity, subgroup analyses, or meta-regression). | N/A |
| | 21c | Report results for adverse events separately for each intervention. | 13-17 |
| DISCUSSION | 22 | Provide a concise summary of the main findings with the strength and shortcomings of evidence for each main outcome. | 18-19 |
| 23. Limitations | 23a | Discuss limitations of either the overview or included studies (or both) (e.g. different eligibility criteria, limitations of searching reviews, language restrictions, publication and selection bias). | 19-20 |
| Section/Topic       | (Sub-) item # | Checklist item                                                                                                                                                                                                 | Reported on page # |
|--------------------|--------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|
| 24. Conclusions    | 23b          | Report possible limitations of the included reviews related to harms (issues of missing data and information, definitions of harms, rare adverse effects).                                                       | 18-19             |
|                    | 24a          | Provide a general interpretation of the results in coherence with the review findings and present implications for practice; consider the harms equally as carefully as the benefits and in the context of other evidence. | 20                |
|                    | 24b          | Present implications for future research.                                                                                                                                                                     | 18-20             |
| 25. Contributions  | 25           | Provide contributions of authors.                                                                                                                                                                            | 26                |
| of authors         |              |                                                                                                                                                                                                            |                   |
| 26. Dual (co-)authorship | 26        | Report about dual (co-)authorship in the limitation or declarations of interest section.                                                                                                                                 | N/A               |
| 27. Funding or     | 27a          | Indicate sources of financial and other support for the OoSRs (direct funding) or for the authors (indirect funding), or report no funding.                                                                 | 26                |
| other support      | 27b          | Provide name for the overview funder and/or sponsor, or for the authors’ supporters.                                                                                                                                 | 6, 26             |
|                    | 27c          | Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in conducted the OoSRs.                                                                                                                                 | 6, 26             |
Appendix B: Database Search Strategy and List of Grey Literature search sites

**Multi-database search Strategy**

1. exp "Sleep Initiation and Maintenance Disorders"/
2. (insomni* or hyposomni*).tw,kw.
3. (sleep* adj3 initiat* adj3 (disorder* or dysfunction* or problem*)).tw,kw.
4. (sleep* adj3 (mainten* or maintain*) adj3 (disorder* or dysfunction* or problem*)).tw,kw.
5. ((difficult* or disturb* or inabilit* or unable* or problem* or reduced) adj3 (asleep or sleep*)).tw,kw.
6. sleepless*.tw,kw.
7. (early adj1 (awake* or wake or wakes or waking)).tw,kw.
8. or/1-7 [INSOMNIA]
9. exp Child/ not (exp Aadult/ and exp Child/)
10. exp Infant/ not (exp Adult/ and exp Infant/)
11. 8 not (9 or 10) [CHILD-ONLY REMOVED]
12. exp Animals/ not (exp Animals/ and Humans/)
13. 11 not 12 [ANIMAL-ONLY REMOVED]
14. (comment or editorial or interview or news).pt.
15. (letter not (letter and randomized controlled trial)).pt.
16. 13 not (14 or 15) [OPINION PIECES REMOVED]
17. limit 16 to systematic reviews
18. meta analysis.pt.
19. exp meta-analysis as topic/
20. (meta-analy* or metanaly* or metaanaly* or met analy* or integrative research or integrative review* or integrative review* or research integration or research review* or collaborative review*).tw,kw.
21. (systematic review* or systematic review* or evidence-based review* or evidence-based review* or (evidence adj3 (review* or review*)) or meta-review* or meta-review* or meta-synthes* or "review of reviews" or technology assessment* or HTA or HTAs).tw,kw.
22. exp Technology assessment, biomedical/
23. (cochrane or health technology assessment or evidence report).jw.
24. (network adj (MA or MAs)).tw,kw.
25. (NMA or NMAs).tw,kw.
26. indirect comparison?.tw,kw.
27. (indirect treatment* adj1 comparison?).tw,kw.
28. (mixed treatment* adj1 comparison?).tw,kw.
29. (multiple treatment* adj1 comparison?).tw,kw.
30. (multi-treatment* adj1 comparison?).tw,kw.
31. simultaneous comparison?.tw,kw.
32. mixed comparison?.tw,kw.
33. or/18-32
34. 16 and 33
35. 17 or 34 [SYSTEMATIC REVIEWS]
36. 35 use ppez [MEDLINE RECORDS]
37. exp insomnia/
38. (insomni* or hyposomni*).tw,kw.
39. (sleep* adj3 initiat* adj3 (disorder* or dysfunction* or problem*)).tw,kw.
40. (sleep* adj3 (mainten* or maintain*) adj3 (disorder* or dysfunction* or problem*)).tw,kw.
41. ((difficult* or disturb* or inabilit* or unable* or problem* or reduced) adj3 (asleep or sleep*)).tw,kw.
42. sleepless*.tw,kw.
43. (early adj1 (awake* or wake or wakes or waking)).tw,kw.
44. or/37-43 [INSOMNIA]
45. exp juvenile/ not (exp juvenile/ and exp adult/)
46. exp Child/ not (exp Adult/ and exp Child/)
47. exp Infant/ not (exp Adult/ and exp Infant/)
48. or/45-47
49. 44 not 48 [CHILD-ONLY REMOVED]
50. exp animal experimentation/ or exp models animal/ or exp animal experiment/ or nonhuman/ or exp vertebrate/
51. exp human/ or exp human experimentation/ or exp human experiment/
52. 50 not 51
53. 49 not 52 [ANIMAL-ONLY REMOVED]
54. editorial.pt.
55. letter.pt. not (letter.pt. and randomized controlled trial/)
56. 53 not (54 or 55) [OPINION PIECES REMOVED]
57. meta-analysis/
58. "systematic review"/
59. "meta analysis (topic)"/
60. (meta-ana* or metanal* or metaanalyzer* or met analyzer* or integrative research or integrative review* or integrative review* or research integration or research review* or collaborative review*).tw,kw.
61. (systematic review* or systematic review* or evidence-based review* or evidence-based review* or (evidence adj3 (review* or review*)) or meta-review* or meta-review* or meta-synthes* or "review of reviews" or technology assessment* or HTA or HTAs).tw,kw.
62. biomedical technology assessment/
63. (cochrane or health technology assessment or evidence report).jw.
64. (network adj (MA or MAs)).tw,kw.
65. (NMA or NMAs).tw,kw.
66. indirect comparison?.tw,kw.
67. (indirect treatment* adj1 comparison?).tw,kw.
68. (mixed treatment* adj1 comparison?).tw,kw.
69. (multiple treatment* adj1 comparison?).tw,kw.
70. (multi-treatment* adj1 comparison?).tw,kw.
71. simultaneous comparison?.tw,kw.
72. mixed comparison?.tw,kw.
73. or/57-72
74. 56 and 73 [SYSTEMATIC REVIEWS]
75. 74 use emcnd [EMBASE RECORDS]
76. Insomnia/
77. (insomni* or hyposomni*).tw,kw.
78. (sleep* adj3 initiat* adj3 (disorder* or dysfunction* or problem*)).tw,kw.
79. (sleep* adj3 (mainten* or maintain*) adj3 (disorder* or dysfunction* or problem*)).tw,kw.
80. ((difficult* or disturb* or inabilit* or unable* or problem* or reduced) adj3 (asleep or sleep*)).tw,kw.
81. sleepless*.tw,kw.
82. (early adj1 (awake* or wake or wakes or waking)).tw,kw.
83. or/76-82 [INSOMNIA]
84. Meta Analysis/
85. (meta-analy* or metanaly* or metaanaly* or met analy* or integrative research or integrative review* or integrative review* or research integration or research review* or collaborative review*).tw,kw.
86. (systematic review* or systematic review* or evidence-based review* or evidence-based review* or (evidence adj3 (review* or review*)) or meta-review* or meta-review* or meta-synthes* or "review of reviews" or technology assessment* or HTA or HTAs).tw,kw.
87. (network adj (MA or MAs)).tw,kw.
88. (NMA or NMAs).tw,kw.
89. indirect comparison??.tw,kw.
90. (indirect treatment* adj1 comparison?).tw,kw.
91. (mixed treatment* adj1 comparison?).tw,kw.
92. (multiple treatment* adj1 comparison?).tw,kw.
93. (multi-treatment* adj1 comparison?).tw,kw.
94. simultaneous comparison?.tw,kw.
95. mixed comparison?.tw,kw.
96. or/84-95
97. 83 and 96 [SYSTEMATIC REVIEWS]
98. 97 use ppez
99. 97 use emcnd
100. 97 not (98 or 99) [PSYCINFO RECORDS]
101. 36 or 75 or 100 [ALL DATABASES]

List of Grey Literature search sites

- Health Technology Assessment Sites
  - Canadian Agency for Drugs and Technologies in Health (www.cadth.ca)
  - Agency for Healthcare Research and Quality (www.ahrq.gov)
  - The International Network of Agencies for Health Technology Assessment (www.inahta.org)
  - National Institute for Health and Care Excellence (www.nice.org.uk)
- International prospective register of systematic reviews (PROSPERO: https://www.crd.york.ac.uk/prospero/)
### Appendix C: Review, participant, and intervention characteristics

| Author, Year | Country | Sample size | Literature search dates | # and type of included studies | Age and Sex [mean (SD)]; % female | Co-morbidities | Treatment comparison (doses [mg]) | Delivery method and setting | Frequency; duration of treatment; length of follow-up (range, weeks) |
|--------------|---------|-------------|--------------------------|-------------------------------|----------------------------------|----------------|----------------------------------|-----------------------------|------------------------------------------------------------------------------------------------|
| Ballesio, 2017 | Germany | 4,317 | 1986-2014 | 47 RCTs | 51.9 (NR); 62.8% | None | CBT-I group v control | | |
| | | | | Intervention: 2,448 | Control: 1,869 | | CBT-I individual v control | | | |
| | | | | | | | CBT-I self-help v control | | NR; NR; NR |
| | | | | 1986-2014 | | | Group behavioural therapy v control | | |

**Systematic Reviews with Meta-analysis (n=35)**

| Brasure, 2015 | USA | 5764 | 2004-2015 | 46 RCTs | NR | Pain, chronic low back pain, hearing impairment | Zolpidem (10 or 15mg) v placebo outpatient | “as needed”; NR; 4 to 34.76 |
|---------------|-----|-----|-----------|---------|-----|----------------------------------|-----------------------------|------------------------------------------------------------------------------------------------|
| | | | | | | | Doxepin (1, 3, or 6 mg) v placebo outpatient | NR; NR; 4 to 12 |
| | | | | | | | Suvorexant (15 or 20mg) v placebo | NR; NR; 4 |
| | | | | | | | CBT-I v control (placebo/sham treatment, wait-list, no treatment, or sleep hygiene/sleep education) | Once a week; ≤1 hour; 4 to 104 |
| | | | | | | | Individual or group (in-person), Phone, Self-help (books, handouts, or electronic resources); outpatient | | |
| | | | | | | | Group behavioural therapy v control | | |
| Author, Year      | Country | # and type of included studies | Sample size | Literature search dates | Age and Sex [mean (SD)]; % female | Treatment comparison (doses [mg]) | Delivery method and setting | Co-morbidities | Frequency; duration of treatment; length of follow-up (range, weeks) |
|-------------------|---------|--------------------------------|-------------|-------------------------|-----------------------------------|----------------------------------|-----------------------------|-----------------|---------------------------------------------------------------|
| Buscemi, 2004     | Canada  | 139 RCTs                        | NR          | NR-2003                 | NR                                | Melatonin (0.1, 0.3, 0.5, 1, 2, 3, 5, or 6 mg) v placebo | Oral - sustained-release, fast-release, or immediate-release | Sleep restriction v control |
|                   |         |                                |             |                         |                                   |                                  |                             | Relaxation therapy v control |
|                   |         |                                |             |                         |                                   |                                  |                             | Behavioural intervention or brief behavioral therapy v control |
|                   |         |                                |             |                         |                                   |                                  |                             | Outpatient |
|                   |         |                                |             |                         |                                   |                                  |                             | Control conditions: sham treatment/placebo, wait-list control, no treatment, or sleep hygiene/sleep education |
| Buscemi, 2005     | Canada  | 97 RCTs                         | NR          | NR-2004                 | NR                                | Flurazepam (15 or 30 mg) v placebo | Temazepam (15, 20, or 30 mg) v placebo | Triazolam (0.125, 0.25, or 0.5 mg) v placebo |
|                   |         |                                |             |                         |                                   |                                  |                             | Zolpidem (5, 10, 15, or 20 mg) v placebo |
|                   |         |                                |             |                         |                                   |                                  |                             | Zopiclone (7.5 mg) v placebo |
|                   |         |                                |             |                         |                                   |                                  |                             | Melatonin (0.1, 0.3, 0.5, 1, 2, 3, or 5 mg) v placebo |
|                   |         |                                |             |                         |                                   |                                  |                             | Doxepin (25 mg or 25 -50 mg) v placebo |
|                   |         |                                |             |                         |                                   |                                  |                             | Trazodone (50 mg; 150 -250 mg) v placebo |
|                   |         |                                |             |                         |                                   |                                  |                             | CBT v placebo |
| Author, Year | Country | # and type of included studies | Sample size | Literature search dates | Age and Sex [mean (SD)]; % female | Treatment comparison (doses [mg]) | Co-morbidities | Delivery method and setting | Frequency; duration of treatment; length of follow-up (range, weeks) |
|--------------|---------|--------------------------------|-------------|-------------------------|-----------------------------------|--------------------------------|---------------|-----------------------------|---------------------------------------------------------------|
| Cheng, 2012  | Hong Kong | 6 RCTs                          | 431         | 1990-2011               | Cancer-related insomnia           | CBT + relaxation v placebo       | CBT + relaxation v placebo | Computer or mobile phone; Home-based                          | NR; 5 to 9; 3 to 26                                           |
| Ferracioli-Oda, 2013 | USA       | 19 RCTs                          | 1683        | NR                     | Delayed sleep phase disorder, REM sleep behaviour disorder | Melatonin (0.1, 0.3, 0.5, 1, 2, 3, or 5 mg) v placebo | CBT-I (sleep hygiene, stimulus control, relaxation training, sleep restriction, cognitive restructuring, relapse prevention, psychoeducation) v control (wait-list control, sleep-monitoring) | NR; NR; 1 to 26                                           |
| Ferracioli-Oda, 2013 | USA       | 19 RCTs                          | 1683        | NR                     | Delayed sleep phase disorder, REM sleep behaviour disorder | Melatonin (0.1, 0.3, 0.5, 1, 2, 3, or 5 mg) v placebo | CBT-I (sleep hygiene, stimulus control, relaxation training, sleep restriction, cognitive restructuring, relapse prevention, psychoeducation) v control (wait-list control, sleep-monitoring) | NR; NR; 1 to 26                                           |
| Author, Year | Country       | # and type of included studies | Sample size | Literature search dates | Age and Sex [mean (SD)]; % female | Co-morbidities | Treatment comparison (doses [mg]) | Delivery method and setting | Literature search dates | Frequency; duration of treatment; length of follow-up (range, weeks) |
|--------------|---------------|--------------------------------|-------------|-------------------------|-----------------------------------|----------------|-----------------------------------|-----------------------------|-------------------------|---------------------------------------------------------------------|
| Gong, 2016   | China         | 6 RCTs                         | 330         | Inception-2015          | NR                                | Depression, cancer | Mindfulness based stress reduction, mindfulness meditation, or mindfulness based therapy for insomnia v control (wait-list control, sleep hygiene education, self-monitoring) | Mindfulness based stress reduction, mindfulness meditation, or mindfulness based therapy for insomnia v control (wait-list control, sleep hygiene education, self-monitoring) | Inception-2015 | NR; NR; 6 -8                                                              |
| Ho, 2015     | Hong Kong     | 20 RCTs                        | 2411        | Inception-2013          | 49.3 (NR); 74.2%                  | None            | CBT (stimulus control, sleep restriction, sleep hygiene, relaxation, cognitive therapy) v control (wait-list control, routine care, or no treatment) | Self-help; home              | Inception-2013 | NR; NR; 4 to 52                                                             |
| Ho, 2016     | Hong Kong     | 11 RCTs                        | Intervention: 303 Control: 290 | Inception-2014          | 45.3 (NR); 35.6%                  | PTSD, depression | CBT (image rehearsal therapy, exposure, rescripting and relaxation therapy, mind-body bridging, behavioural sleep intervention) v control (wait list control, sleep hygiene, or placebo) | Individual or group delivery | Inception-2014 | NR; 2 -12; 1 to 26                                                          |
| Hwang, 2016  | South Korea   | 37                             | 13 RCTs     | 24 Quasi-experimental   | NR                                | NR              | Behavioural therapy v control (unspecified)                                | Behavioural therapy v control (unspecified)                          | 206 Quasi-experimental | NR; NR; NR                                                                  |
| Irwin, 2006  | United States | 23 RCTs                        | NR          | 1966-2004               | NR                                | None            | CBT (relaxation/biofeedback/hypnosis, sleep compression/restriction, paradoxical intention) v control (unspecified) | CBT (relaxation/biofeedback/hypnosis, sleep compression/restriction, paradoxical intention) v control (unspecified) | 1966-2004 | NR; NR; NR                                                                  |
| Johnson, 2016|               | 8 RCTs                         | NR          |                         | NR                                | NR              | CBT-I v control (wait-list control, treatment as usual, sleep)              | CBT-I v control (wait-list control, treatment as usual, sleep)          |                         | NR; NR; 13 to 52                                                            |
| Author, Year | Country | # and type of included studies | Sample size | Literature search dates | Age and Sex [mean (SD)]; % female | Co-morbidities | Treatment comparison (doses [mg]) | Delivery method and setting | Frequency; duration of treatment; length of follow-up (range, weeks) |
|--------------|---------|-------------------------------|-------------|-------------------------|----------------------------------|----------------|----------------------------------|-----------------------------|-------------------------------------------------|
| Canada       | 752     | Intervention: 434 Control: 318 | Cancer      | Inception-2014          | 56.6 (NR); 61.8%                  | None           | Suvorexant (10 -80mg/day) v placebo | Individual, group, video or online-based          | NR; NR; 4 to 52                                   |
| Kishi, 2015  | Japan   | 4 RCTs                        | 3076        | NR-2015                 | 56.6 (NR); 61.8%                  | None           | Suvorexant (10 -80mg/day) v placebo | Individual, group, video or online-based          | NR; NR; 4 to 52                                   |
| Koffel, 2015 | USA     | 8 RCTs                        | NR          | NR-2013                 | NR                               | Chronic pain, cancer, fibromyalgia, chronic illness, arthritis | CBT-I (stimulus control, sleep restriction, addressing dysfunctional beliefs about sleep) v control (wait-list, treatment as usual, placebo) | >1 session; NR; 13.04 to 52                       |
| Kuriyama, 2017 | Japan | 4 RCTs                        | 3076        | NR-2016                 | 56.3 (15.3); 61.5%                | None           | Suvorexant (10, 15, 20, 30, 40, or 80mg/d) v placebo | Group delivery; community-based                  | NR; NR; 4 to 52                                   |
| Lee, NA [unpublished] | South Korea | 18 RCTs                      | NR          | NR-2014                 | NR                               | None           | Melatonin (0.1, 0.3, 1, 2, 5, 12, or 75 mg; 0.05, 0.1, or 0.15 mg/kg) v placebo | Transbuccal; sustained release, fast release, controlled release, or prolonged release | NR; 4 days to 26 weeks; NR                      |
| Liu, 2017    | China   | 7 RCTs                        | NR          | NR-2014                 | NR                               | None           | Doxepin (1, 3, or 6 mg) v placebo | Individual, group, video or online-based          | NR; NR; NR                                    |
| Author, Year       | Country | Sample size | Literature search dates | # and type of included studies | Age and Sex | Co-morbidities | Treatment comparison (doses [mg]) | Delivery method and setting | Frequency; duration of treatment; length of follow-up (range, weeks) |
|-------------------|---------|-------------|--------------------------|--------------------------------|-------------|----------------|-----------------------------------|-------------------------------|-------------------------------------------------|
| McCleery, 2016    | UK      | 222         | NR-2016                  | 3 RCTs                         | NR          | Dementia       | Melatonin (5 or 1 mg immediate-release, 2 or 2.5 mg slow-release) v placebo | Tablet; long-term care and community care | Nightly (1-2 hours before bedtime); NR; 8 to 28 |
| Montgomery, 2003  | USA     | 282         | Inception 2002           | 6 RCTs                         | NR          | Parasomnia, sleep apnea | CBT (sleep hygiene, stimulus control, muscle relaxation, sleep restriction, cognitive therapy, education, imagery training) v control (wait-list control, placebo) | Group or individual delivery | NR; NR; 13 to 104 |
| Navarro-Bravo, 2015 | Spain  | 699         | NR-2012                  | 9 RCTs                         | NR          | Cancer survivor, depression, restless leg syndrome, osteoarthritis | CBT (sleep restriction, stimulus control, sleep education/hygiene) v control (placebo, wait-list control, stress management and wellness training, treatment as usual, sleep hygiene/education) | | NR; NR; 5 to 8 |
| Okajima, 2011     | Japan   | 454         | 1990-2009                | 14 RCTs                        | NR          | None           | CBT (sleep hygiene education, sleep restriction, stimulus control, cognitive therapy, relaxation, paradoxical intention) v control (placebo, wait-list control, treatment as usual, sleep hygiene education) | Individual or group delivery | 1 – 8 sessions; NR; 4 to 104 |
| Sateia, 2017      | USA     | 129 RCTs    | NR-2016                  | 129 RCTs                       | NR          | None           | Temazepam (15 mg) v placebo | | NR; 5 days to 8 weeks; NR |
|                   |         | 46 in MA    |                          |                                |             |                | Zolpidem (10 mg) v placebo | | NR; 2 to 32; NR |
|                   |         |             |                          |                                |             |                | Melatonin (2 mg) v placebo | | Nightly; 3; NR |
| Author, Year | Country | Sample size | Literature search dates | # and type of included studies | Age and Sex [mean (SD)]; % female | Co-morbidities | Treatment comparison (doses [mg]) | Delivery method and setting | Frequency; duration of treatment; length of follow-up (range, weeks) |
|-------------|---------|-------------|-------------------------|-------------------------------|----------------------------------|----------------|----------------------------------|-----------------------------|-------------------------------------------------------------------|
| Seda, 2015  | USA     | NR          | NR-2016                 | NR                           | PTSD, nightmares                 | NR             | Doxepin (3 mg) v placebo          | Face-to-face, group, self-help; outpatient                        | NR; 2 nights to 12 weeks; NR                                      |
| Seyffert, 2016 | USA   | 2392        | NR-2015                 | NR                           | Major depression                 | Diphenhydramine (50 mg) v placebo | Imagery rehearsal therapy v CBT (stimulus control, sleep restriction therapy) + Imagery rehearsal therapy | Weekly; NR; 4 to 48                                               |
| Soldatos, 1999 | Greece | 1276        | 1966-1997               | 75 (designs NR)              | None                             | Triazolam (0.25 or 0.5 mg) v placebo | CBT (sleep education, stimulus control, sleep restriction, relaxation, sleep hygiene, cognitive techniques) v control (wait-list control, internet control, treatment as usual) | NR; 1 to 42 nights; NR                                               |
| Tang, 2015   | UK      | 1066        | 965 in MA               | 11 RCTs                      | Chronic pain, cancer, back pain, arthritis | CBT-I (psychoeducation, sleep hygiene, stimulus control, sleep restriction, cognitive therapy, relaxation) v control (waitlist, treatment as usual, sleep hygiene advice, healthy eating/nutrition advice) | Face-to-face, phone, internet, group or individual delivery        | 3 to 7 sessions averaging 69 to 120 minutes; 60 days; 13 to 52   |
| Trauer, 2015 | Australia | 1162        | Inception-2015          | 20 RCTs                      | None                             | CBT (cognitive therapy, stimulus control, sleep restriction, relaxation, sleep hygiene) v control (wait-list, treatment as usual, sleep hygiene, sham, placebo) | Group or individual delivery with aids such as telephone,          | NR; NR; 4 to 48                                                   |
| Author, Year | Country | # and type of included studies | Sample size | Literature search dates | Age and Sex [mean (SD)]; % female | Treatment comparison (doses [mg]) | Delivery method and setting | Co-morbidities | Literature search dates | Sample size | Literature search dates | Treatment comparison (doses [mg]) | Delivery method and setting | Co-morbidities |
|--------------|---------|--------------------------------|-------------|--------------------------|----------------------------------|----------------------------------|-----------------------------|----------------|--------------------------|-------------|--------------------------|----------------------------------|-----------------------------|----------------|
| van Straten, 2009 | Netherlands | 10 RCTs 9 in MA | 1000 Intervention: 580 | Control: 420 | NR | Alcohol dependence, chronic disease | CBT (self-help, stimulus control, sleep restriction, cognitive therapy, sleep hygiene, relaxation, in-bed exercises) v wait-list control | Audiotape, videotape, written materials; internet + face-to-face, telephone, or e-mail support; home delivery (self-help) | NR-2007 | | | Weekly; NR; 17 to 43.5 |
| van Straten, 2007 | Netherlands | 87 RCTs | 6303 Intervention: 3724 | Control: 2579 | NR | chronic pain; cancer; hearing problems; post-traumatic stress disorder; chronic obstructive pulmonary disease | CBT (relaxation, sleep restriction, stimulus control, paradoxical intention, identifying and challenging dysfunctional thought) v control (wait-list, no treatment, psycho-education, placebo) | Group, individual, phone, or self-help delivery | NR-2015 | | | NR; 2 to 16 sessions; NR |
| Xu, 2015 | China | 6 RCTs | 484 | | NR | Dementia | Melatonin (1.5, 2.5, 2.9, 3.5, 6, 8.5, or 10mg) v placebo sustained- or immediate-release | NR | NR-2013 | | | NR; NR; 1.43 to 10 |
| Yang, 2014 | China | 3 RCTs | 184 | | NR | Dialysis-dependent patients with end stage renal disease | CBT + relaxation v control (sleep hygiene, treatment as usual) | Relaxation training delivered via CD | NR | | | Daily (relaxation), 3 to 4 sessions weekly (CBT); NR; 4 to 8 |
| Author, Year | Country | # and type of included studies | Sample size | Literature search dates | Age and Sex | Treatment comparison (doses [mg]) | Co-morbidities | Delivery method and setting | Frequency; duration of treatment; length of follow-up (range, weeks) |
|--------------|---------|--------------------------------|-------------|-------------------------|-------------|----------------------------------|----------------|-----------------------------|------------------------------------------------------------------|
| Ye, 2016     | China   | 14 RCTs                         | 1604        | NR-2106                 | NR          | CBT (sleep hygiene education, cognitive restructuring, stimulus control, sleep restriction, relaxation therapy, hierarchy development, imagery training, scheduled pseudo desensitization, breathing control) v control (wait-list, treatment as usual, internet/email/telephone based control) | Cancer, depression | CBT delivered over the internet | NR; NR; 4 to 52                                                  |
| Yuan, 2010   | China   | 4 RCTs                          | 171         | NR-2009                 | NR          | Doxepin (1 mg) v placebo          | None           | Doxepin (3 mg) v placebo         | NR; NR; NR; NR                                                    |
|              |         |                                 | 169         |                         |             | Doxepin (6 mg) v placebo          |                | Doxepin (25 mg) v placebo        | NR; NR; NR; NR                                                    |
| Zachariae, 2016 | Denmark | 11 RCTs                         | 1460        | 1991-2015               | NR          | CBT (stimulus control, sleep hygiene, cognitive therapy, sleep restriction, relaxation technique) v control (wait-list control, treatment as usual, active control) | Cancer         | Internet/home delivery               | NR; NR; 4 to 48                                                   |
| Zhang, 2016  | China   | 9 RCTs                          | NR          | NR-2015                 | NR          | Melatonin (2, 2.5, 3, 5, 6, 8.5, or 50 mg/d) v placebo | Alzheimer's disease, Parkinson's disease, REM sleep behavior disorder |                                                                 | NR; 2 to 24; NR                                                   |
| Anderson, 2014 | USA     | 12 RCTs                         | NR          | 8 design unspecified    | depression/major | Quetiapine (25mg; increased to 50 or 75 mg) – pre-/post-intervention comparison |                                                                 | Daily; 2 to 12 weeks; NR                                           |
| Author, Year | Country | # and type of included studies | Sample size | Literature search dates | Age and Sex | Co-morbidities | Treatment comparison (doses [mg]) | Delivery method and setting | Frequency; duration of treatment; length of follow-up (range, weeks) |
|--------------|---------|-------------------------------|------------|-------------------------|-------------|----------------|---------------------------------|-----------------------------|-----------------------------------------------------|
| Bellon, 2006 | USA     | NR                            | 15 RCTs    | NR                      | [mean (SD)]; % female | depressive disorder, bipolar disorder, breast cancer, Parkinson’s disease, schizophrenia, polysubstance abuse (withdrawal) | Oral; inpatient | Quetiapine (25 -100mg; 340 mg) vs Placebo | Oral |
| Bogdanov, 2017 | Australia | 4 RCTs 3 Quasi-experimental  | NR         | NR                      | Mean range 27 – 54 | Traumatic brain injury | CBT v control (unspecific) | NR; 60 minutes; 4 to 13 |
| Brooks, 2014  | USA     | 4 RCTs 1 Quasi-experimental   | NR         | NR                      | Individual, in-person | Alcohol use | Progressive relaxation training v control (unspecific) | 5 to 9 sessions; NR; 26 |
| Chase, 1997   | NR      | 5 RCTs                        | NR         | Melatonin (1, 2, 5, or 75 mg) | NR; NR; NR | Melatonin (1, 2, 5, or 75 mg) | NR; NR; NR |
| Author, Year | Country | Sample size | Literature search dates | Treatment comparison (doses [mg]) | Delivery method and setting | Co-morbidities | Frequency; duration of treatment; length of follow-up (range, weeks) |
|--------------|---------|-------------|-------------------------|----------------------------------|-----------------------------|----------------|-------------------------------------------------------------------|
| USA          | 66      | Patients with at least one chronic disease | Controlled sustained release | | | |
| Chiesa, 2009 | Italy   | 3 Observational | NR | Pharmacotherapy (unspecified) + Mindfulness (unspecified) | NR; NR; NR |
| Cimolai, 2007 | Canada  | 8 RCTs | NR | Zopiclone (7.5 mg) – pre-/post- intervention comparison Zopiclone (7.5 mg) vs Triazolam Zopiclone (7.5 mg) vs Zolpidem Zopiclone (7.5 mg) vs Flurazepam Zopiclone (7.5 mg) vs. Temazepam | NR; NR; NR |
| Citrome, 2014 | USA     | 4 RCTs Interventions: 1279 Control: 1274 | NR | Suvorexant (15 or 20 mg) v placebo | SR; NR; 12 |
| Coe, 2012    | USA     | 2 RCTs 1 NRCT | None | Quetiapine (25 mg titrated up to 75mg) – pre-/post-intervention comparison | NR; NR; 2 to 6 |
| Costello, 2014 | USA    | 4 RCTs | NR | Melatonin (0.3, 1, 2, or 5 mg) v placebo Oral; sustained release | Daily; NR; NR |
| Culpepper, 2015 | USA   | 11 RCTs | NR | Melatonin (0.3, 1, 2, or 5 mg) v placebo Fast release capsule; sustained-release synthetic tablet; prolonged-release tablet | Daily; NR; 1 to 29 |
|               |         | 1590      | None | Diphenhydramine (50 mg) v placebo | Daily; NR; 1 day to 4 weeks |
| Author, Year | Country | # and type of included studies | Sample size | Literature search dates | Age and Sex | Co-morbidities | Treatment comparison (doses [mg]) | Delivery method and setting | Frequency; duration of treatment; length of follow-up (range, weeks) |
|--------------|---------|-------------------------------|-------------|-------------------------|-------------|----------------|----------------------------------|-----------------------------|---------------------------------------------------------------|
| Dickerson, 2014 | USA | 7 RCTs | 352 | NR | NR | Cancer | CBT – pre-/post- intervention comparison | CBT vs control (usual treatment, waitlist crossover, waitlist control) | Weekly; NR; 4 to 8 |
| | | Intervention: 220 Control:132 | | | | | EEG biofeedback v wait-list control | | NR; NR; NR |
| Hellstrom, 2011 | Sweden | 3 RCTs | 209 | NR | NR | NR | Mental imagery v usual care | In-person; inpatient | Daily; NR; NR |
| | | Intervention: 103 Control:106 | | | | | | |
| Howell, 2014 | Canada | 7 RCTs | NR | Cancer | NR | NR | CBT (sleep hygiene, sleep restriction, stimulus control, cognitive restructuring, relaxation therapies) v control (usual care, wait-list control, health eating and nutrition, sleep education and hygiene, no treatment) | Individual delivery | Weekly; NR; 8 to 74 |
| Ishak, 2012 | USA | 7 | NR | Breast, prostate gynecological, bowel cancer | Zopiclone (NR) vs Placebo Zolpidem (10 mg) vs Zolpidem (10 mg) | NR | 5 nights/week + placebo 2 nights/week or once-daily; NR; 2 |
| Author, Year | Country | # and type of included studies | Sample size | Literature search dates | Age and Sex [mean (SD)]; % female | Treatment comparison (doses [mg]) | Delivery method and setting | Co-morbidities | Frequency; duration of treatment; length of follow-up (range, weeks) |
|-------------|---------|--------------------------------|-------------|------------------------|-----------------------------------|---------------------------------|--------------------------|---------------|-------------------------------------------------------------|
| Kolla, 2011 | USA     | 4 RCTs 2 NRCTs 240            | NR          | Alcohol recovery       | CBT vs control (placebo, no treatment, unspecified, usual care) | CBT group vs CBT individual: NR; NR; 14 to 52 | Weekly; NR; 4 to 24 | CBT components: psychoeducation, sleep hygiene, stimulus control, sleep restriction, relaxation exercises, cognitive restructuring | |
|             |         |                                |             |                        | Triazolam (0.5 -1 mg) – pre-/post- intervention comparison Oral | Trazodone (50 -200 mg) v placebo Oral | NR; NR; 4 to 24 | |
|             |         |                                |             |                        | Quetiapine (300 -800mg) – pre-/post- intervention comparison | Quetiapine (300 -800mg) – pre-/post- intervention comparison | NR; NR; 16 | |
|             |         |                                |             |                        | Oral | Oral | |
| Mayers, 2005 | UK      | 6 RCTs 466                    | NR          | Depression, dysthymia  | Zolpidem (10 mg) v placebo Oral | Trazodone (50, 75, or 100 mg) v placebo Doxepin (25 – 50 mg) vs placebo Trazodone (50 mg) vs Zolpidem (10 mg) | Oral | NR; NR; NR |
|             |         |                                |             |                        | | | | NR; NR; 2; NR |
| Author, Year | Country | # and type of included studies | Sample size | Literature search dates | Age and Sex | Treatment comparison (doses [mg]) | Delivery method and setting | Co-morbidities | Frequency; duration of treatment; length of follow-up (range, weeks) |
|--------------|---------|-------------------------------|-------------|-------------------------|-------------|----------------------------------|----------------------------|----------------|---------------------------------------------------------------------|
| McCurry, 2007 | USA     | 11 (designs unspecified)      | NR          | NR                      | Medical Illness | CBT vs control (delayed treatment, wait-list control, placebo, stress management) | Individual delivery | CBT components: sleep hygiene/education, relaxation, sleep restriction/compression, stimulus control | Weekly; NR; NR |
|              |         | 53.3 (10.2); NR               |             |                         |              | | | Sleep restriction therapy, nap sleep restriction therapy, sleep compression, or sleep compression guidance v control (sleep hygiene, placebo, wait-list control) | Weekly; NR; NR |
|              |         |                               |             |                         |              | | | Individual delivery | |
| Mendelson, 2005 | USA     | 18 (designs unspecified)      | NR          | NR                      | Depression  | Zolpidem (10 mg) v placebo | Nightly; NR; NR | Trazodone (50 to 600 mg) – pre-/post- intervention comparison | NR; NR; NR |
|              |         | 1667 Intervention: 1195 Control: 472 |             |                         |              | | | Trazodone (50 to 300 mg) vs placebo | Nightly; NR; NR |
|              |         | 53.3 (10.2); NR               |             |                         |              | | | Trazodone (50 mg) vs Zolpidem (10 mg) | Nightly; NR; NR |
| Miller, 2014  | USA     | 9 4 RCTs                      | 53.3 (10.2); NR |                         |              | Sleep restriction therapy v control (relaxation therapy, | NR; NR; 13 to 52 |
|              |         |                               |             |                         |              | | | | |
| Author, Year | Country | # and type of included studies | Sample size | Literature search dates | Age and Sex | Treatment comparison (doses [mg]) | Co-morbidities | Delivery method and setting | Frequency; duration of treatment; length of follow-up (range, weeks) |
|--------------|---------|--------------------------------|-------------|-------------------------|-------------|-----------------------------------|----------------|-------------------------------|--------------------------------------------------------------|
| UK | UK | 1 NRCT  
4 Observational | 380 | | | | | | |
| Swainston Harrison, 2005 | New Zealand | 3 RCTs | 145 | Intervention: 102  
Control: 43 | None | Triazolam (0.5 mg) v placebo  
Tablet; bedtime | None | Zolpidem (10 mg) vs Placebo  
Zolpidem (10 mg) vs Triazolam  
Tablet; bedtime | NR; NR; 4 |
| Tamrat, 2013 | USA | 8  
4 RCTs  
2 NRCTs  
2 Observational | 508 | | | | Cancer, post-coronary artery bypass grafting, psychiatric disease [all hospitalized patients] | Relaxation techniques, audiotape guided imagery, or relaxation tapes v control (usual care, solitary activity, baseline) | Inpatient setting |
| Taylor, 2014 | USA | 16 RCTs | 571 | | | | Depression, post-traumatic stress disorder, alcohol dependence, hypnotic | CBT (stimulus control, sleep restriction, relaxation therapy, cognitive therapy, image rehearsal therapy, medication withdrawal) v control (wait-list, usual care, sleep hygiene, hypnotic/medication withdrawal) | NR; 2 -10 sessions; NR |
| Vande Griend, 2012 | USA | 16 RCTs | NR | | | | Alcohol detoxification, | Trazodone (50 mg) vs Placebo  
Doxepin (1, 3, 6, 25, or 50 mg) vs placebo  
Trazodone (50 mg) vs Zolpidem (NR) | NR; 1 to 4 weeks; NR  
NR; 1 night to 12 weeks  
NR; NR; 2; NR |
| Author, Year | Country | # and type of included studies | Sample size | Literature search dates | Age and Sex | Treatment comparison (doses [mg]) | Delivery method and setting | Co-morbidities | Treatment comparison (doses [mg]) | Frequency; duration of treatment; length of follow-up (range, weeks) |
|--------------|---------|--------------------------------|-------------|-------------------------|-------------|-----------------------------------|---------------------------|---------------|-----------------------------------|---------------------------------------------------------------|
| Venables, 2014 | UK      | 22 16 RCTs 5 Quasi-experimental 1 Observational | 1794        | NR                      | adult cancer patients undergoing curative treatment | Self-help CBT – pre-/post- intervention comparison | Video; home | methadone-maintained | Diphenhydramine (50 mg) v placebo | NR; 5 to 28 days; NR                                        |
| Vural, 2014   | Netherlands | 5 4 RCTs 1 NRCTs               | 207         | NR                      | NR          | Melatonin (0.4, 0.5, 2, or 4 mg) v control (unspecified) sustained release transbuccal patch or immediate release | CBT (stimulus control, sleep restriction, cognitive therapy, sleep hygiene education, sleep scheduling) vs control (quasi desensitization, self-monitoring, sleep hygiene, wait list) | Nightly (bedtime); 4 to 42 days; 1 to 24 | | |
| Wang, 2005    | Taiwan  | 6 RCTs                          | 255         | NR                      | NR          | CBT (stimulus control, sleep restriction, sleep hygiene education) vs relaxation | Behavioural therapy (stimulus control, relaxation therapy, sleep education) v stimulus control | | | NR; NR; 12 to 104 |
| Wine, 2009    |        | 3 NRCTs                         | NR          | Quetiapine (25 -75, or 12.5 -50mg) – pre-/post- | | | | | Bedtime, as needed; NR; 6 |
| Author, Year | Country | # and type of included studies | Sample size | Literature search dates | Age and Sex [mean (SD)]; % female | Co-morbidities | Treatment comparison (doses [mg]) | Delivery method and setting | Frequency; duration of treatment; length of follow-up (range, weeks) |
|-------------|---------|-------------------------------|-------------|------------------------|----------------------------------|---------------|-----------------------------------|-----------------------------|---------------------------------------------------------------|
| Yeung, 2015 | Hong Kong | 8 RCTs | Total:1513 | 8 RCTs | NR | Anxiety, depression | Doxepin (3, 6, or 25-300 mg) v placebo Oral | Tablet | NR; NR; 4 to 12 |
| USA         |         | Total:50 | Posttraumatic stress disorder, Parkinson's disease | 50 | Intervention comparison | Quetiapine (25 -300mg) v untreated control | Tablet | to 12 | Bedtime, as needed; NR; 6 |
### Appendix D: AMSTAR Results

| Author, Year | 1. PICO components | 2. A priori design | 3. Rationale for study selection | 4. Literature search | 5. Duplicate Selection | 6. Duplicate Abstraction | 7. List of excluded studies | 8. Description of included studies | 9a. RoB in RCTs | 9b. RoB in non-randomized studies | 10. Funding sources | 11. Appropriate MA methods | 12. Used RoB in MA | 13. Used RoB in interpreting results | 14. Discussion of heterogeneity | 15. Publication bias | 16. Conflict of Interest | Overall Rating |
|--------------|-------------------|-------------------|-------------------------------|-------------------|-----------------------|------------------------|-------------------------------|-------------------------------|----------------|-------------------------------|----------------|----------------|----------------|-------------------|----------------|-------------------------|-----------------|
| Ballesio, 2017 | Y                  | Y                 | Y                             | Partial           | Y                     | Y                      | Y                            | Y                             | Y              | Y                             | Y              | Y              | Y              | Y                  | Y              | Y                      | High             |
| Brasure, 2015  | Y                  | Y                 | Y                             | Y                 | N                     | Y                      | Y                            | Y                             | Y              | Y                             | Y              | Y              | N              | Y                  | Y              | N                      | High             |
| Buscemi, 2004  | Y                  | Partial           | Y                             | Y                 | Y                     | Y                      | Y                            | Partial           | Y              | Y                             | Y              | Y              | Y              | Partial           | Y              | Y                      | High             |
| Buscemi, 2005  | Y                  | N                 | N                             | Partial           | Y                     | Y                      | N                            | Partial           | Y              | Y                             | Y              | Y              | Y              | Y                  | Y              | Y                      | High             |
| Cheng, 2012    | Y                  | N                 | N                             | Y                 | N                     | N                      | N                            | N                             | Y              | Y                             | Y              | N              | N              | Y                  | N              | N                      | Low              |
| Ferracioli, 2013| Y                  | N                 | N                             | N                 | Y                     | N                      | Partial           | N                             | Y              | Y                             | Y              | N              | N              | Y                  | Y              | Y                      | Critically Low    |
| Gong, 2016     | Y                  | N                 | Partial           | Y                  | Y                     | Partial           | Y                             | Y                             | Y              | Y                             | Y              | N              | N              | Y                  | Y              | Y                      | Low              |
| Author, Year | 1. PICOs components | 2. A priori design | 3. Rationale for study selection | 4. Literature search | 5. Duplicate Selection | 6. Duplicate Abstraction | 7. List of excluded studies | 8. Description of included studies | 9a. RoB in RCTs | 9b. RoB in non-randomized studies | 10. Funding sources | 11. Appropriate MA methods | 12. Used RoB in MA interpretation | 14. Discussion of heterogeneity | 15. Publication bias | 16. Conflict of Interest | Overall Rating |
|-------------|------------------|-----------------|------------------|------------------|------------------|------------------|------------------|------------------|----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|----------------|
| Ho, 2015    | Y                | N               | N                | Partial          | Y                | Y                | Y                | N                | Y              | Y               | N               | Y               | Y               | N               | Y               | N               | Low            |
| Ho, 2016    | Y                | N               | N                | Partial          | Y                | N                | N                | Partial          | Y              | Y               | Includes only RCTs | N               | Y               | N               | Y               | N               | Low            |
| Hwang, 2016 | Y                | N               | N                | Partial          | Partial          | Y                | Y                | N                | N               | Partial          | N               | N               | N               | N               | N               | N               | Critically Low |
| Irwin, 2006 | Y                | N               | N                | Partial          | Partial          | Y                | Y                | N                | N               | Partial          | Includes only RCTs | N               | Y               | N               | N               | N               | Critically Low |
| Johnson, 2016 | Y              | Y               | Y               | Y                | Y                | N                | Partial          | Y                | Y               | N               | Includes only RCTs | N               | Y               | N               | Y               | Y               | Moderate       |
| Kishi, 2015 | N                | N               | N                | Partial          | Partial          | Y                | N                | N                | N               | Partial          | Includes only RCTs | N               | Y               | Y               | Y               | Y               | Moderate       |
| Koffel, 2015 | N                | N               | Y                | Partial          | N                | N                | N                | Y                | N               | Partial          | Includes only RCTs | Y               | N               | N               | N               | N               | Critically Low |
| Kuriyama, 2017 | N             | N               | N                | Y                | Y                | Y                | N                | Y                | Y               | Includes only RCTs | N               | Y               | Y               | N               | N               | N               | Moderate       |
| Lee, NR     | Y                | N               | N                | Y                | Y                | Y                | N                | Partial          | Y              | Y               | Includes only RCTs | N               | Y               | N               | N               | N               | Critically Low |
| Author, Year | 1. PICO components | 2. A priori design | 3. Rationale for study selection | 4. Literature search | 5. Duplicate Selection | 6. Duplicate Abstraction | 7. List of excluded studies | 8. Description of included studies | 9a. RoB in RCTs | 9b. RoB in non-randomized studies | 10. Funding sources | 11. Appropriate MA methods | 12. Used RoB in MA | 13. Used RoB in interpreting results | 14. Discussion of heterogeneity | 15. Publication bias | 16. Conflict of Interest | Overall Rating |
|-------------|-------------------|-----------------|-------------------------------|-------------------|-------------------|-----------------|-------------------|-------------------|-------------------|-------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Liu, 2017   | Y                 | Partial Y       | N                             | Partial Y         | Y                 | N               | N                 | N                 | Y                 | Y                 | Includes only RCTs | N               | Y               | Y               | N               | Y               | Y               | Y               | Critically Low  |
| McCleery,   | Y                 | Partial Y       | Y                             | Partial Y         | Y                 | Y               | Y                 | Y                 | Partial Y         | Partial Y         | Includes only RCTs | N               | Y               | Y               | Y               | Y               | N               | Y               | High            |
| 2016        |                   |                 |                               |                   |                   |                 |                   |                   |                   |                   |                 |                  |                  |                  |                  |                  |                  |                  |
| Montgomery,  | Y                 | N               | N                             | Partial Y         | Y                 | N               | N                 | Y                 | Y                 | Y                 | Includes only RCTs | N               | Y               | N               | Y               | Y               | Y               | Y               | High            |
| 2003        |                   |                 |                               |                   |                   |                 |                   |                   |                   |                   |                 |                  |                  |                  |                  |                  |                  |                  |
| Navarro-Bravo, 2015 | Y | N | N | Partial Y | Y | Y | N | Partial Y | Y | Y | Includes only RCTs | N | Y | N | Y | Y | Y | Moderate |
| Okajima, 2011 | Y | N | N | N | N | N | N | Y | N | Y | Includes only RCTs | N | N | N | N | N | Y | N | Critically Low |
| Sateia, 2017 | Y | N | N | N | Y | N | N | Partial Y | Partial Y | Y | Y | Y | Y | N | Y | N | Y | Y | Critically Low |
| Seda, 2015  | Y | N | N | Partial Y | N | N | N | Partial Y | N | Y | N | N | Y | Y | N | Y | N | Y | Low |
| Seyffert, 2016 | Y | Partial Y | N | Y | N | Y | N | Partial Y | Y | Y | Y | Y | N | Y | Y | N | Y | Y | Low |
| Soldatos, 2009 | Y | N | N | N | N | N | N | Partial Y | N | N | Y | Y | N | N | N | N | N | N | Critically Low |
| Author, Year       | 1. PICO components | 2. A priori design | 3. Rationale for study selection | 4. Literature search | 5. Duplicate Selection | 6. Duplicate Abstraction | 7. List of excluded studies | 8. Description of included studies | 9a. RoB in RCTs | 9b. RoB in non-randomized studies | 10. Funding sources | 11. Appropriate MA methods | 12. Used RoB in MA | 13. Used RoB in interpreting results | 14. Discussion of heterogeneity | 15. Publication bias | 16. Conflict of Interest | Overall Rating |
|-------------------|---------------------|-------------------|---------------------------------|---------------------|------------------------|-------------------------|----------------------------|-------------------------------|----------------|-------------------------------|----------------|----------------|----------------|---------------------------------|-----------------------------|---------------------|-----------------------------|----------------|---------------------|
| Tang, 2015        | Y                   | Y                 | N                               | Partial Y           | Y                      | Y                       | Y                          | Y                             | N              | Y                              | N              | Y              | N              | Y                              | Y                           | Y                   | Y                           | Y              | Moderate |
| Trauer, 2015      | Y                   | Y                 | N                               | Y                   | Y                      | Y                       | N                          | Partial Y                     | Y              | Y                              | N              | Y              | N              | Y                              | Y                           | Y                   | Y                           | Y              | Moderate |
| van Straten, 2007 | Y                   | N                 | N                               | Y                   | Y                      | Y                       | N                          | Y                             | Y              | Y                              | N              | Y              | Y              | Y                              | Y                           | Y                   | Y                           | N              | Low       |
| van Straten, 2009 | Y                   | N                 | N                               | Partial Y           | N                      | N                       | N                          | Partial Y                     | Y              | Y                              | N              | Y              | Y              | Y                              | Y                           | N                   | Y                           | N              | Moderate |
| Xu, 2015          | Y                   | N                 | N                               | Partial Y           | Y                      | N                       | Partial Y                  | Y                             | N              | N                              | N              | Y              | Y              | Y                              | Y                           | Y                   | Y                           | N              | Moderate |
| Yang, 2014        | Y                   | Y                 | N                               | Partial Y           | Y                      | Y                       | Partial Y                  | Y                             | Partial Y                  | Y              | Y                              | N              | Y              | Y              | Y                              | Y                           | Y                   | Y                           | N              | Moderate |
| Ye, 2016          | Y                   | Partial Y         | N                               | Partial Y           | Y                      | Y                       | Y                          | Partial Y                     | Y              | Y                              | N              | Y              | N              | Y                              | Y                           | Y                   | Y                           | N              | Moderate |
| Yuan, 2010        | Y                   | N                 | N                               | Partial Y           | Y                      | Y                       | Partial Y                  | Y                             | N              | N                              | Y              | N              | N              | Y                              | Y                           | Y                   | N                           | N              | Low       |
| Zachariae, 2016   | Y                   | Y                 | N                               | Partial Y           | Y                      | N                       | Partial Y                  | Y                             | Y              | Y                              | N              | Y              | N              | Y                              | Y                           | Y                   | Y                           | Y              | Moderate |
| Author, Year | 1. PICO components | 2. A priori design | 3. Rationale for study selection | 4. Literature search | 5. Duplicate Selection | 6. Duplicate Abstraction | 7. List of excluded studies | 8. Description of included studies | 9a. RoB in RCTs | 9b. RoB in non-randomized studies | 10. Funding sources | 11. Appropriate MA methods | 12. Used RoB in MA | 13. Used RoB in interpreting results | 14. Discussion of heterogeneity | 15. Publication bias | 16. Conflict of Interest | Overall Rating |
|--------------|-------------------|-------------------|-------------------------------|-------------------|----------------------|------------------------|-------------------------|-----------------------------|-----------------|--------------------------|----------------|------------------------|----------------|----------------------------|----------------|-------------------------|-----------------|
| Zhang, 2016  | Y                 | N                 | N                             | Partial           | Y                    | Y                      | includes only RCTs      | Y                           | N               | N                        | N             | Y                      | N             | N                      | Y              | Y                      | Partial Low     |

Systematic reviews without meta-analysis (n=29)

| Author, Year | 1. PICO components | 2. A priori design | 3. Rationale for study selection | 4. Literature search | 5. Duplicate Selection | 6. Duplicate Abstraction | 7. List of excluded studies | 8. Description of included studies | 9a. RoB in RCTs | 9b. RoB in non-randomized studies | 10. Funding sources | 11. Appropriate MA methods | 12. Used RoB in MA | 13. Used RoB in interpreting results | 14. Discussion of heterogeneity | 15. Publication bias | 16. Conflict of Interest | Overall Rating |
|--------------|-------------------|-------------------|-------------------------------|-------------------|----------------------|------------------------|-------------------------|-----------------------------|-----------------|--------------------------|----------------|------------------------|----------------|----------------------------|----------------|-------------------------|-----------------|
| Anderson, 2014 | N                  | N                 | N                             | Partial           | Y                    | N                      | No MA                   | No MA                       | N               | No MA                    | No MA           | N                      | No MA         | N                      | Critically Low  |
| Bellon, 2006  | N                  | N                 | N                             | Partial           | Y                    | N                      | No MA                   | No MA                       | N               | No MA                    | No MA           | N                      | No MA         | N                      | Critically Low  |
| Bogdanov, 2017 | N                  | N                 | N                             | Partial           | Y                    | Y                      | No MA                   | No MA                       | Y               | No MA                    | No MA           | Y                      | Low           | No MA                   | Low             |
| Brooks, 2014  | N                  | N                 | N                             | Partial           | Y                    | Partial                | Partial                 | No MA                       | N               | No MA                    | No MA           | Y                      | Low           | No MA                   | Low             |
| Chase, 1997   | N                  | N                 | N                             | Partial           | Y                    | N                      | No MA                   | No MA                       | N               | No MA                    | No MA           | N                      | Critically Low  |
| Chiesa, 2009  | Y                  | N                 | Y                             | Partial           | Y                    | Y                      | No MA                   | No MA                       | N               | No MA                    | No MA           | N                      | Low           | No MA                   | Low             |
| Cimolai, 2007 | N                  | N                 | N                             | Partial           | Y                    | N                      | No MA                   | No MA                       | N               | No MA                    | No MA           | Y                      | Critically Low  |
| Citrome, 2014  | N                 | N                 | N                             | Partial           | Y                    | N                      | No MA                   | No MA                       | N               | No MA                    | No MA           | Y                      | Critically Low  |
| Coe, 2012     | N                  | N                 | N                             | Partial           | Y                    | N                      | No MA                   | No MA                       | N               | No MA                    | No MA           | Y                      | Critically Low  |
| Costello, 2014 | Y                 | N                 | Y                             | Partial           | Y                    | Y                      | Includes only RCTs      | Y                           | No MA           | No MA                    | No MA           | Y                      | No MA         | Moderate                | Critically Low  |
| Culpepper, 2015 | Y                | Partial        | Y                             | Partial           | Y                    | N                      | Includes only RCTs      | N                           | No MA           | No MA                    | No MA           | Y                      | No MA         | Critically Low           | Critically Low  |
| Author, Year          | 1. PICO components | 2. A priori design | 3. Rationale for study selection | 4. Literature search | 5. Duplicate Selection | 6. Duplicate Abstraction | 7. List of excluded studies | 8. Description of included studies | 9a. RoB in RCTs | 9b. RoB in non-randomized studies | 10. Funding sources | 11. Appropriate MA methods | 12. Used RoB in MA methods | 13. Used RoB in interpreting results | 14. Discussion of heterogeneity | 15. Publication bias | 16. Conflict of Interest | Overall Rating |
|----------------------|--------------------|--------------------|-------------------------------|-------------------|------------------------|------------------------|----------------------------|-------------------------------|----------------|----------------------------------|----------------|-----------------------------|----------------|---------------------------------|----------------|-------------------------------|-----------------|-----------------------------|
| Dickerson, 2014      | Y                  | Partial            | Y                             | Partial           | Y                      | Partial                | Partial                    | Partial                       | Partial        | Partial                        | N              | No MA                        | Y               | Y                             | No MA           | Y                             | No MA           | High                         |
| Hellstrom, 2011      | N                  | Partial            | N                             | Partial           | Y                      | N                      | Partial                    | Partial                       | Partial        | Partial                        | No MA          | No MA                       | Y               | N                             | No MA           |.create Overall Rating: Moderate|
| Howell, 2014         | N                  | Partial            | Y                             | Partial           | N                      | N                      | Partial                    | Partial                       | N              | Partial                        | No MA          | No MA                       | No MA           | N                             | Y               | Moderate                    |
| Ishak, 2012          | N                  | Partial            | N                             | Partial           | Y                      | N                      | Partial                    | Partial                       | N              | Partial                        | No MA          | No MA                       | No MA           | N                             | Y               | Low                          |
| Kolla, 2011          | N                  | N                  | N                             | Partial           | Y                      | N                      | N                          | N                            | No MA          | Partial                        | No MA          | No MA                       | No MA           | N                             | No MA           | Critically Low               |
| Mayers, 2005         | Y                  | N                  | Y                             | Partial           | N                      | N                      | N                          | Partial                       | N              | Partial                        | No MA          | No MA                       | No MA           | N                             | No MA           | Critically Low               |
| McCurry, 2007        | Y                  | N                  | N                             | N                | N                      | N                      | Y                          | Partial                       | N              | Partial                        | No MA          | No MA                       | No MA           | N                             | No MA           | Critically Low               |
| Mendelson, 2005      | N                  | N                  | N                             | Partial           | Y                      | N                      | N                          | N                            | N              | N                             | No MA          | No MA                       | No MA           | N                             | No MA           | Critically Low               |
| Miller, 2014         | Y                  | N                  | N                             | Partial           | Y                      | N                      | N                          | N                            | N              | N                             | No MA          | No MA                       | No MA           | N                             | No MA           | High                         |
| Swainston Harrison, 2005 | Y                  | Partial            | Y                             | Partial           | N                      | N                      | N                          | N                            | No MA          | Partial                        | No MA          | No MA                       | No MA           | N                             | No MA           | Critically Low               |
| Tamrat, 2013         | Y                  | Partial            | N                             | N                | Y                      | Y                      | Y                          | N                            | No MA          | Partial                        | No MA          | No MA                       | No MA           | N                             | No MA           | Low                          |
| Taylor, 2014         | N                  | N                  | N                             | Partial           | Y                      | N                      | Y                          | Partial                       | N              | Partial                        | No MA          | No MA                       | No MA           | N                             | No MA           | Critically Low               |
| Author, Year    | 1. PICO components | 2. A priori design | 3. Rationale for study selection | 4. Literature search | 5. Duplicate Selection | 6. Duplicate Abstraction | 7. List of excluded studies | 8. Description of included studies | 9a. RoB in RCTs | 9b. RoB in non-randomized studies | 10. Funding sources | 11. Appropriate MA methods | 12. Used RoB in MA | 13. Used RoB in interpreting results | 14. Discussion of heterogeneity | 15. Publication bias | 16. Conflict of Interest | Overall Rating |
|----------------|-------------------|---------------------|---------------------------------|---------------------|------------------------|-------------------------|--------------------------|-------------------------------|----------------|-------------------------------|----------------|-------------------------|----------------|-----------------------------|------------------|--------------------------|------------------|------------------------|
| Vande Griend, 2012 | N                  | N                   | N                               | Partial Y           | N                      | N                       | Partial Y                | N                             | N              | Includes only RCTs           | N              | No MA                   | N              | N                         | N                | Y                       | Critically Low     |
| Venables, 2014    | N                  | N                   | N                               | Partial Y           | N                      | N                       | Partial Y                | N                             | N              | No MA                        | No MA          | No MA                  | No MA          | N                         | No MA             | N                       | Critically Low     |
| Vural, 2014       | Y                  | N                   | N                               | Partial Y           | Y                      | N                       | Partial Y                | Y                             | No MA           | No MA                        | No MA          | No MA                  | No MA          | N                         | No MA             | Y                       | Critically Low     |
| Wang, 2005        | Y                  | Partial Y           | Y                               | Partial Y           | Y                      | Partial Y               | N                       | Partial Y                | N                             | No MA           | No MA                        | No MA          | No MA                  | Y               | N                         | No MA             | Moderate               |
| Wine, 2009        | N                  | N                   | N                               | Partial Y           | N                      | N                       | Partial Y                | N                             | N              | Includes only RCTs           | N              | No MA                   | No MA          | N                         | No MA             | N                       | Critically Low     |
| Yeung, 2015       | Y                  | Partial Y           | N                               | Y                   | Y                      | Y                       | Partial Y                | Y                             | Y              | Includes only RCTs           | Y              | No MA                   | No MA          | Y                         | No MA             | Moderate               |
# Appendix E: Detailed Tables of Results

## Table E1. Benzodiazepines

| Author, Year  | AMSTAR rating | Intervention and sample size | # of studies | Measurement method                          | Pooled Estimates (MA) or Narrative Results (from SR with no MA)* |
|---------------|---------------|------------------------------|--------------|-----------------------------------------------|---------------------------------------------------------------|
| **Sleep onset latency** | | | | | |
| Buscemi, 2005 Meta-analysis | High | Flurazepam: 317 | 10 | sleep diary, polysomnography | Mean difference [95% CI]: -23.21 [-34.26, -12.16] I-squared: 51.8% |
| | | Placebo: 215 | | | |
| | | Temazepam: 128 | 4 | sleep diary, polysomnography | Mean difference [95% CI]: -11.61 [-23.64, 0.42] I-squared: 84% |
| | | Placebo: 78 | | | |
| | | Triazolam: 290 | 8 | sleep diary, polysomnography | Mean difference [95% CI]: -19.69 [-28.36, -11.01] I-squared: 69.2% |
| | | Placebo: 249 | | | |
| Sateia, 2017 Meta-analysis | Critically Low | Temazepam: 36 | 2 | subjective measure | Mean difference [95% CI]: -20.06 [-39.05, -1.07] I-squared: 68% |
| | | Placebo: 36 | | | |
| Soldatos, 1999 Meta-analysis | Critically Low | Triazolam: NR | 28 | sleep laboratory | Mean difference [95% CI]: -15.5 [-19.5, -11.4] I-squared: NR |
| | | Placebo: NR | | | |
| **Total sleep time** | | | | | |
| Sateia, 2017 Meta-analysis | Critically Low | Temazepam: 36 | 2 | subjective measure | Mean difference [95% CI]: 64.41 [8.07, 120.76] I-squared: 59% |
| | | Placebo: 36 | | | |
| Soldatos, 1999 Meta-analysis | Critically Low | Triazolam: NR | 12 | sleep laboratory | Mean difference [95% CI]: 49.2 [36, 62.5] I-squared: NR |
| | | Placebo: NR | | | |
| Kolla, 2011 Systematic Review | Critically Low | Triazolam: 23 (enrolled); 12 (analysis) | 1 | sleep diaries | Significant improvement in depth and duration of sleep |
| Author, Year Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA)* |
|-----------------------------|---------------|-----------------------------|--------------|--------------------|---------------------------------------------------------------|
| **Swainston Harrison, 2005 Systematic Review** | Critically Low | Triazolam | 1 | NR | Change in outcome (p-value): +41 vs +25 minutes (p<0.05) |
| Total sample: 16 | Placebo | |

**Wake after sleep onset**

| Buscemi, 2005 Meta-analysis | High | Temazepam: 38 | 2 | sleep diary, polysomnography | Mean difference [95% CI]: -23.66 [-36.57, -10.76] I-squared: 0% |
|-----------------------------|------|----------------|-----|-----------------------------|---------------------------------------------------------------|
| Placebo: 39 | | |
| | Triazolam: 30 | 2 | sleep diary, polysomnography | Mean difference [95% CI]: -39.96 [-64.47, -15.45] I-squared: 0% |
| Placebo: 27 | | |

**Sleep quality**

| Sateia, 2017 Meta-analysis | Critically Low | Temazepam: 39 | 2 | subjective measure | Mean difference [95% CI]: 0.25 [-0.20, 0.70] I-squared: 0% |
|-----------------------------|---------------|----------------|-----|--------------------|---------------------------------------------------------------|
| Placebo: 39 | | |

*Bolded results indicate statistical significance as reported by review*

**Table E2. Non-benzodiazepines**

| Author, Year Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-----------------------------|---------------|-----------------------------|--------------|--------------------|---------------------------------------------------------------|
| **Sleep onset latency** |
| **Brasure, 2015 Meta-analysis** | High | Zolpidem: 181 | 4 | subjective sleep latency, minutes | Mean difference [95% CI]: -14.95 [-22.10, -7.80] I-squared: 0% |
| Placebo: 192 | | |
| Zolpidem: 177 | 2 | subjective report, minutes | Mean difference [95% CI]: -14.8 [-23.41, -6.19] I-squared: 0% |
| Placebo: 178 | | |

| **Buscemi, 2005 Meta-analysis** | High | Zolpidem: 997 | 17 | sleep diary, polysomnography | Mean difference [95% CI]: -12.75 [-16.42, -9.08] I-squared: 4.5% |
|-----------------------------|------|----------------|-----|-----------------------------|---------------------------------------------------------------|
| Placebo: 808 | | |
| Zopiclone: 178 | 5 | sleep diary, polysomnography | Mean difference [95% CI]: -30.91 [-49.37, -12.44] I-squared: 73.9% |
| Placebo: 178 | | |

| **Sateia, 2017 Meta-analysis** | Critically Low | Zolpidem: 181 | 5 | polysomnography | Mean difference [95% CI]: -11.65 [-19.15, -4.15] I-squared: 78% |
|-----------------------------|---------------|----------------|-----|--------------------|---------------------------------------------------------------|
| Placebo: 185 | | |
| Author, Year Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-----------------------------|---------------|------------------------------|-------------|-------------------|---------------------------------------------------------------|
| Zolpidem: 543               | 10            | subjective measure          |             |                   | Mean difference [95% CI]: -19.55 [-24.90, -14.20] I-squared: 95% |
| Placebo: 558                |               |                              |             |                   |                                                               |
| Zolpidem: NR                | 29            | sleep laboratory             |             |                   | Mean difference [95% CI]: -17.6 [-23.2, -12] I-squared: NR    |
| Placebo: NR                 |               |                              |             |                   |                                                               |
| Zopiclone: NR              | 14            | sleep laboratory             |             |                   | Mean difference [95% CI]: -19.1 [-26.7, -11.5] I-squared: NR   |
| Placebo: NR                |               |                              |             |                   |                                                               |
| Zolpidem: NR               |               |                              |             |                   | Significant decrease in sleep latency compared to placebo (p<0.05) |
| Placebo: NR                |               |                              |             |                   |                                                               |
| Total sample: 306           |               |                              |             |                   |                                                               |
| Total sample: 22            |               |                              |             |                   | Significant increase in total sleep time compared to placebo (p<0.05) |

**Total sleep time**

| Author, Year Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-----------------------------|---------------|------------------------------|-------------|-------------------|---------------------------------------------------------------|
| Zolpidem: 82                | 3             | subjective report            |             |                   | Mean difference [95% CI]: 22.95 [2.01, 43.88] I-squared: 0%    |
| Placebo: 85                 |               |                              |             |                   |                                                               |
| Zolpidem: 55                | 2             | PSG                          |             |                   | Mean difference [95% CI]: 28.91 [10.85, 46.97] I-squared: 49%   |
| Placebo: 57                 |               |                              |             |                   |                                                               |
| Zolpidem: 435               | 8             | subjective measure           |             |                   | Mean difference [95% CI]: 30.04 [15.12, 44.96] I-squared: 71%    |
| Placebo: 455                |               |                              |             |                   |                                                               |
| Zolpidem: NR                | 23            | sleep laboratory             |             |                   | Mean difference [95% CI]: 32 [21.7, 42.3] I-squared: NR          |
| Placebo: NR                 |               |                              |             |                   |                                                               |
| Zopiclone: NR              | 13            | sleep laboratory             |             |                   | Mean difference [95% CI]: 56.3 [37.3, 75.4] I-squared: NR        |
| Placebo: NR                |               |                              |             |                   |                                                               |
| Zolpidem: NR               |               |                              |             |                   | Significant increase in total sleep time compared to placebo (p<0.05) |
| Placebo: NR                |               |                              |             |                   |                                                               |
| Total sample: 16            |               |                              |             |                   | Change in outcome (p-value): +35 vs +29 minutes (p<0.05)         |

**Total sample: 306**
| Author, Year | Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|--------------|---------------|---------------|-----------------------------|--------------|---------------------|-------------------------------------------------------------|
| **Wake after sleep onset** | | | | | | |
| Buscemi, 2005 Meta-analysis | Critically Low | Zolpidem: 345 Placebo: 345 | 7 | sleep diary polysomnography | Mean difference [95% CI]: -8.46[-20.17, 3.26] I-squared: 64.1% |
| Sateia, 2017 Meta-analysis | Critically Low | Zolpidem: 55 Placebo: 57 | 2 | polysomnography | Mean difference [95% CI]: -25.46 [-32.99, -17.94] I-squared: 0% |
| Sateia, 2017 Meta-analysis | Critically Low | Zolpidem: 384 Placebo: 400 | 6 | subjective measure | Mean difference [95% CI]: -13.57 [-19.84, -7.30] I-squared: 92% |
| **Sleep Quality** | | | | | | |
| Brasure, 2015 Meta-analysis | High | Zolpidem: 289 Placebo: 268 | 3 | participants reporting improvement | Mean difference [95% CI]: 1.4 [1.20, 1.65] I-squared: 14% |
| Sateia, 2017 Meta-analysis | Critically Low | Zolpidem: 314 Placebo: 324 | 6 | subjective measure | Standardized mean difference [95% CI]: 0.64 [0.03, 1.26] I-squared: 92% |
| Mayers, 2005 Systematic Review | Critically Low | Zolpidem Placebo Total sample: 306 | 1 | NR | Significant improvement on sleep quality compared to placebo (p=0.0003) |
| **Sleep efficiency** | | | | | | |
| Mendelson, 2005 Systematic Review | Critically Low | Zolpidem Placebo Total sample: 306 | 1 | self-reported | Relative to placebo, patients reported significant improvement in sleep efficiency during week 1 (p < 0.02) |

**Notes:**
- **Pooled Estimates (MA):** Pooled estimates from meta-analysis.
- **Narrative Results (from SR with no MA):** Narrative results from systematic reviews without meta-analysis.
- **Significant improvement:** Indicates a statistically significant improvement compared to placebo.
- **I-squared:** Percentage of total variation across studies that is due to heterogeneity rather than chance.
| Author, Year       | Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-------------------|----------------|---------------|-------------------------------|--------------|-------------------|-------------------------------------------------------------|
| Sateia, 2017      | Meta-analysis  | Critically Low | Zolpidem: 111 Placebo: 115    | 4            | polysomnography   | Mean difference[95% CI]: 6.12 [4.39, 7.85]  I-squared: 35%  |
| Swainston Harrison, 2005 | Systematic Review | Critically Low | Zolpidem Placebo Total sample: 69 | 1            | NR                | Change in outcome (p-value): -3 vs +5 min (p=NS)           |
|                   |                |               | Zolpidem Triazolam Total sample: 86 | 2            | NR                | Change in outcome (p-value): +10 vs -6 min (p<0.01) -3 vs -15 min (p=NS) |
| **Health-related quality of life** |               |               | Zopiclone Placebo Total sample: 1006 | 2            | 23-item questionnaire developed by sleep experts; QOLI | Contradicting evidence between both studies. No differences found in QoL between subjects treated with zopiclone and placebo |
| **Hangover/morning sedation** | Low           |               | Zopiclone Flurazepam Placebo Total sample: 789 | 1            | SF-36             | Both groups demonstrated improvement with treatment (p=0.005). The continuous group demonstrated greater increase in mean MOS than the discontinuous group. |
| **Addiction, dependence, or diversion** | Critically Low |               | Zopiclone No comparator (pre- post-intervention) Total sample: 119 | 3            | NR                | After 3 weeks of treatment, zopiclone has no effect on early morning performance and free of residual sedative activity |
|                   |                |               | Zopiclone Triazolam Total sample: 48 | 1            | NR                | One study found no carry over effect after 3 weeks of treatment; the second one found that after 7-8 weeks of treatment, return of sleep variables to pre-treatment baseline after withdrawal, and 1 of 11 patients had marked rebound insomnia and daytime anxiety for the first week off; and the third study after 3 mos of treatment, found withdrawal effects despite tapering dose |
|                   |                |               | Zopiclone Zolpidem Total sample: 248 | 1            | NR                | Worse psychomotor deterioration after triazolam than zopiclone, 3 of 24 zopiclone patients felt agitated early after withdrawal |
|                   |                |               |                                |              |                   | After 2 weeks of treatment, zopiclone group had 15.4% with rebound insomnia |
| Author, Year Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-----------------------------|---------------|------------------------------|--------------|--------------------|---------------------------------------------------------------|
| *bolded results indicate statistical significance as reported by review* |

### Table E3. Suvorexant

| Author, Year Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-----------------------------|---------------|------------------------------|--------------|--------------------|---------------------------------------------------------------|
| **Sleep onset latency**     |               |                              |              |                    |                                                               |
| Brasure, 2015 Meta-analysis | High         | Suvorexant: 425 Placebo: 664 | 2            | subjective report  | Mean change [95% CI]: -5.97 [-10.01, -1.92] I-squared: 0%      |
| Kishi, 2015 Meta-analysis   | Moderate      | Suvorexant: 936 Placebo: 953 | 3            | sleep diary        | Mean difference [95% CI]: -7.62 [-11.03, -4.21] I-squared: 0% |
|                            |              | Suvorexant: 349 Placebo: 659 | 3            | polysomnography    | Mean difference [95% CI]: -10.82 [-16.72, -4.93] I-squared: 35% |
| Kuriyama, 2017 Meta-analysis| Moderate      | Suvorexant: NR Placebo: NR  | 3            | sleep diary, PSG   | Mean difference [95% CI]: -9.45 [-13.26, -5.65] I-squared: 13.3% |
|                            |              | Suvorexant: NR Placebo: NR  | 3            | polysomnography    | Mean difference [95% CI]: -6.39 [-12.85, 0.07] I-squared: 67.1% |
| Citrome, 2014 Systematic Review | Critically Low | Suvorexant: 15; 20 mg: 425 Placebo: 688 | 2            | sleep diary        | Change in outcome [least squares mean difference (p-value)]: -5.9 minutes (p<0.01) Proportion of respondents with >15% improvement: 69.9% vs 66%; NNT: 26 (p=NS) Suvorexant was superior to placebo for sleep latency both through patient-assessed and polysomnography means |
|                            |              | Suvorexant: 30; 40 mg: 688 Placebo: 664 | 2            | polysomnography    | Change in outcome [least squares mean difference (p-value)]: -10.8 minutes (p<0.001) Proportion of respondents with >15% improvement: 76.5% vs 66%; NNT 10 (95% CI 7 to 18) |
|                            |              | Suvorexant: 30; 40 mg: 590 Placebo: 585 | 2            | polysomnography    | Change in outcome [least squares mean difference (p-value)]: -6.4 minutes (p<0.01) |
| Study                                      | Rating        | Treatment | Placebo | Type of Data | Total Sleep Time | Change in Outcome | Wake After Sleep Onset |
|-------------------------------------------|---------------|-----------|---------|--------------|------------------|-------------------|------------------------|
| Kishi, 2015                               | Moderate      | Suvorexant: 936 | Placebo: 953 | 3 sleep diary | Mean difference [95% CI]: | -20.16 min [-25.01, -15.30] I-squared: 0% |
| Kuriyama, 2017                            | Moderate      | Suvorexant: NR  | Placebo: NR | 3 sleep diary, PSG | Mean difference [95% CI]: | 18.55 min [12.52, 24.58] I-squared: 0% |
| Brasure, 2015                             | High          | Suvorexant: 425 | Placebo: 664 | 2 subjective report | Mean change [95% CI]: | 15.97 min [4.73, 27.22] I-squared: 63% |
| Citrome, 2014 Systematic Review           | Critically Low| Suvorexant (15, 20 mg): 425 | Placebo: 664 | 2 sleep diary | Change in outcome [least squares mean difference (p-value)]: | 16 minutes (p<0.001) |
|                                           |               | Suvorexant (30, 40 mg): 688 | Placebo: 664 |               | Proportion of respondents with >15% increase: | 50.1% v 41.9%; NNT 13 (95% CI 17 to 46) |
|                                           |               | Suvorexant: NR  | Placebo: NR | 3 sleep diary | Mean difference [95% CI]: | -7.51 [-12.46, -2.56] I-squared: 0% |
|                                           |               | Suvorexant: NR  | Placebo: NR | 3 polysomnography | Mean difference [95% CI]: | -24.19 [-33.81, -14.58] I-squared: 69.7% |
| Kishi, 2015                               | Moderate      | Suvorexant: 955 | Placebo: 960 | 3 sleep diary | Mean difference [95% CI]: | -7.75 [-10.87, -4.62] I-squared: 0% |
| Suvorexant: 317                           |               | Placebo: 542 | 2 polysomnography | Mean difference [95% CI]: | -25.32 [-31.52, -19.39] I-squared: 0% |
| Kuriyama, 2017                            | Moderate      | Suvorexant: NR  | Placebo: NR | 3 sleep diary | Mean difference [95% CI]: | -7.51 [-12.46, -2.56] I-squared: 0% |
| Suvorexant: NR                            |               | Placebo: NR | 3 polysomnography | Mean difference [95% CI]: | -24.19 [-33.81, -14.58] I-squared: 69.7% |
| Citrome, 2014 Systematic Review           | Critically Low| Suvorexant (15, 20 mg): 425 | Placebo: 660 | 2 polysomnography | Change in outcome [least squares mean difference (p-value)]: | -4.7 minutes (p<0.0001) |
|                                           |               | Suvorexant (30, 40 mg): 683 | Placebo: 660 |               | Proportion of respondents with >15% improvement: | 75.8% v 69.4%; NNT 16 (95% CI 9 to 102) |
|                                           |               | Suvorexant (15, 20 mg): 343 | Placebo: 585 | 2 polysomnography | Change in outcome [least squares mean difference (p-value)]: | -23.1 minutes (p<0.001) |
|                                           |               | Suvorexant (30, 40 mg): 683 | Placebo: 660 | 2 sleep diary | Change in outcome [least squares mean difference (p-value)]: | -7.8 minutes (p<0.001) |
|                                           |               | Suvorexant (15, 20 mg): 343 | Placebo: 585 |               | Proportion of respondents with >15% improvement: | 77.5% v 69.4%; NNT 13 (95% CI 8 to 30) |
## Sleep quality

| Study                          | Level | Suvorexant (30, 40 mg) | Placebo | Method | Change in outcome: least squares mean difference (p-value): |
|-------------------------------|-------|------------------------|---------|--------|----------------------------------------------------------|
| Kishi, 2015 Meta-analysis     | Moderate | 590                    | 585     | polysomnography | -25.9 minutes (p<0.001) |

## Insomnia severity index

| Study                          | Level | Suvorexant | Placebo | Method | Change in outcome: mean difference [95% CI]: |
|-------------------------------|-------|------------|---------|--------|------------------------------------------|
| Kishi, 2015 Meta-analysis     | Moderate | 955        | 960     | polysomnography | 0.17 [-0.25, -0.09] I-squared: 0% |
| Kuriyama, 2017 Meta-analysis  | Moderate | NR         | NR      | ISI    | -1.42 [-1.85, -0.98] I-squared: 0% |

## Sleep diary; 4-point scale

| Study                          | Level | Suvorexant (30, 40 mg) | Placebo | Method | Proportion of respondents with >6 point improvement: |
|-------------------------------|-------|------------------------|---------|--------|-----------------------------------------------------|
| Citrome, 2014 Systematic Review | Critically Low | 411                    | 638     | ISI    | 55.5% v 42.2%; NNT 8 (95% CI 6 to 14) |
| Suvorexant (30, 40 mg)        |       | 656                    | Placebo | ISI    | 54.9% v 42.2%; NNT 8 (95% CI 6 to 14) |

## Hangover/morning sedation

| Study                          | Level | Suvorexant | Placebo | Method | Change in outcome: risk ratio [95% CI]: |
|-------------------------------|-------|------------|---------|--------|----------------------------------------|
| Kishi, 2015 Meta-analysis     | Moderate | 1784       | 1025    | NR     | 3.34 [1.08, 10.32] I-squared: 0% |
| Kuriyama, 2017 Meta-analysis  | Moderate | 2027       | 1274    | "excessive daytime sleepiness" | 3.05 [1.10, 8.48] I-squared: 0% |

## Accidental Injury

| Study                          | Level | Suvorexant | Placebo | Method | Change in outcome: relative risk [95% CI]: |
|-------------------------------|-------|------------|---------|--------|------------------------------------------|
| Kishi, 2015 Meta-analysis     | Moderate | 1784       | 1025    | "Motor vehicle accidents/violation" | 1.16 [0.52, 2.60] I-squared: 14% |
| Kuriyama, 2017 Meta-analysis  | Moderate | 1784       | 1025    | "Falls" | 0.84 [0.44, 1.62] I-squared: 0% |
| Suvorexant (30, 40 mg)        |       | 1784       | 1025    | "Motor vehicle accident/violation" | 1.16 [0.39, 3.40] I-squared: 50.2% |

## Addiction, dependence, diversion

| Study                          | Level | Suvorexant | Placebo | Method | Change in outcome: relative risk [95% CI]: |
|-------------------------------|-------|------------|---------|--------|------------------------------------------|
| Kishi, 2015 Meta-analysis     | Moderate | 1784       | 1025    | "events suggesting drug abuse potential" | 1.05 [0.67, 1.65] I-squared: 0% |
| Kuriyama, 2017 Meta-analysis  | Moderate | 1784       | 1025    | "Potential drug abuse" | 1.05 [0.66, 1.65] I-squared: 0% |
| Author, Year | Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|--------------|----------------|---------------|-----------------------------|--------------|-------------------|----------------------------------------------------------------|
| **Sleep onset latency** | | | | | | |
| Buscemi, 2005 | Meta-analysis | High | Doxepin 25mg: 40 Placebo: 40 | 3 | sleep diary, polysomnography | Mean difference [95% CI]: -6.65 [-10.68, -2.63] I-squared: 49.3% |
| | | | Doxepin 3mg: 282 Placebo: 276 | 4 | polysomnography | Mean difference [95% CI]: -2.3 [-6.22, 1.62] I-squared: 0% |
| | | Critically Low | Doxepin 3mg: 148 Placebo: 143 | 2 | subjective measure | Mean difference [95% CI]: -9.35 [-21.89, 3.19] I-squared: 55% |
| | | | Doxepin 6mg: 209 Placebo: 206 | 3 | polysomnography | Mean difference [95% CI]: -5.29 [-9.25, -1.34] I-squared: 0% |
| Sateia, 2017 | Meta-analysis | Critically Low | Doxepin 1mg: 140 Placebo: 139 | 2 | NR | Mean difference [95% CI]: -0.85 [-5.82, 4.13] I-squared: NR |
| | | | Doxepin 3mg: 140 Placebo: 139 | 2 | NR | Mean difference [95% CI]: 0.37 [-0.66, 1.40] I-squared: NR |
| | | | Doxepin 6mg: 141 Placebo: 139 | 2 | NR | Mean difference [95% CI]: 0.37 [-0.66 to 1.40] I-squared: NR |
| | | | Doxepin 25mg: 30 Placebo: 30 | 2 | NR | Mean difference [95% CI]: -8.69 [-13.72 to -3.67] I-squared: NR |
| Yuan, 2010 | Meta-analysis | Low | | | | |
| | | | Doxepin 1mg: 140 Placebo: 139 | 2 | NR | Mean difference [95% CI]: -0.85 [-5.82, 4.13] I-squared: NR |
| | | | Doxepin 3mg: 140 Placebo: 139 | 2 | NR | Mean difference [95% CI]: 0.37 [-0.66, 1.40] I-squared: NR |
| | | | Doxepin 6mg: 141 Placebo: 139 | 2 | NR | Mean difference [95% CI]: 0.37 [-0.66 to 1.40] I-squared: NR |
| | | | Doxepin 25mg: 30 Placebo: 30 | 2 | NR | Mean difference [95% CI]: -8.69 [-13.72 to -3.67] I-squared: NR |
| Buscemi, 2005 | Meta-analysis | High | Trazodone (50mg, 150-250mg): 100 Placebo: 108 | 2 | sleep diary, polysomnography | Mean difference [95% CI]: -12.21 [-22.26, -2.15] I-squared: 0% |
| | | | Doxepin Placebo | NR | self-report | Adults <65 y: 3 mg doxepin had negative impact on sleep latency in short term (1-2 nights) results, 6 mg doxepin had positive impact on sleep latency in the short term (1-2 nights) | Adults >65y: 3 mg doxepin had negative impact on sleep latency in both short- and long-term (4 weeks) treatment; 6 mg doxepin had positive results at short-term but negative results at long-term |
| Mayers, 2005 | Systematic Review | Critically Low | Doxepin: NR Placebo: NR | NR | polysomnography questionnaire (7-point Likert scale) | Mixed results: polysomnography and questionnaire data showed significant improvement compared to placebo in some trials (p<0.05); non-significant change found in other trials |
| Vande Griend, 2012 | Systematic Review | Critically Low | Doxepin: NR Placebo: NR | 6 | polysomnography questionnaire | Adults <65 y: 3 mg doxepin had negative impact on sleep latency in short term (1-2 nights) results, 6 mg doxepin had positive impact on sleep latency in the short term (1-2 nights) | Adults >65y: 3 mg doxepin had negative impact on sleep latency in both short- and long-term (4 weeks) treatment; 6 mg doxepin had positive results at short-term but negative results at long-term |
| Yeung, 2015 | Systematic Review | Moderate | Doxepin: NR Placebo: NR | NR | self-report | Adults <65 y: 3 mg doxepin had negative impact on sleep latency in short term (1-2 nights) results, 6 mg doxepin had positive impact on sleep latency in the short term (1-2 nights) | Adults >65y: 3 mg doxepin had negative impact on sleep latency in both short- and long-term (4 weeks) treatment; 6 mg doxepin had positive results at short-term but negative results at long-term |
| Study                        | Critically Low          | Intervention | Control | Sample Size | Outcome Measures | Findings |
|------------------------------|-------------------------|--------------|---------|-------------|------------------|----------|
| Mayers, 2005 Systematic Review | Critically Low          | Trazodone    | Placebo | 323         | NR, polysomnography | Adults <65y: 3 and 6 mg had mixed results in short-term and negative results in long-term; Adults >65y: 3 mg doxepin had mixed results in short term and negative results in long-term; 6 mg doxepin had negative results in short term, no assessment of long-term effect |
| Mendelson, 2005 Systematic Review | Critically Low          | Trazodone    | Placebo; unspecified control | 306         | NR, self-reported | Relative to placebo, patients reported significant improvement during week 1 (p<0.02); during week 2, the trazodone group did not differ significantly from the placebo group. |
| Vande Griend, 2012 Systematic Review | Critically Low          | Trazodone: NR | Placebo: NR | 306         | polysomnography | No significant changes in sleep latency found between groups |
| Liu, 2017 Meta-analysis      | Critically Low          | Doxepin: 743 | Placebo: 733 | 7           | polysomnography | Standardized mean difference [95% CI]: 0.61 [0.50, 0.71] I-squared: 15% |
| Brasure, 2015 Meta-analysis  | High                    | Doxepin: 289 | Placebo: 205 | 2           | subjective report, in minutes | Mean change [95% CI]: 23.85 [12.04, 35.65] I-squared: 0% |
| Study                        | Meta-analysis Level | Meta-analysis Type | Doxepin Dose | Placebo Dose | Study Design | Outcome Measure | Mean Difference [95% CI] | I-squared |
|------------------------------|---------------------|--------------------|--------------|--------------|--------------|-----------------|-------------------------|-----------|
| Sateia, 2017                 | Critically Low      | Meta-analysis      | Doxepin (3mg): 282 | Placebo: 276 | polysomnography | Mean difference [95% CI]: 26.14 [18.49, 33.79] I-squared: 0% |
|                             |                     |                    | Doxepin (3mg): 148 | Placebo: 143 | subjective measure | Mean difference [95% CI]: 43.57 [5.16, 81.98] I-squared: 82% |
|                             |                     |                    | Doxepin (6mg): 209 | Placebo: 206 | PSG           | Mean difference [95% CI]: 32.27 [24.24, 40.30] I-squared: 0% |
|                             |                     |                    | Doxepin (6mg): 204 | Placebo: 197 | subjective measure | Mean difference [95% CI]: 18.84 [-1.65, 39.34] I-squared: 56% |
| Yuan, 2010                   | Low                 | Meta-analysis      | Doxepin (1mg): 140 | Placebo: 139 | NR            | Mean difference [95% CI]: 17.24 [7.43, 27.05] I-squared: NR |
|                             |                     |                    | Doxepin (25mg): 30 | Placebo: 30 | NR            | Mean difference [95% CI]: 70.74 [42.61, 98.88] I-squared: NR |
|                             |                     |                    | Doxepin (3mg): 140 | Placebo: 139 | NR            | Mean difference [95% CI]: 27.95 [17.99, 37.90] I-squared: NR |
|                             |                     |                    | Doxepin (6mg): 141 | Placebo: 139 | NR            | Mean difference [95% CI]: 33.78 [24.44, 43.11] I-squared: NR |
| Mayers, 2005 Systematic Review | Critically Low   | Systematic Review  | Doxepin | Placebo | Total sample: 10 | Doxepin significantly improved total sleep time compared to placebo (p-value not reported) |
| Vande Griend, 2012 Systematic Review | Critically Low  | Systematic Review  | Doxepin: NR | Placebo: NR | polysomnography | Doxepin increased total sleep time by 25-51 minutes across the trials; 6 of the found a significant difference compared to placebo (p<0.05) |
| Yeung, 2015 Systematic Review  | Moderate            | Systematic Review  | Doxepin: NR | Placebo: NR | NR | self-report |
|                             |                     |                    | Adults <65y: mixed results for 3 mg doxepin over 1-2 nights, a single trial showed improvement at 4 weeks; multiple trials showed positive improvement for 6 mg doxepin over 1-2 nights, a single trial showed improvement at 4 weeks |
|                             |                     |                    | Adults >65y: 3mg and 6mg doxepin showed positive results over 1-2 nights; results were maintained for 3 mg doxepin only |
|                             |                     |                    | NR | polysomnography |
|                             |                     |                    | Adults <65y: multiple trials found positive results for 3mg and 6mg doxepin over 1-2 nights, the effect was maintained at 4 weeks for 6mg doxepin only |
|                             |                     |                    | Adults >65y: positive results for 3mg and 6mg doxepin over 1-2 nights, the effect was maintained at 4 weeks for 3 mg doxepin; no long-term data on 6mg doxepin was available |
| Study                          | Methodology     | Design/Quality | Intervention/Comparator | Total Sample | Study Type | Outcome                          |
|-------------------------------|-----------------|----------------|-------------------------|--------------|------------|----------------------------------|
| **Mayers, 2005**              | Systematic Review | Critically Low | Trazodone Placebo       | 323          |            | Both trials found a **significant increase** in total sleep time compared to placebo ($p<0.05$; $p=0.003$) |
|                               |                 |                | Trazodone (50 v 75 v 100mg): 75 |              |            | Total sleep time was **significantly longer** with 50mg and 75mg doses compared to 100mg ($p$-value NR); no significant difference was found between 50mg and 75mg doses ($p$-value NR) |
|                               |                 |                | No comparator (multiple doses) | 1            | self-rated |                                   |
| **Mendelson, 2005**           | Systematic Review | Critically Low | Trazodone Placebo; unspecified control | 63           | polysomnography | Mixed results: 2 trials found **significant improvement** in total sleep time compared to placebo ($p<0.05$); 1 trial found no significant change between groups |
|                               |                 |                | Trazodone: 39 | 3            | polysomnography | Mixed results: 2 trials found **significant increase** in total sleep time compared to baseline ($p<0.05$); 3 trials found no significant change from baseline |
|                               |                 |                | No comparator (pre-post-intervention) | 5            | polysomnography |                                   |
| **Vande Griend, 2012**        | Systematic Review | Critically Low | Trazodone: NR | 2            | sleep diaries polysomnography | No significant differences between groups |
|                               |                 |                | Placebo: NR |              |            |                                   |
|                               |                 |                | Total sample: 306 |              |            |                                   |
| **Vande Griend, 2012**        | Systematic Review | Critically Low | Trazodone | 1            | NR | No significant differences found between zolpidem and trazodone |
|                               |                 |                | Zolpidem |              |            |                                   |
|                               |                 |                | Total sample: 306 |              |            |                                   |

**Wake after sleep onset**

| Study                          | Methodology     | Design/Quality | Intervention/Comparator | Total Sample | Study Type | Outcome                          |
|-------------------------------|-----------------|----------------|-------------------------|--------------|------------|----------------------------------|
| **Sateia, 2017**              | Meta-analysis   | Critically Low | Doxepin (3mg): 282 Placebo: 276 | 4 polysomnography | polysomnography | Mean difference [95% CI]: **-22.17 [-29.62, -14.72] I-squared: 23%** |
|                               |                 |                | Doxepin (6mg): 209 Placebo: 206 | 3 polysomnography | polysomnography | Mean difference [95% CI]: **-23.4 [-30.34, -16.46] I-squared: 0%** |
|                               |                 |                | Doxepin (6mg): 204 Placebo: 197 | 2 Subjective measure | polysomnography | Mean difference [95% CI]: **-14.39 [-24.86, -3.93] I-squared: 0%** |
| **Yuan, 2010**                | Meta-analysis   | Low            | Doxepin (1mg): 140 Placebo: 139 | 2             | NR | Mean difference [95% CI]: **-3.57 [-7.46, 0.32] I-squared: NR** |
|                               |                 |                | Doxepin (25mg): 30 Placebo: 30 | 2             | NR | Mean difference [95% CI]: **-10.23 [-14.82, -5.64] I-squared: NR** |
|                               |                 |                | Doxepin (3mg): 140 Placebo: 139 | 2             | NR | Mean difference [95% CI]: **-5.71 [-9.39, -2.02] I-squared: NR** |
|                               |                 |                | Doxepin (6mg): 141 Placebo: 139 | 2             | NR | Mean difference [95% CI]: **-7.36 [-10.69, -4.03] I-squared: NR** |
| Study                                      | Quality | Methodology            | Treatment          | Comparator        | Sample Size | Outcome Measure | Result Description                                                                 |
|-------------------------------------------|---------|------------------------|--------------------|-------------------|-------------|-----------------|------------------------------------------------------------------------------------|
| Vande Griend, 2012                        | Critically Low | Doxepin: NR | Placebo: NR | 7 polysomnography questionnaire (Likert-type scale) | Doxepin reduced WASO by 5-20 minutes across the trials; 6 out of 7 trials found a significant difference compared to placebo \( (p<0.05) \) |
| Yeung, 2015                                | Moderate | Doxepin: NR | Placebo: NR | 6 self-report | Adults <65y: mixed results for 3mg and 6mg doxepin over 1-2 nights, 3mg and 6mg doxepin showed positive results at 4 weeks; Adults >65y: positive results for 3mg doxepin over 1-2 nights, negative results for 6mg doxepin over 1-2 nights and at 4 weeks |
| Kolla, 2011                                | Critically Low | Trazodone | Placebo | 1 polysomnography | Improved WASO was observed in trazodone participants compared to placebo |
| Mayers, 2005                               | Critically Low | Trazodone | Placebo | 1 NR | Significant improvement in WASO compared to placebo \( (p=0.04) \) |
| Mendelson, 2005                            | Critically Low | Trazodone | Placebo; unspecified control | 1 self-reported | Relative to placebo, patients reported significant improvement during week 1 \( (p<0.02) \); during week 2, the trazodone group did not differ significantly from the placebo group. |
| Vande Griend, 2012                        | Critically Low | Trazodone: NR | Placebo: NR | 2 polysomnography | Mixed result: 1 trial found significant improvement \( (p<0.05) \); 1 trial found no significant change from baseline |
| Mayers, 2005                               | Critically Low | Trazodone | Zolpidem | 1 NR | No significant differences found between zolpidem and trazodone |
| Vande Griend, 2012                        | Critically Low | Trazodone | Zolpidem | 1 daily questionnaire | No significant differences found between zolpidem and trazodone |

*Sleep Quality*
| Study                        | Methodology | Study Type | Intervention | Comparator | Outcome measure | Study Outcome |
|-----------------------------|-------------|------------|--------------|------------|----------------|---------------|
| Sateia, 2017                | Meta-analysis | Critically Low | Doxepin (3mg): 148 | Placebo: 143 | 2 subjective measure | Standardized mean difference [95% CI]: 0.57 [0.26 to 0.88] I-squared: 43% |
|                            |             |            | Doxepin (6mg): 204 | Placebo: 200 | 2 subjective measure | Standardized mean difference [95% CI]: 0.28 [0.06 to 0.49] I-squared: 15% |
| Mayers, 2005 Systematic Review | Critically Low | Doxepin Placebo Total sample: 57 | 2 NR | | Doxepin significantly improved sleep quality relative to placebo (p<0.001) |
| Kolla, 2011 Systematic Review | Critically Low | Trazodone placebo Total sample: 173 | 1 Pittsburgh Sleep Quality Index | | Sleep quality improved significantly in trazodone group during active treatment phase |
| Mayers, 2005 Systematic Review | Critically Low | Trazodone Placebo Total sample: 323 | 2 NR; Pittsburgh Sleep Quality Index | | Sleep quality significantly improved compared to placebo in one trial (p=0.003), and almost reached significance in the other (p=0.06) but significantly higher proportion of patients in this trial showed improvement on sleep quality compared to placebo (0.004) |
| Mendelson, 2005 Systematic Review | Critically Low | Trazodone placebo; unspecified control Total sample: 767 | 5 self-reported (1); Pittsburgh Sleep Quality Index (1); Leeds sleep evaluation questionnaire (3) | | Relative to placebo, patients reported significant improvement during week 1 (p<0.02); during week 2, the trazodone group did not differ significantly from the placebo group; 3 trials reported significant improvements throughout the 6-week treatment period for "quality of sleep."(p<0.001); Pittsburgh Sleep Quality Index improvements were similar for the placebo and trazodone groups |
|                           |             |            | Trazodone 9 No comparator (pre- post-intervention) Total sample: 306 | 1 visual analog scale | In the subjective ratings, sleep quality improved significantly during weeks 1 and 2 (p<0.001) but not during week 3 |
| Mayers, 2005 Systematic Review | Critically Low | Trazodone Zolpidem Total sample: 306 | 1 NR | | No significant differences found between zolpidem and trazodone |

**Sleep Efficiency**

| Study                        | Methodology | Study Type | Intervention | Comparator | Outcome measure | Study Outcome |
|-----------------------------|-------------|------------|--------------|------------|----------------|---------------|
| Sateia, 2017                | Meta-analysis | Critically Low | Doxepin (3mg): 214 | Placebo: 209 | 3 polysomnography | Mean difference [95% CI]: 6.78 [4.50 to 9.07] I-squared: 17% |
|                            |             |            | Doxepin (6mg): 141 | Placebo: 139 | 2 polysomnography | Mean difference [95% CI]: 7.06 [5.12 to 9.01] I-squared: 0% |
| Yuan, 2010 Meta-analysis     | Low         |            | Doxepin (1mg): 140 | Placebo: 139 | 2 NR | Mean difference [95% CI]: 3.59 [1.55 to 5.63] I-squared: NR |
|                            |             |            | Doxepin (25mg): 30 | Placebo: 30 | 2 NR | Mean difference [95% CI]: 12.58 [7.60, 17.56] I-squared: NR |
| Study                          | Quality       | Dosage 1 | Dosage 2 | N | ISI   | Effect Size | Notes                                                                 |
|-------------------------------|---------------|----------|----------|---|-------|-------------|------------------------------------------------------------------------|
| **Doxepin**                   |               |          |          |   |       |             |                                                                        |
| Mayers, 2005                  | Critically Low| Doxepin  | Placebo  | 2 | NR    | Mean difference [95% CI]: 5.82 [3.75 to 7.90] | I-squared: NR |
|                               |               | 140      | 139      |   |       |              |                                                                        |
| Vande Griend, 2012            | Critically Low| Doxepin  | Placebo  | 1 | NR    | Mean difference [95% CI]: 7.07 [5.12 to 9.01] | I-squared: NR |
|                               |               | 141      | 139      |   |       |              |                                                                        |
| Yeung, 2015                   | Moderate      | Doxepin  | Placebo  | 1 | polysomnography | Sleep efficiency significantly improved compared to placebo (p<0.05) |                                                                        |
|                               |               | NR       | NR       |   |       |              |                                                                        |
| Mendelson, 2005               | Critically Low| Trazodone| Placebo  | 3 | polysomnography | Mixed result: 2 trials found significant improvements in sleep efficiency compared to placebo (p<0.05); 1 trial found no significant change compared to placebo |                                                                        |
|                               |               | 20       | NR       |   |       |              |                                                                        |
| Vande Griend, 2012            | Critically Low| Trazodone| Placebo  | 2 | sleep diaries; polysomnography | Mixed result: 1 study found significant difference between groups (p<0.05, polysomnography data only); 1 study found no difference between group (polysomnography and sleep diary data) |                                                                        |
|                               |               | NR       | NR       |   |       |              |                                                                        |
| **Trazodone**                 |               |          |          |   |       |             |                                                                        |
| Mendelson, 2005               | Critically Low| Trazodone| unspecified control | 3 | polysomnography | Mixed result: 1 trial found significant improvements in sleep efficiency compared to baseline (p<0.05); 2 trials found no significant change from baseline |                                                                        |
|                               |               | 20       |          |   |       |              |                                                                        |
| Vande Griend, 2012            | Critically Low| Trazodone| Placebo  | 2 | polysomnography | Mixed result: 1 study found significant difference between groups (p<0.05, polysomnography data only); 1 study found no difference between group (polysomnography and sleep diary data) |                                                                        |
|                               |               | NR       | NR       |   |       |              |                                                                        |

**Insomnia Severity Index**

| Study                          | Quality       | Dosage 1 | Dosage 2 | N | ISI   | Effect Size | Notes                                                                 |
|-------------------------------|---------------|----------|----------|---|-------|-------------|------------------------------------------------------------------------|
| Brasure, 2015                 | High          | Doxepin  | Placebo  | 2 | ISI   | Mean change [95% CI]: -1.74 [-2.59 to -0.88] | I-squared: 0% |
|                               |               | 289      | 205      |   |       |              |                                                                        |

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*NR* = Not reported.
| Author, Year | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|--------------|---------------|-----------------------------|--------------|--------------------|-------------------------------------------------------------|
| **Sleep onset latency** | | | | | |
| Anderson, 2014 Systematic Review | Critically Low | Quetiapine: 18 No comparator (pre-post-intervention) Total sample: 18 | 1 | polysomnography | Change in outcome: 395.6 +/- 62.3 (p<0.05 compared to baseline) |
| | | Placebo: 8 | | | |
| | | 2 | patient-recorded sleep logs | Change in outcome: 395.6 +/- 62.3 (p<0.05 compared to baseline) |
| | | Quetiapine: 32 Placebo: 8 | 1 | polysomnography or actigraphy | Change in outcome: 22±17 v 24±19 minutes (p=NS); 82±65 v 29±23 minutes (p<0.05) |
| | | Total sample: 52 | | | |
| | | 2 | NR | Change in outcome: 22±17 v 24±19 minutes (p=NS); 82±65 v 29±23 minutes (p<0.05) |
| Wine, 2009 Systematic Review | Critically Low | Quetiapine: 18 No comparator (pre-post-intervention) Total sample: 18 | 1 | polysomnography | Change in outcome: 22±17 v 24±19 minutes (p=NS); 82±65 v 29±23 minutes (p<0.05) |
| | | Placebo: 8 | | | |
| | | 2 | patient-recorded sleep logs | Change in outcome: 22±17 v 24±19 minutes (p=NS); 82±65 v 29±23 minutes (p<0.05) |
| | | Quetiapine: 32 Placebo: 8 | 1 | polysomnography or actigraphy | Change in outcome: 22±17 v 24±19 minutes (p=NS); 82±65 v 29±23 minutes (p<0.05) |
| | | Total sample: 52 | | | |
| | | 2 | NR | Change in outcome: 22±17 v 24±19 minutes (p=NS); 82±65 v 29±23 minutes (p<0.05) |
| **Total Sleep Time** | | | | | |
| Anderson, 2014 Systematic Review | Critically Low | Quetiapine: 18 No comparator (pre-post-intervention) Total sample: 52 | 2 | polysomnography or actigraphy | Change in outcome: 347.5 +/- 100.9 v 361.9 +/- 85.4 (p=NS); 432 +/- 66 v 390 +/- 54 (p=NS) |
| | | Placebo: 8 | | | |
| | | 1 | objective; from baseline to week 6 | TST significantly improved from baseline compared to week 6 (p=0.03) |
| Wine, 2009 Systematic Review | Critically Low | Quetiapine: 18 No comparator (pre-post-intervention) Total sample: 18 | 1 | polysomnography or actigraphy | Change in outcome: 347.5 +/- 100.9 v 361.9 +/- 85.4 (p=NS); 432 +/- 66 v 390 +/- 54 (p=NS) |
| | | Placebo: 8 | | | |
| | | 1 | NR | TST significantly improved from baseline compared to week 6 (p=0.03) |
| | | Quetiapine: Untreated control (pre-post-intervention) Total sample: 18 | 1 | NR | Significant decrease in TST vs baseline for quetiapine |

**Sleep Quality**
| Study                  | Type            | Quality | Quetiapine | Comparator | Sample Size | Outcome Measure | Changes                                                                 |
|-----------------------|-----------------|---------|------------|------------|-------------|-----------------|------------------------------------------------------------------------|
| Anderson, 2014        | Systematic Review | Critically Low | 84         | No comparator (pre-post-intervention) | 3 | PSQI; Spiegel Sleep Questionnaire | **Significant improvements** on PSQI global scores (p<0.001); 75% improvement in global score for SSQ (p-value not reported) |
| Coe, 2014             | Systematic Review | Critically Low | 18         | No comparison | 1 | PSQI; actigraphy | **Significant improvement** in PSQI scores from baseline and compared to placebo (p<0.001) |
| Kolla, 2011           | Systematic Review | Critically Low | 28         | No comparator (pre-post-intervention) | 1 | HAM-D's sleep question subset | Middle and late insomnia was **significantly reduced** at 2 weeks, no other sleep data presented |
| Wine, 2009            | Systematic Review | Critically Low | 18         | No comparator (pre-post-intervention) | 1 | PSQI | PSQI decreased total scores with use of quetiapine vs baseline |
| **Sleep Satisfaction**|                 |          |            |            |             |                 |                                                                        |
| Anderson, 2014        | Systematic Review | Critically Low | 18         | No comparator (pre-post-intervention) | 1 | Visual analogue scale | Non-significant improvement based on visual analog scale (p=0.505) |
| **Sleep Efficiency**  |                 |          |            |            |             |                 |                                                                        |
| Anderson, 2014        | Systematic Review | Critically Low | 18         | No comparator (pre-post-intervention) | 1 | Polysomnography | Change in outcome (p-value): 89.9±8.2 (p<0.05) |
| Coe, 2014             | Systematic Review | Critically Low | 18         | No comparator (pre-post-intervention) | 1 | Polysomnography or actigraphy | Change in outcome (p-value): 82.7±9.1 v 77.0±7.9 (p<0.05) |
| Wine, 2009            | Systematic Review | Critically Low | 18         | No comparator (pre-post-intervention) | 1 | Objective measure | Sleep efficiency **significantly improved** from baseline compared to week 6 (p=0.02) |
| **Insomnia Severity Index** |                 |          |            |            |             |                 |                                                                        |
| Anderson, 2014        | Systematic Review | Critically Low | 6          | No comparator (pre-post-intervention) | 1 | ISI | In 5 of 6 patients, the ISI score moved from moderate insomnia to absence of insomnia at week 1 and was maintained |

**Hangover/Morning Sedation**
Daytime sedation was **significantly more common** in the quetiapine group (compared to placebo, p-value not reported)

| Author, Year | Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|--------------|----------------|---------------|------------------------------|--------------|--------------------|---------------------------------------------------------------|
| Anderson, 2014 | Systematic Review | Critically Low | Quetiapine Placebo; no therapy | 2 | NR | |

**Table E6. Melatonin**

| Author, Year | Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|--------------|----------------|---------------|------------------------------|--------------|--------------------|---------------------------------------------------------------|
| **Sleep onset latency** | | | | | | |
| Buscemi, 2005 | Meta-analysis | High | Melatonin: 103 Placebo: 103 | 8 | sleep diary polysomnography | Mean difference [95% CI]: -8.25 [-14.45, -2.04] I-squared: 44.2% |
| Buscemi, 2004 | Meta-analysis | High | Melatonin: 178 Placebo: 167 | 12 | NR | Mean difference [95% CI]: -10.66 [-17.61, -3.72] I-squared: 81.5% |
| Ferracioli-Oda, 2013 | Meta-analysis | Critically Low | Melatonin: NR Placebo: NR | 8 | polysomnography or actigraphy | Mean difference [95% CI]: 5.5 [2.29, 7.81] I-squared: NR |
| Lee, NA | Meta-analysis | Critically Low | Melatonin: NR Placebo: NR | 12 | sleep diary polysomnography or actigraphy | Mean difference [95% CI]: -3.71 [-6.78, -0.63] I-squared: 39% |
| Bellon, 2006 | Systematic Review | Critically Low | Melatonin: NR Placebo: NR | 13 | subjective polysomnography actigraphy | Adults: 3 studies significant improvement (p<0.05); 1 study non-significant improvement; 1 study improved subjectively and non-significant change on polysomnography Elderly: 2 studies non-significant improvement; 2 studies no change; 1 study **significant improvement (P<0.05)** Schizophrenia, Dementia, and medically ill patients: 3 studies, non-significant improvement |
| Culpepper, 2015 | Systematic Review | Critically Low | Melatonin Placebo: Total sample: 772 | 3 | polysomnography actigraphy sleep diary | No significant difference between groups (melatonin vs placebo) |
| Vural, 2014 | Systematic Review | Critically Low | Melatonin Control Total sample: 14 | 1 | NR | **Significant decrease** in sleep latency with morning and nighttime melatonin doses; **significant decrease** in sleep latency to 10mins of persistent sleep with early and continuous melatonin doses |

**Total Sleep Time**

| Author, Year | Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|--------------|----------------|---------------|------------------------------|--------------|--------------------|---------------------------------------------------------------|
| Buscemi, 2004 | Meta-analysis | High | Melatonin: NR Placebo: NR | 11 | NR | Mean difference [95% CI]: 4 [-10.5, 18.5] I-squared: 67.6% |
| Ferracioli-Oda, 2013 | Meta-analysis | Critically Low | Melatonin: NR Placebo: NR | 10 | polysomnography actigraphy | Mean change [95% CI]: 0.34 [-11.19, 11.87] I-squared: NR |
| Author, Year      | Study Type             | Quality   | Melatonin: NR     | Placebo: NR     | N  | Methodologies                          | Effect Size       |
|-------------------|------------------------|-----------|-------------------|----------------|----|----------------------------------------|-------------------|
| Lee, NA           | Meta-analysis          | Critically Low | Melatonin: NR     | Placebo: NR     | 11 | sleep diary, polysomnography, actigraphy | Mean difference [95% CI]: 3.3 [7.04, 13.65] I-squared: 12% |
| McCleery, 2016    | Meta-analysis          | High      | Melatonin: 119    | Placebo: 65     | 2  | actigraphy                             | Mean difference [95% CI]: 10.68 [-16.22, 37.59] I-squared: 0% |
| Xu, 2015          | Meta-analysis          | Moderate  | Melatonin: 257    | Placebo: light therapy: 240 | 8  | actigraphy                             | Mean difference [95% CI]: 24.36 [3.26, 45.46] I-squared: 59% |
| Zhang, 2016       | Meta-analysis          | Critically Low | Melatonin: 101    | Placebo: 96     | 4  | polysomnography, actigraphy            | Mean difference [95% CI]: 12.38 [-10.38, 35.15] I-squared: 34% |
| Bellon, 2006      | Systematic review      | Critically Low | Melatonin: NR     | Placebo: NR     | 15 | subjective polysomnography, actigraphy | Adult patients: 2 studies report no change; 2 report significant improvement: 1 reports subjective improvement but no change on PSG Elderly patients: 4 studies report no change Schizophrenia, dementia, Alzheimer's patients: 3 studies, non-significant improvement Medically ill patients: 1 study, significant improvement |
| Chase, 1997       | Systematic review      | Critically Low | Melatonin Placebo | Total sample: 25 | 2  | wrist actigraphy; subjective report    | 1 study found no change in total sleep time; 1 study found Melatonin treatment resulted in a significant effect on reported time asleep |
| Costello, 2014    | Systematic review      | Moderate   | Melatonin Placebo | Total sample: 791 | 1  | National sleep foundation diary; Pittsburgh Sleep Quality Index | Melatonin (Circadin) significantly increased sleep time compared to placebo (p=0.035) |
| Culpepper, 2015   | Systematic review      | Critically Low | Melatonin Placebo | Total sample: 50 | 2  | sleep diary, polysomnography, actigraphy | Change in outcome (p-value): -15.4 vs -5.5 minutes (p<0.01) [1 study] 1 study: No significant difference between groups (melatonin vs placebo); 1 study: Significant reduction in sleep latency (p<0.01) |
| Wake after sleep onset |                |            |                   |                |    |                                        |                   |
| Buscemi, 2005     | Meta-analysis          | High      | Melatonin: 68     | Placebo: 68     | 5  | sleep diary, polysomnography           | Mean difference [95% CI]: -9.65 [-33.57, 14.26] I-squared: 89.8% |
| Buscemi, 2004     | Meta-analysis          | High      | Melatonin: NR     | Placebo: NR     | 5  | NR                                     | Mean difference [95% CI]: -1.4 [-21.8, 19] I-squared: 84% |
|                   |                        |           | Melatonin: NR     | Placebo: NR     | 3  | NR                                     | Mean difference [95% CI]: -6.3 [-16.6, 3.9] I-squared: 35.3% |
| Zhang, 2016       | Meta-analysis          | Critically Low | Melatonin: 75     | Placebo: 69     | 2  | polysomnography, actigraphy            | Mean difference [95% CI]: 10.93 [-6.07, 27.92] I-squared: 0% |
| Study                                      | Methodology | Score | Intervention | Control | Sample Size | Study Design | Measures                          | Outcome |
|--------------------------------------------|-------------|-------|--------------|---------|-------------|--------------|-----------------------------------|---------|
| Chase, 1997                                | Systematic Review | Critically Low | Melatonin | Placebo | Total sample: 12 | 1 | wrist actigraphy | Change in outcome (p-value): 49 minutes v 73 minutes (p<0.001) |
| Vural, 2014                                | Systematic Review | Critically Low | Melatonin | Control | Total sample: 12 | 1 | NR | Significant decrease in wake after sleep onset in melatonin group |

**Sleep Quality**

| Study                                      | Methodology | Score | Intervention | Control | Sample Size | Study Design | Measures                          | Outcome |
|--------------------------------------------|-------------|-------|--------------|---------|-------------|--------------|-----------------------------------|---------|
| Buscemi, 2004                              | Meta-analysis | High | Melatonin: NR | Placebo: NR | 2 | NR | Standardized mean difference [95% CI]: 0.5 [-0.1, 1.1] I-squared: 0% |
| Ferracioli-Oda, 2013                       | Meta-analysis | Critically Low | Melatonin: NR | Placebo: NR | 14 | polysomnography actigraphy sleep scales questionnaires sleep logs | Mean change [95% CI]: 0.22 [0.13, 0.32] I-squared: 0% |
| McCleery, 2016                             | Meta-analysis | High | Melatonin: 111 Lactose placebo: 53 | 2 | carer-rated sleep quality | Standardized mean difference [95% CI]: 0.04 [-0.29, 0.38] I-squared: 46% |
| Lee, NA                                    | Meta-analysis | Critically Low | Melatonin: 675 Placebo: 672 | 10 | Leeds Sleep Evaluation Questionnaire – Quality of Sleep; The Pittsburgh Sleep Quality Index Component 1; The Northside Hospital Sleep Medicine Institute Test; Daily Sleep Questionnaire | Standardized mean difference [95% CI]: 0.16 [-0.06, 0.39] I-squared: 58% |
| Sateia, 2017                               | Meta-analysis | Critically Low | Melatonin: 233 Placebo: 228 | 3 | subjective measure | Standardized mean difference [95% CI]: 0.21 [-0.36, 0.77] I-squared: 83% |
| Bellon, 2006                               | Systematic Review | Critically Low | Melatonin: NR Placebo: NR | 11 | subjective polysomnography actigraphy | Adult patients: 4 studies showed significant improvement; 2 studies no change Elderly patients: 2 studies no change Medically ill patients: 1 study significant improvement Dementia or Alzheimer’s patients: 2 studies, no change |
| Chase, 1997                                | Systematic Review | Critically Low | Melatonin | Placebo | Total sample: 10 | 1 | daily sleep questionnaire | No statistical difference between groups noted, except patients in melatonin group had significantly improved perceived quality of sleep (p<0.03) |
| Study                                      | Methodology | Quality | Treatment          | Comparator          | Total Sample | Measures                                                                 | Results                                                                 |
|-------------------------------------------|-------------|---------|--------------------|--------------------|--------------|---------------------------------------------------------------------------|-------------------------------------------------------------------------|
| Costello, 2014                            | Systematic Review | Moderate | Melatonin          | Placebo            | 54           | sleep diary; subjective sleep quality questionnaire; Daily Sleep Questionnaire; Stanford Sleepiness Scale; Visual Analog Scale | Melatonin did not affect sleep quality in patients with primary insomnia; melatonin **significantly improved** sleep quality compared to placebo, indicating that controlled-release melatonin may effectively facilitate discontinuation of benzodiazepine therapy while maintaining good sleep quality; melatonin 5 mg resulted in an improvement in overall subjective sleep quality (*p*=0.03) compared to 1 mg and placebo. |
| Culpepper, 2015                           | Systematic Review | Critically Low | Melatonin          | Placebo            | 48           | sleep questionnaire: visual analogue scale; 38-item Northside Hospital Sleep Medicine Institute test | Change in outcome (p-value): 1.78 vs 3.44 (*p*<0.05)  
1 study: No significant difference between groups (melatonin vs placebo);  
1 study: **Significantly improved** sleep quality |
| Vural, 2014                                | Systematic Review | Critically Low | Melatonin          | Control            | 27           | polysomnography sleep diary (2)                                          | Significant increase in sleep quality in melatonin group |
| Vural, 2014                                | Systematic Review | Critically Low | Melatonin          | Control            | 112          | % nights scored good; % good mood                                        | Significant increase in % nights scored good and significant increase in % good mood in melatonin group |
| Buscemi, 2004                              | Meta-analysis | High     | Melatonin: 117     | Placebo: 117       | 9            | NR                                                                        | Mean difference [95% CI]: 1.45 [-0.66, 3.56] I-squared: 62.8% |
| McCleery, 2016                            | Meta-analysis | High     | Melatonin: 104     | Placebo: 47        | 1            | Actigraphy                                                               | Mean difference [95% CI]: -0.01 [-0.04, 0.03] I-squared: 0% |
| Xu, 2015                                  | Meta-analysis | Moderate | Melatonin: 232     | Placebo: light therapy: 214 | 6            | Actigraphy                                                               | Mean difference [95% CI]: 1.78 [-0.13, 3.70] I-squared: 25% |
| Lee, NA                                   | Meta-analysis | Critically Low | Melatonin: 123     | Placebo: 125       | 8            | sleep diary; polysomnography actigraphy                                 | Mean difference [95% CI]: **2.74 [0.41, 5.88]** I-squared: 54% |
| Zhang, 2016                                | Meta-analysis | Critically Low | Melatonin: 75      | Placebo: 69        | 2            | polysomnography actigraphy                                              | Mean difference [95% CI]: -0.01 [-0.04, 0.02] I-squared: 0% |
| Author, Year | Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|--------------|----------------|----------------|-----------------------------|-------------|--------------------|---------------------------------------------------------------|
| **Sleep onset latency** | | | | | | |
| Bellon, 2006 Systematic Review | Critically Low | Melatonin: NR Placebo: NR | 12 | subjective polysomnography actigraphy | Adult patients: No change across all studies Elderly patients: 2 studies no change; 2 studies **significant improvement** Schizophrenia patients: 1 study **significant improvement** Dementia or Alzheimer’s: 2 studies, no change |
| Chase, 1997 Systematic Review | Critically Low | Melatonin Placebo Total sample: 35 | 2 | wrist actigraphy | Proportion of respondents (p-value): 83% v 75% (p<0.001) Increase in sleep efficiency: A significant difference in sleep efficiency was noted in the elderly without sleep disorders and compared with those with insomnia (p<0.0001) |
| Culpepper, 2015 Systematic Review | Critically Low | Melatonin Placebo Total sample: 40 | 1 | Actigraphy | No significant difference between groups |
| Vural, 2014 Systematic Review | Critically Low | Melatonin Control Total sample: 42 | 1 | NR | **Significant increase** in quality of life in melatonin group |

**Health-related Quality of Life**

| Author, Year | Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|--------------|----------------|----------------|-----------------------------|-------------|--------------------|---------------------------------------------------------------|
| Sateia, 2017 Meta-analysis | Critically Low | Diphenhydramine: 79 patients Placebo: 84 patients | 2 | subjective measure | Mean difference [95% CI]; -2.47 [-8.17, 3.23] I-squared: 0% |
| Culpepper, 2015 Systematic Review | Critically Low | Diphenhydramine Placebo Total sample: 226 | 3 | sleep diary | Change in outcome (p-value): 34.2 vs 36.8 mins (p=NS); 21.6 vs 23.8 mins (p=NS); **138.5 vs 99.9 mins (p<0.05)** |
| Vande Griend, 2012 Systematic Review | Critically Low | Diphenhydramine Placebo Total sample: 332 | 4 | sleep diaries questionnaire polysomnography | Overall, the outcomes analyzed from all four trials provided mixed results, with the majority not being statistically different than placebo (P > 0.05); 3 studies found no difference compared to placebo and 2 studies found the drug was superior to placebo |

**Total Sleep Time**

| Author, Year | Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|--------------|----------------|----------------|-----------------------------|-------------|--------------------|---------------------------------------------------------------|
| Sateia, 2017 Meta-analysis | Critically Low | Diphenhydramine: 77 patients Placebo: 84 patients | 2 | subjective measure | Mean difference [95% CI]; 17.86 [-3.79, 39.51] I-squared: 0% |
| Study                          | Critically Low | Treatment | Placebo | Total Sample | Outcome | Change in outcome (p-value): |
|-------------------------------|----------------|-----------|---------|--------------|---------|-----------------------------|
| Culpepper, 2015 Systematic Review | Critically Low | Diphenhydramine | Placebo | 204          | sleep diary | 6.6 vs 6.3 minutes (p=NS); No change (p=NS); No significant changes in TST compared to placebo |
| Vande Griend, 2012 Systematic Review | Critically Low | Diphenhydramine | Placebo | 332          | sleep diary | Overall, the outcomes analyzed from all four trials provided mixed results, with the majority not being statistically different than placebo (P > 0.05); 4 studies found no significant difference between groups; 1 study found drug to be superior |
| Vande Griend, 2012 Systematic Review | Critically Low | Diphenhydramine | Placebo | 17           | questionnaire | Overall, the outcomes analyzed from all four trials provided mixed results, with the majority not being statistically different than placebo (p>0.05) |
| Culpepper, 2015 Systematic Review | Critically Low | Diphenhydramine | Placebo | 20           | sleep diary | No significant treatment difference for sleep quality |
| Vande Griend, 2012 Systematic Review | Critically Low | Diphenhydramine | Placebo | 204          | sleep diary | Overall, the outcomes analyzed from all four trials provided mixed results, with the majority not being statistically different than placebo (p>0.05); Sleep diary data showed significant improvement (p<0.05); polysomnography data showed no difference compared to placebo |
| Insomnia Severity Index       |                | Diphenhydramine | Placebo | 184          | ISI      | 9.39 vs 11.63 (p<0.01) | Significantly lower ISI with diphenhydramine after 2 weeks |
| Author, Year | AMSTAR Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-------------|-----------------------|---------------|-----------------------------|--------------|-------------------|---------------------------------------------------------------|
| **Sleep onset latency** | | | CBT-I: 626 | | | |
| | sham treatment/ placebo, wait-list control, no treatment, or sleep hygiene/sleep education: 620 | 15 | subjective report | Mean difference [95% CI]: | -12.7 [-18.23, -7.18] I-squared: 78% |
| Brasure, 2015 | Meta-analysis | High | CBT-I: 108 [older adults] | placebo, wait-list control, no treatment, or sleep hygiene/sleep education: 83 | 3 | subjective report | Mean difference [95% CI]: | -9.98 [-16.48, -3.48] I-squared: 0% |
| | | | CBT-I: 61 [adults with chronic pain] | passive control (placebo or sham treatment or wait-list): 61 | 3 | subjective report | Mean difference [95% CI]: | -26.5 [-43.25, -9.75] I-squared: 77% |
| Cheng, 2012 | Meta-analysis | Low | CBT - sleep hygiene; stimulus control; relaxation training; sleep restriction; cognitive restructuring: NR | wait list control: NR | 4 | sleep diary | Standardized mean difference [95% CI]: | -0.55 [-0.80, -0.30] I-squared: 0% |
| Ho, 2016 | Meta-analysis | Low | CBT- image rehearsal therapy; exposure, re-scripting and relaxation therapy; mind-body bridging; behavioural sleep intervention: NR | wait list control; sleep hygiene: NR | 4 | sleep diary | Standardized mean difference [95% CI]: | -0.83 [-1.19, -0.47] I-squared: 0% |
| Irwin, 2006 | Meta-analysis | Critically Low | CBT – relaxation, biofeedback, hypnosis, sleep compression/restriction, paradoxical intention: NR | control: NR | 21 | self-report | Cohen’s d [95% CI]: | -0.52 [-0.68 to -0.82] Q-statistic: 74.66 |
| Author, Year Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-----------------------------|---------------|-----------------------------|--------------|--------------------|-------------------------------------------------------------|
| Johnson, 2016 Meta-analysis | Moderate      | CBT-I with both cognitive and behavioral components: 423 | 8            | sleep diary        | Cohen’s $d$ [95% CI]: $0.27$ [0.11 to 0.44] I-squared: 0.2% |
| Koffel, 2015 Meta-analysis  | Critically Low | group CBT-I - stimulus control, sleep restriction, and addressing dysfunctional beliefs about sleep: NR | 6            | sleep diary        | Mean effect size [95% CI]: $0.47$ [0.27; 0.66] I-squared: NR |
| Montgomery, 2003 Meta-analysis | High         | CBT - sleep hygiene; stimulus control; muscle relaxation; sleep restriction; cognitive therapy; education; imagery training: 86 | 3            | sleep diary        | Mean difference [95% CI]: $-3$ [-8.92, 2.92] I-squared: 0% |
| Navarro-Bravo, 2015 Meta-analysis | Moderate | CBT - sleep restriction, stimulus control, sleep education/hygiene: NR | 7            | sleep diary; actigraphy; sleep evaluation (4-item questionnaire); | Cohen’s $d$ [95% CI]: $-0.46$ [-0.76, -0.15] Chi square: 19.88; 0.003 |
| Seyffert, 2016 Meta-analysis | Low           | Internet-based CBT - sleep education, stimulus control, sleep restriction, relaxation, sleep hygiene, cognitive techniques: NR | 7            | sleep diary        | Mean difference [95% CI]: $-10.68$ [-16.00, -5.37] I-squared: 4.3% |
| Author, Year | AMSTAR Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|--------------|----------------------|--------------|-----------------------------|--------------|-------------------|-------------------------------------------------------------|
| van Straten, 2007 | Meta-analysis | Low | CBT - relaxation; sleep restriction; stimulus control; paradoxical intention; identifying and challenging dysfunctional thoughts: NR | 108 | sleep diary | Hedges g [95% CI]: 0.57 [0.50, 0.65] I-squared: 48% |
| | | | waitlist control; no treatment; placebo; psycho-education: NR | | | |
| van Straten, 2009 | Meta-analysis | Moderate | CBT (self-help): stimulus-control; sleep restriction; cognitive therapy; sleep hygiene; relaxation; in-bed exercises: NR | 8 | sleep diary | Cohen’s d [95% CI]: 0.29 [0.15, 0.43] I-squared: 0% |
| | | | waiting list: NR | | | |
| Ye, 2016 | Meta-analysis | Moderate | CBT - sleep hygiene education; cognitive restructuring; stimulus control; sleep restriction; relaxation therapy; hierarchy development; imagery training; scheduled pseudo desensitization; breathing control: 1006 | 15 | NR | Mean difference [95% CI]: -18.41 [-23.21, 13.60] I-squared: 62% |
| | | | wait-list control, treatment as usual; internet + email; internet + telephone; telephone; internet-based control: 1004 | | | |
| Brooks, 2014 | Systematic Review | Low | CBT-I (unspecified) | 1 | daily sleep diary; Pittsburgh Sleep Quality Index; actigraphy | Improved self-reported sleep latency maintained for 6 months post-treatment; not corroborated by actigraphy |
| | | | Control (unspecified) | | | |
| | | | Total sample: 60 | | | |
| Ishak, 2012 | Systematic Review | Low | CBT (unspecified) | 1 | SF-36 | Significant reductions in sleep latency for CBT compared to placebo (p<0.01) |
| | | | Placebo; no treatment; usual care | | | |
| | | | Total sample: 209 | | | |
| Author, Year Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-----------------------------|---------------|-------------------------------|--------------|-------------------|---------------------------------------------------------------|
| Dickerson, 2014 Systematic Review | High | CBT (unspecified): Control: usual treatment; waitlist crossover; waitlist control; control; usual treatment | 1 | actigraphy | Mean change [95% CI]: -0.42 [-0.80 to -0.01] CBT moderate effect in decreasing insomnia symptoms |
| Venables, 2014 Systematic Review | Critically Low | group CBT: 660 No comparator (pre- post-intervention) professionally administered CBT: 615 No comparator (pre- post-intervention) | 8 | NR | The group CBT studies obtained improvements in all sleep parameters, group delivered CBT sessions may be slightly more effective than individual sessions |
| Wang, 2005 Systematic Review | Moderate | CBT: stimulus control; sleep restriction; cognitive therapy; sleep hygiene education; sleep scheduling control; Quasi desensitization; self-monitoring control; sleep hygiene recommendations; waiting-list control | 1 | sleep diary; wrist actigraphy | Change in outcome: CBT: 61→28mins; control: 74→70mins CBT significantly improved sleep latency compared to control with sustained mean reduction by 50% in CBT group (p<0.05) |
| Ho, 2015 Meta-analysis | Low | Multi-component CBT - stimulus control, sleep restriction, sleep hygiene, relaxation and/or cognitive therapy: NR waiting-list control; routine care or no treatment: NR | 8 | sleep diary | Hedges g [95% CI]: -0.70 [-1.0, -0.4] I-squared: 77% |
| Author, Year Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-----------------------------|---------------|------------------------------|--------------|--------------------|----------------------------------------------------------------|
| Trauer, 2015 Meta-analysis  | Moderate      | Multi-modal CBT - cognitive therapy, stimulus control, sleep restriction, relaxation, sleep hygiene: NR | 16           | sleep diary        | Mean difference [95% CI]: 
-19.03 [-23.93, 14.12] I-squared: 41.9% |
|                            |               | Wait-list control, treatment as usual, Sleep hygiene, sham, placebo: NR |              |                    |                                                                  |
| Buscemi, 2005 Meta-analysis | High          | Multi-component CBT - Paradoxical Intention; Sleep compression; Stimulus control:152 | 9            | sleep diary        | Mean difference [95% CI]: 
-4.57 [-9.75, 0.61] I-squared: 12.5% |
|                            |               | Placebo: 124                  |              |                    |                                                                  |
| Okajima, 2011 Meta-analysis | Critically Low | Multi-component CBT - sleep hygiene education; sleep restriction; stimulus control; cognitive therapy; relaxation; paradoxical intention: NR | 7            | sleep diary        | Cohen’s d [95% CI]: 
0.4 [0.21, 0.57] I-squared: NR |
|                            |               | wait-list control, placebo; sleep hygiene education; control(unspecified); treatment as usual: NR |              |                    |                                                                  |
|                            |               |                               | 2            | polysomnography; actigraphy | Cohen’s d [95% CI}: 
0.59 [0.08, 1.02] I-squared: NR |
| Zachariae, 2016 Meta-analysis | Moderate      | Multi-component CBT - stimulus control, sleep hygiene; cognitive therapy; sleep restriction; relaxation techniques: NR | 10           | NR                 | Hedges g [95% CI]: 
0.41 [0.29, 0.53] I-squared: 0% |
|                            |               | Wait-list control, treatment as usual: NR |              |                    |                                                                  |
| Author, Year Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|------------------------------|---------------|-----------------------------|--------------|-------------------|-------------------------------------------------------------|
| Howell, 2014 Systematic Review | Moderate       | Multi-component CBT - sleep hygiene, sleep restriction, stimulus control, cognitive restructuring, and relaxation therapies | 3            | sleep diary       | Sleep latency had **significant improvement** in all studies post CBT intervention (values not reported) |
| McCurry, 2007 Systematic Review | Critically Low | Multi-component CBT - sleep hygiene, relaxation, sleep compression, cognitive behavioural therapy, stimulus control delayed treatment; wait-list control, placebo; stress management | 1            | sleep logs        | CBT **significantly decreased** sleep latency compared to stress management (p-values not reported) |
| Yang, 2014 Meta-analysis      | Moderate       | CBT + relaxation (sleep hygiene; relaxation CD): 13 Sleep hygiene education; treatment as usual: 13 | 1            | NR                | Standardized mean difference [95% CI]: **1.33 [0.46, 2.19] I-squared: 0%** |
| Buscemi, 2005 Meta-analysis   | High           | CBT + relaxation: relaxation training; cognitive control; stimulus control; group relaxation; aggressive muscle relaxation; cognitive distraction: 45 placebo: 46 | 4            | sleep diary       | Mean difference [95% CI]: **-21.5 [-42.2, -0.8] I-squared: 74.4%** |
| van Straten, 2009 Meta-analysis | Moderate      | CBT (self-help): stimulus-control; sleep restriction; cognitive therapy; sleep hygiene; relaxation; in-bed exercises: NR | 3            | sleep diary       | Cohen’s d [95% CI]: **-0.37 [-0.73, -0.02] I-squared: 0%** |
| Author, Year Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-----------------------------|---------------|------------------------------|--------------|-------------------|-------------------------------------------------------------|
| Buscemi, 2005 Meta-analysis | High          | CBT + relaxation - relaxation training; cognitive control; stimulus control; progressive muscle relaxation; EMG biofeedback; group relaxation: 18 | 2            | sleep diary       | Mean difference [95% CI]: -9.2 [-37.9, 19.5] I-squared: 37.1% |
|                             |               | CBT + relaxation - relaxation training; stimulus control; aggressive muscle relaxation; cognitive distraction: 23 | 2            | sleep diary       | Mean difference [95% CI]: -4.6 [-20.7, 11.5] I-squared: 0%   |
|                             |               | CBT - cognitive therapy; sleep restriction; stimulus control; sleep hygiene: 24 | 2            | sleep diary       | Mean difference [95% CI]: 0.22 [-0.03, 0.46] I-squared: 0%   |

**Total Sleep Time**

| Brasure, 2015 Meta-analysis | High          | CBT-I: 621 | Sham treatment/placebo, wait list control, no treatment, or sleep hygiene/sleep education: 612 | 15 | subjective report | Mean difference [95% CI]: 14.24 [2.08, 26.39] I-squared: 56% |

| Cheng, 2012 Meta-analysis  | Low           | CBT - sleep hygiene; stimulus control; relaxation training; sleep restriction; cognitive restructuring: NR | 4  | sleep diary       | Standardized mean difference [95% CI]: 0.22 [-0.03, 0.46] I-squared: 0% |
|                            |               | wait list control: NR |                 |                  |                                                             |

| Ho, 2016 Meta-analysis     | Low           | CBT - image rehearsal therapy; exposure, re-scripting and relaxation therapy; mind-body bridging; behavioural sleep intervention: NR | 4  | sleep diary       | Standardized mean difference [95% CI]: 0.39 [-0.05, 0.84] I-squared: 38% |
|                            |               | wait list control; sleep hygiene: NR |                 |                  |                                                             |

| Irwin, 2006 Meta-analysis  | Critically Low | CBT – relaxation, biofeedback, hypnosis, sleep compression/restriction paradoxical intention: NR | 16 | self-report       | Cohen’s $d$ [95% CI]: 0.17 [-0.13, 0.48] Q-statistic: 50.27 |
| Author, Year Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-----------------------------|---------------|------------------------------|-------------|--------------------|---------------------------------------------------------------|
| Koffel, 2015 Meta-analysis  | Critically Low | group CBT-I - stimulus control, sleep restriction, and addressing dysfunctional beliefs about sleep: NR wait list, treatment as usual, placebo: NR | 6           | sleep diary        | Mean effect size [95% CI]: -0.04 [-0.32, 0.23] I-squared: NR |
| Montgomery, 2003 Meta-analysis | High | CBT - sleep hygiene; stimulus control; muscle relaxation; sleep restriction; cognitive therapy; education; imagery training: 76 wait-list control, placebo: 67 CBT - sleep hygiene; stimulus control; muscle relaxation; sleep restriction; cognitive therapy; education; imagery training: 30 wait-list control, placebo: 29 | 4           | Sleep Diary        | Mean difference [95% CI]: -14.56 [-36.13, 7.01] I-squared: 0% |
| Navarro-Bravo, 2015 Meta-analysis | Moderate | CBT - sleep restriction, stimulus control, sleep education/hygiene: NR placebo; wait list control; stress management and wellness training; treatment as usual; sleep hygiene/education: NR | 8           | polysomnography actigraphy sleep evaluation (4-item questionnaire) | Cohen’s d [95% CI]: 0.11 [-0.15, 0.37] Chi square: 17.56; 0.014 |
| Seyffert, 2016 Meta-analysis | Low | Internet-based CBT - sleep education, stimulus control, sleep restriction, relaxation, sleep hygiene, cognitive techniques: NR Wait-list control, internet control, Treatment as usual: NR | 8           | sleep diary        | Mean difference [95% CI]: 19.57 [8.56, 30.58] I-squared: 24.7% |
| Author, Year | Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|--------------|----------------|---------------|-----------------------------|--------------|-------------------|--------------------------------------------------------------|
| van Straten, 2007 | Meta-analysis | Low | CBT - relaxation; sleep restriction; stimulus control; paradoxical intention; identifying and challenging dysfunctional thoughts: NR waitlist control; no treatment; placebo; psycho-education: NR | 91 | sleep diary | Hedges g [95% CI]: 0.16 [0.08, 0.24] I-squared: 47% |
| van Straten, 2009 | Meta-analysis | Moderate | CBT - self-help: stimulus-control; sleep restriction; cognitive therapy; sleep hygiene; relaxation; in-bed exercises: NR | 8 | sleep diary | Cohen’s d [95% CI]: -0.01 [-0.14, 0.14] I-squared: 18.8% |
| Ye, 2016 | Meta-analysis | Moderate | CBT - sleep hygiene education; cognitive restructuring; stimulus control; sleep restriction; relaxation therapy; hierarchy development; imagery training; scheduled pseudo desensitization; breathing control: 1006 wait-list control, treatment as usual; internet + email; internet + telephone; telephone; internet-based control: 1003 | 15 | sleep diary | Mean difference [95% CI]: 22.3 [16.38, 28.23] I-squared: 12% |
| Dickerson, 2014 | Systematic Review | High | CBT usual treatment; waitlist crossover; waitlist control; control; usual treatment | 1 | actigraphy | Change in outcome: CBT vs placebo: -0.81 [-1.21, -0.42] CBT had a moderate effect in decreasing insomnia symptoms |
|              |               |               | Total sample: 150 CBT: 12 |               | sleep diary | Change in outcome: Pre-/post scores: 0.47 [-0.27, 1.350] |
| Author, Year Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-----------------------------|---------------|-----------------------------|--------------|-------------------|----------------------------------------------------------|
| Venables, 2014 Systematic Review | Critically Low | group CBT: 660               | 8            | NR                | 7 of 8 studies obtained improvements in total sleep time; group delivered CBT sessions may be slightly more effective than individual sessions. |
|                            |               | No comparator (pre- post-intervention) |               |                   |                                                                         |
|                            |               | professionally administered CBT: 615 |               |                   |                                                                         |
|                            |               | No comparator (pre- post-intervention) | 8            | actigraphy sleep diary | 4 of 8 studies reported increased TST in the intervention group, 4 of 8 found no significant increase in TST in the intervention or control groups |
| Ho, 2015 Meta-analysis     | Low           | Multi-component CBT - stimulus control, sleep restriction, sleep hygiene, relaxation and/or cognitive therapy: NR | 8            | sleep diary       | Hedges g [95% CI]: 0.31 [0.0, 0.6] I-squared: 78% |
|                            |               | waiting-list control; routine care or no treatment: NR |               |                   |                                                                         |
| Okajima, 2011 Meta-analysis | Critically Low | Multi-component CBT - sleep hygiene education; sleep restriction; stimulus control; cognitive therapy; relaxation; paradoxical intention: NR | 7            | sleep diary       | Cohen’s d [95% CI]: 0.21 [0.03, 0.39] I-squared: NR |
|                            |               | wait-list control, placebo; sleep hygiene education; control(unspecified); treatment as usual: NR | 2            | polysomnography actigraphy | Cohen’s d [95% CI]: 0.71 [0.21, 1.12] I-squared: NR |
| Trauer, 2015 Meta-analysis  | Moderate       | Multi-component CBT - cognitive therapy, stimulus control, sleep restriction, relaxation, sleep hygiene: NR | 16           | sleep diary       | Mean difference [95% CI]: 7.61 [-0.51, 15.74] I-squared: 3.1% |
|                            |               | WLC/TAU, Sleep hygiene, sham, placebo: NR |               |                   |                                                                         |
| Author, Year Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-----------------------------|---------------|------------------------------|--------------|--------------------|---------------------------------------------------------------|
| Zachariae, 2016 Meta-analysis | Moderate | Multi-component CBT - stimulus control, sleep hygiene, cognitive therapy, sleep restriction, relaxation techniques: NR | 10 | NR | Hedges g [95% CI]: 0.29 [0.17, 0.42] I-squared: 5.4% |
| Howell, 2014 Systematic Review | Moderate | Multi-component CBT - sleep hygiene, sleep restriction, stimulus control, cognitive restructuring, and relaxation therapies | 2 | actigraphy | Non-significant change was identified between control and treatment groups for total sleep time |
| van Straten, 2009 Meta-analysis | Moderate | self-help CBT: stimulus-control; sleep restriction; cognitive therapy; sleep hygiene; relaxation; in-bed exercises: NR | 3 | sleep diary | Cohen’s d [95% CI]: -0.05 [-0.40, 0.31] I-squared: 50.9% |
| Seyffert, 2016 Meta-analysis | Low | Internet-based CBT - sleep education, stimulus control, sleep restriction, relaxation, sleep hygiene, cognitive techniques: NR | 2 | sleep diary | Mean difference [95% CI]: 0.73 [-311.8, 313.3] I-squared: 75% |
| Wang, 2005 Systematic Review | Moderate | Relaxation therapy | 1 | sleep log polysomnography | Change in outcome: CBT: 352.1→372.4 mins; relaxation: 352.1→337.9 mins |
| Author, Year | Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|--------------|----------------|---------------|-----------------------------|--------------|--------------------|---------------------------------------------------------------|
| Brasure, 2015 | Meta-analysis | High       | CBT-I: 412 [general adult population] sham treatment/ placebo, wait-list control, no treatment, or sleep hygiene/sleep education: 420 | 11           | subjective report  | Mean difference [95% CI]: -22.33 [-37.44, -7.21] I-squared: 89% |
|              |                |             | CBT-I: 124 [older adults] placebo, wait-list control, no treatment, or sleep hygiene/sleep education: 96 | 4            | subjective report  | Mean difference [95% CI]: -26.96 [-35.73, -18.19] I-squared: 0% |
|              |                |             | CBT-I: 61 [adults with chronic pain] passive control (placebo or sham treatment or wait-list): 61 | 3            | subjective report  | Mean difference [95% CI]: -38.18 [-65.57, -10.78] I-squared: 0.82% |
| Cheng, 2012  | Meta-analysis  | Low         | CBT - sleep hygiene; stimulus control; relaxation training; sleep restriction; cognitive restructuring: NR wait list control: NR | 4            | sleep diary       | Standardized mean difference [95% CI]: -0.18 [-0.43, 0.06] I-squared: 55% |
| Ho, 2016     | Meta-analysis  | Low         | CBT - image rehearsal therapy; exposure, re-scripting and relaxation therapy; mind-body bridging; behavioural sleep intervention: NR wait list control; sleep hygiene: NR | 4            | sleep diary       | Standardized mean difference [95% CI]: -1.02 [-1.32, -0.66] I-squared: 0% |
| Irwin, 2006  | Meta-analysis  | Critically Low | CBT – relaxation, biofeedback, hypnosis, sleep compression/restriction, paradoxical intention: NR control: NR | 15           | self-report       | Cohen’s $d$ [95% CI]: -0.64 [-0.82, -0.47] Q-statistic: 21.65 |
| Author, Year | AMSTAR rating | Intervention and sample size                                                                 | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-------------|---------------|---------------------------------------------------------------------------------------------|--------------|-------------------|---------------------------------------------------------------|
| Johnson, 2016 Meta-analysis | Moderate | CBT-I - with both cognitive and behavioral components: 423 waitlist control; treatment-as-usual; sleep education; behavioral placebo; mindfulness-based stress reduction: 297 | 8            | sleep diary       | Cohen’s $d$ [95% CI]: 0.29 [0.10 to 0.48] I-squared: 30.1%    |
| Koffel, 2015 Meta-analysis | Critically Low | group CBT-I - stimulus control, sleep restriction, and addressing dysfunctional beliefs about sleep: NR wait list, treatment as usual, placebo: NR | 6            | sleep diary       | Mean effect size [95% CI]: 0.65 [0.26, 1.04] I-squared: NR     |
| Montgomery, 2003 Meta-analysis | High | CBT - sleep hygiene; stimulus control; muscle relaxation; sleep restriction; cognitive therapy; education; imagery training: 95 wait-list control, placebo: 64 CBT -sleep hygiene; stimulus control; muscle relaxation; sleep restriction; cognitive therapy; education; imagery training: 30 wait-list control, placebo: 29 | 4, 2         | Sleep Diary, polysomnography | Mean difference [95% CI]: -24.36 [-41.14, -7.57] I-squared: 55% -21.84 [-37.30, -6.38] I-squared: 55% |
| Navarro-Bravo, 2015 Meta-analysis | Moderate | CBT - sleep restriction, stimulus control, sleep education/hygiene: NR placebo; wait list control; stress management and wellness training; treatment as usual; sleep hygiene/education: NR sleep diary polysomnography actigraphy sleep evaluation (4-item questionnaire) | 7            |                   | Cohen’s $d$ [95% CI]: -0.68 [-1.11, -0.26] Chi square: 34.43; 0.000 |
| Author, Year | AMSTAR Synthesis type | AMSTAR rating | Intervention and sample size                                                                                           | # of studies | Measurement method          | Pooled Estimates (MA) or Narrative Results (from SR with no MA)                                                                 |
|--------------|-----------------------|--------------|----------------------------------------------------------------------------------------------------------------------|--------------|----------------------------|---------------------------------------------------------------------------------------------------------------------------|
| Seyffert, 2016 | Meta-analysis        | Low          | Internet-based CBT - sleep education, stimulus control, sleep restriction, relaxation, sleep hygiene, cognitive techniques: NR wait-list control, Internet control, TAU: NR | 6            | Sleep diary                | Mean difference [95% CI]: -20.44 [-34.87, -6.01] I-squared: 69.3%                                                        |
| van Straten, 2007 | Meta-analysis       | Moderate     | CBT - relaxation; sleep restriction; stimulus control; paradoxical intention; identifying and challenging dysfunctional thoughts: NR waitlist control; no treatment; placebo; psycho-education: NR | 71           | sleep diary                | Hedges g [95% CI]: 0.63 [0.53, 0.73] I-squared: 60%                                                                     |
| van Straten, 2009 | Meta-analysis       | Moderate     | CBT -self-help: stimulus-control; sleep restriction; cognitive therapy; sleep hygiene; relaxation; in-bed exercises: NR waiting list: NR | 6            | sleep diary                | Cohen’s d [95% CI]: 0.3 [0.13, 0.48] I-squared: 63.9%                                                                    |
| Ye, 2016       | Meta-analysis        | Moderate     | CBT - sleep hygiene education; cognitive restructuring; stimulus control; sleep restriction; relaxation therapy; hierarchy development; imagery training; scheduled pseudo desensitization; breathing control: 828 wait-list control, treatment as usual; internet + email; internet + telephone; telephone; internet-based control: 827 | 11           | sleep diary                | Mean difference [95% CI]: -22.31 [-31.11, -13.50] I-squared: 76%                                                         |
| Brooks, 2014   | Systematic Review   | Low          | CBT-I: NR                                                                                                                                                  | 1            | daily sleep diary; Pittsburgh Sleep Quality Index; actigraphy | WASO improved in treatment group based on self-reported data and effect remained for 6 months post-treatment; not corroborated by actigraphy |
| Author, Year Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-----------------------------|---------------|------------------------------|--------------|-------------------|---------------------------------------------------------------|
| Dickerson, 2014 Systematic Review | High | CBT (unspecified); usual treatment; waitlist crossover; waitlist control; control; usual treatment | 1 | Actigraphy | Change in outcome: CBT vs placebo: **-0.50 [-0.89 to -0.1]**; CBT showed a moderate effect in decreasing insomnia symptoms compared to control |
| Total sample: 150 | | CBT (unspecified): 12 | | | |
| | No comparator (pre- post-intervention) | 1 | sleep diary | | Change in outcome: Pre/post scores -1.18 [-2.45 to 0.62] |
| | | | | | |
| Venables, 2014 Systematic Review | Critically Low | group CBT: 660 | 8 | NR | 8 of 8 studies demonstrated improvement in WASO (p-values not reported); results demonstrate that group delivered CBT sessions may be slightly more effective than individual sessions |
| | | professionally administered CBT: 615 | | actigraphy sleep diary | 8 of 8 studies in professionally administered CBT reported an increase in WASO (p-values not reported) |
| | | No comparison | | | |
| Wang, 2005 Systematic Review | Moderate | CBT - stimulus control; sleep restriction; cognitive therapy; sleep hygiene education; sleep scheduling control; Quasi desensitization; self-monitoring control; sleep hygiene recommendations; waiting-list control | 3 | polysomnography sleep log | **significant improvement** in WASO for CBT compared to placebo (p<0.05); CBT group averaged a 52% reduction in WASO from study entry to 3-month follow-up time point; 60% of CBT group and none of control group achieved the criterion for clinically significant WASO improvement |
| Total sample: 162 | | | | | |
| Ho, 2015 Meta-analysis | Low | Multi-component CBT - stimulus control, sleep restriction, sleep hygiene, relaxation and/or cognitive therapy; NR | 6 | sleep diary | Hedges g [95% CI]: **-0.74 [-1.3, -0.2]** I-squared: 93% |
| Author, Year Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|----------------------------|---------------|------------------------------|--------------|-------------------|-----------------------------------------------------------|
| Okajima, 2011 Meta-analysis | Critically Low | Multi-component CBT - sleep hygiene education; sleep restriction; stimulus control; cognitive therapy; relaxation; paradoxical intention; NR wait-list control, placebo; sleep hygiene education; control(unspecified); treatment as usual; NR | 6 | sleep diary | Cohen’s $d$ [95% CI]: $0.34 \ [0.15, 0.52]$ I-squared: NR |
| Trauer, 2015 Meta-analysis  | Moderate      | Multi-component CBT - cognitive therapy, stimulus control, sleep restriction, relaxation, sleep hygiene: NR Wait-list control, treatment as usual, Sleep hygiene, sham, placebo: NR | 14 | Sleep diary | Mean difference [95% CI]: -26 [-36.52, 15.48] I-squared: 47.2% |
| Zachariaes, 2016 Meta-analysis | Moderate  | Multi-component CBT - stimulus control, sleep hygiene, cognitive therapy, sleep restriction, relaxation techniques: NR Wait-list control, treatment as usual: NR | 7 | NR | Hedges $g$ [95% CI]: $0.45 \ [0.25, 0.66]$ I-squared: 48.5% |
| Howell, 2014 Systematic Review | Moderate  | Multi-component CBT -sleep hygiene, sleep restriction, stimulus control, cognitive restructuring, and relaxation therapies usual care, wait-list control, healthy eating and nutrition, sleep education and hygiene only, no treatment | 2 | actigraphy sleep diary | 2 of 2 studies found **significant improvement** in WASO for undergoing CBT |
| Author, Year Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-----------------------------|---------------|------------------------------|--------------|-------------------|-------------------------------------------------------------|
| McCurry, 2007 Systematic Review | Critically Low | Multi-component CBT - sleep hygiene, relaxation, sleep compression, cognitive behavioural therapy, stimulus control delayed treatment, wait-list control, placebo; stress management: Total sample: 154 | 3 | sleep logs | CBT **significantly improved** WASO compared to stress management and wait-list control |
| van Straten, 2009 Meta-analysis | Moderate | self-help CBT: stimulus-control; sleep restriction; cognitive therapy; sleep hygiene; relaxation; in-bed exercises: NR In-person CBT: NR | 3 | sleep diary | Cohen’s $d$ [95% CI]: -0.03 [-0.32, 0.38] I-squared: 44.5% |
| Wang, 2005 Systematic Review | Moderate | CBT - stimulus control; sleep restriction; sleep hygiene education Relaxation therapy | 1 | polysomnography sleep log | Change in outcome: CBT: 50.8→30.1 minutes relaxation: 50.8→50.6 minutes **Significant improvement** in WASO for CBT compared to relaxation therapy: CBT recipients reported a 54% reduction whereas relaxation group reported 16% ($p<0.01$) |
| McCurry, 2007 Systematic Review | Critically Low | CBT (unspecified) CBT (unspecified) + Temazepam | 1 | sleep logs | CBT and CBT + temazepam groups both showed **significant improvement** compared to placebo |
| Author, Year | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-------------|---------------|-------------------------------|--------------|--------------------|-------------------------------------------------------------|
| Buscemi, 2005 Meta-analysis | High | CBT + relaxation technique - relaxation training; cognitive control; stimulus control; group relaxation; aggressive muscle relaxation; cognitive distraction: 23 placebo: 26 | 2 | NR | Mean difference [95% CI]: -7.6 [-26.3, 11.1] I-squared: 0% |
| | | Multi-component CBT; Paradoxical Intention; Sleep compression; Stimulus control:128 | 8 | sleep diary | Mean difference [95% CI]: -18.17 [-30.37, -5.98] I-squared: 52.9% |
| | | CBT + relaxation - relaxation training; stimulus control; aggressive muscle relaxation; cognitive distraction: 23 | 2 | NR | Mean difference [95% CI]: 5.1 [-12.0, 22.2] I-squared: 0% |
| | | CBT - cognitive therapy; sleep restriction; stimulus control; sleep hygiene: 24 | | | |
| **Sleep Quality** | | | | | |
| Brasure, 2015 Meta-analysis | High | CBT-I: 296 | 6 | Pittsburgh Sleep Quality Index | Mean difference [95% CI]: -2.1 [-2.87, -1.34] I-squared: 37% |
| Ho, 2016 Meta-analysis | Low | CBT - image rehearsal therapy; exposure, re-scripting and relaxation therapy; mind-body bridging; behavioural sleep intervention: NR wait list control; sleep hygiene: NR | 6 | Pittsburgh sleep quality index | Standardized mean difference [95% CI]: -0.87 [-1.18, -0.56] I-squared: 33% |
| Irwin, 2006 Meta-analysis | Critically Low | CBT – relaxation, biofeedback, hypnosis, sleep compression/restriction, paradoxical intention: NR control: NR | 7 | self-report | Cohen’s d [95% CI]: 0.76 [0.48 to 1.03] Q-statistic: 7.92 |
| Author, Year | AMSTAR Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-------------|----------------------|---------------|------------------------------|-------------|-------------------|------------------------------------------------------------|
| Koffel, 2015 | Meta-analysis | Low | group CBT-I - stimulus control, sleep restriction, and addressing dysfunctional beliefs about sleep; NR wait list, treatment as usual, placebo: NR | 5 | Sleep Diary, Sleep Quality Measures | Mean effect size [95% CI]: 0.4 [-0.14, 0.93] I-squared: NR |
| Navarro-Bravo, 2015 | Meta-analysis | Moderate | CBT - sleep restriction, stimulus control, sleep education/hygiene: NR placebo; wait list control; stress management and wellness training; treatment as usual; sleep hygiene/education: NR | 5 | Pittsburgh Sleep Quality Index | Cohen’s $d$ [95% CI]: -0.59 [-0.59, -0.85] Chi square: 6.85; 0.144 |
| Tang, 2015 | Meta-analysis | Moderate | CBT-I: psychoeducation, sleep hygiene, stimulus control, sleep restriction, cognitive therapy, and relaxation: 510 waitlist, treatment as usual: 455 | 11 | Pittsburgh Sleep Quality Index (PSQI); Insomnia Severity Index (ISI) | Standardized mean difference [95% CI]: 0.78 [0.42, 1.13] I-squared: 84% |
| van Straten, 2007 | Meta-analysis | Low | CBT - relaxation; sleep restriction; stimulus control; paradoxical intention; identifying and challenging dysfunctional thoughts: NR waitlist control; no treatment; placebo; psycho-education: NR | 19 | Pittsburgh sleep quality index | Hedges $g$ [95% CI]: 0.65 [0.51, 0.79] I-squared: 39% |
| van Straten, 2009 | Meta-analysis | Moderate | CBT –self-help: stimulus-control; sleep restriction; cognitive therapy; sleep hygiene; relaxation; in-bed exercises: NR waiting list: NR | 40 | sleep diary | Hedges $g$ [95% CI]: 0.4 [0.24, 0.56] I-squared: 74% |
| Cheng, 2012 | Meta-analysis | Low | sleep hygiene; stimulus control; relaxation training; sleep restriction; cognitive restructuring: NR wait list control: NR | 4 | Pittsburgh sleep quality index | Standardized mean difference [95% CI]: 0.41 [0.16, 0.65] I-squared: 45% |
| Author, Year Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-----------------------------|---------------|------------------------------|--------------|-------------------|---------------------------------------------------------------|
| Bogdanov, 2017 Systematic Review | Low | CBT (unspecified) Control (unspecified) Total sample: 3 | 1 | Pittsburgh sleep quality index | No clinically meaningful improvement in either group |
| Venables, 2014 Systematic Review | Critically Low | professionally administered CBT: 215 No comparator (pre- post-intervention) | 2 | Pittsburgh sleep quality index | Change in outcome [mean change (%)]: 7.3 (37.6) 2 of 2 studies found a reduction in PSQI scores (p-values not reported); neither of the scores decreased to below 5.0, above which is a diagnostic score for insomnia |
| Ho, 2015 Meta-analysis | Low | Multi-component CBT - stimulus control, sleep restriction, sleep hygiene, relaxation and/or cognitive therapy: NR waiting-list control; routine care or no treatment: NR | 4 | sleep diary | Hedges g [95% CI]: 0.43 [0.2, 0.6] I-squared: 0% |
| Okajima, 2011 Meta-analysis | Critically Low | Multi-component CBT –sleep hygiene education; sleep restriction; stimulus control; cognitive therapy; relaxation; paradoxical intention: NR wait-list control, placebo; sleep hygiene education; control(unspecified); treatment as usual: NR | 2 | Pittsburgh Sleep Quality Index | Cohen’s d [95% CI]: 0.77 [0.48, 0.97] I-squared: NR |
| Zachariae, 2016 Meta-analysis | Moderate | Multi-component CBT –stimulus control, sleep hygiene, cognitive therapy, sleep restriction, relaxation techniques: NR Wait-list control, treatment as usual: NR | 8 | NR | Hedges g [95% CI]: 0.49 [0.30, 0.68] I-squared: 34.5% |
| Author, Year | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|--------------|---------------|-----------------------------|--------------|-------------------|---------------------------------------------------------------|
| Howell, 2014 | Moderate       | Multi-component CBT – sleep hygiene, sleep restriction, stimulus control, cognitive restructuring, and relaxation therapies; usual care, wait-list control, healthy eating and nutrition, sleep education and hygiene only, no treatment | 2            | actigraphy, sleep diary | Significant improvement in all studies post CBT intervention identified for sleep quality (p-values not reported) |
| McCurry, 2007| Critically Low | Multi-component CBT – sleep hygiene, relaxation, sleep compression, cognitive behavioural therapy, stimulus control; delayed treatment, wait-list control, placebo; stress management: | 4            | sleep logs, Pittsburgh sleep quality index | Significant improvement in sleep quality ratings compared to control |
| Buscemi, 2005| High          | CBT + relaxation - relaxation training; cognitive control; stimulus control; group relaxation; aggressive muscle relaxation; cognitive distraction: 23, placebo: 26 | 2            | NR | Mean difference [95% CI]: 0.69 [-0.34, 1.73] I-squared: 65.4% |
| Yang, 2014   | Moderate      | CBT + relaxation - CBT; sleep hygiene; relaxation CD: 93, Sleep hygiene education; treatment as usual: 91, CBT + relaxation - CBT; sleep hygiene; relaxation CD: 56, Sleep hygiene education; treatment as usual: 56 | 3            | global Pittsburgh sleep quality index | Standardized mean difference [95% CI]: **0.85 [0.37, 1.34]** I-squared: 56% |
|              |               |                             | 2            | subjective sleep quality in Pittsburgh Sleep Quality Index | Standardized mean difference [95% CI]: 0.44 [-0.28, 1.17] I-squared: 64% |
| Author, Year Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-----------------------------|---------------|-----------------------------|--------------|-------------------|---------------------------------------------------------------|
| van Straten, 2009 Meta-analysis | Moderate | self-help CBT: stimulus-control; sleep restriction; cognitive therapy; sleep hygiene; relaxation; in-bed exercises: NR | 2 | sleep diary | Cohen’s $d$ [95% CI]: -0.5 [-0.90, 0.02] I-squared: 0% |
| Buscemi, 2005 Meta-analysis | High | CBT + relaxation - relaxation training; stimulus control; aggressive muscle relaxation; cognitive distraction: 23 | 2 | NR | Mean difference [95% CI]: 0.2 [-0.38, 0.77] I-squared: 0% |
| Sleep Satisfaction | | | | | |
| Wang, 2005 Systematic Review | Moderate | CBT - stimulus control; sleep restriction; cognitive therapy; sleep hygiene education; sleep scheduling control; Quasi desensitization; self-monitoring control; sleep hygiene recommendations; waiting-list control | 2 | Dysfunctional attitudes and Beliefs about Sleep (DBAS) evaluation; The Beliefs and Attitudes about Sleep Scale | CBT provided greater improvements in DBAS scores than did placebo, CBT endorsed less dysfunctional beliefs and attitudes about sleep than the placebo group; significantly greater improvement in BAS scores |
| Sleep efficiency | | | | | |
| Cheng, 2012 Meta-analysis | Low | CBT - sleep hygiene: stimulus control; relaxation training; sleep restriction; cognitive restructuring: NR | 4 | sleep diary | Standardized mean difference [95% CI]: 0.4 [0.15, 0.64] I-squared: 63% |
| Ho, 2016 Meta-analysis | Low | CBT - image rehearsal therapy; exposure, re-scripting and relaxation therapy; mind-body bridging; behavioural sleep intervention: NR | 5 | sleep diary | Standardized mean difference [95% CI]: 1.15 [0.75, 1.56] I-squared: 37% |
| Author, Year | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|--------------|---------------|------------------------------|--------------|-------------------|---------------------------------------------------------------|
| Irwin, 2006  | Critically Low | CBT – relaxation, biofeedback, hypnotis, sleep compression/restriction, paradoxical intention: NR | 8            | self-report       | Cohen’s $d$ [95% CI]: $0.52$ [0.28 to 0.75] Q-statistic: 47.85 |
| Johnson, 2016| Moderate       | CBT-I with both cognitive and behavioral components: 423 | 8            | sleep diary       | Cohen’s $d$ [95% CI]: $0.33$ [0.11 to 0.54] I-squared: 41.1% |
| Koffel, 2015 | Critically Low | group CBT-I - stimulus control, sleep restriction, and addressing dysfunctional beliefs about sleep: NR | 6            | sleep diary       | Mean effect size [95% CI]: $0.84$ [0.38, 1.31] I-squared: NR |
| Montgomery, 2003 | High        | CBT - cognitive-behavioural therapy (unspecified); sleep hygiene; stimulus control; muscle relaxation; sleep restriction; cognitive therapy; education; imagery training: 86 | 3            | sleep diary       | Mean difference [95% CI]: -7.49 [-15.45, 0.47] I-squared: 77% |
|              |               | wait-list control, placebo: 57 |              | polysomnography   | Mean difference [95% CI]: -6.25 [-10.18, -2.31] I-squared: 0% |
| Author, Year Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-----------------------------|--------------|------------------------------|--------------|-------------------|-------------------------------------------------------------|
| Navarro-Bravo, 2015 Meta-analysis | Moderate | CBT - sleep restriction, stimulus control, sleep education/hygiene: NR placebo; wait list control; stress management and wellness training; treatment as usual; sleep hygiene/education: NR | 8 | Sleep diary, polysomnography, actigraphy, sleep evaluation (4-item questionnaire) | Cohen’s d [95% CI]: 0.78 [0.34, 1.21] Chi square: 47.56; 0.000 |
| Seyffert, 2016 Meta-analysis | Low | Internet-based CBT - sleep education, stimulus control, sleep restriction, relaxation, sleep hygiene, cognitive techniques: NR Wait-list control, Internet control, treatment as usual: NR | 9 | Sleep diary | Mean difference [95% CI]: 7.22 [5.13, 9.32] I-squared: 39.5% |
| van Straten, 2007 Meta-analysis | Low | CBT - relaxation; sleep restriction; stimulus control; paradoxical intention; identifying and challenging dysfunctional thoughts: NR waitlist control; no treatment; placebo; psycho-education: NR | 79 | Sleep diary | Hedges g [95% CI]: 0.71 [0.61, 0.82] I-squared: 70% |
| van Straten, 2009 Meta-analysis | Moderate | CBT - self-help: stimulus-control; sleep restriction; cognitive therapy; sleep hygiene; relaxation; in-bed exercises: NR waiting list: NR | 7 | Sleep diary | Cohen’s d [95% CI]: 0.26 [0.11, 0.40] I-squared: 65.5% |
| Author, Year | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|--------------|---------------|------------------------------|--------------|-------------------|----------------------------------------------------------------|
| Ye, 2016     | Moderate      | CBT - sleep hygiene education; cognitive restructuring; stimulus control; sleep restriction; relaxation therapy; hierarchy development; imagery training; scheduled pseudo desensitization; breathing control: 1006 wait-list control, treatment as usual; internet + email; internet + telephone; telephone; internet-based control: 1003 | 15           | sleep diary       | Mean difference [95% CI]: **9.58 [7.30, 11.85]** I-squared: 76% |
| Bogdanov, 2017 | Low           | CBT (unspecified) Control (unspecified) Total sample: 11 | 1            | sleep diary       | **Significant improvement** in sleep efficiency compared to control (**p=0.01**) |
| Brooks, 2014  | Low           | CBT-I: 7 No comparator (pre- post-intervention) | 1            | daily sleep diary | Improvement in sleep efficiency (p-values not reported) |
|               |               | CBT-I (unspecified): NR Control (unspecified): NR | 2            | daily sleep diary Pittsburgh Sleep Quality Index actigraphy | Self-reported sleep efficiency improved in treatment group; maintained for 6 months post-treatment; not corroborated by actigraphy |
| Dickerson, 2014 | High         | CBT (unspecified): 12 No comparator (pre- post-intervention) | 1            | sleep diary       | Change in outcome: Pre-/post scores **1.49 [0.88 to 2.79]** Sleep efficiency improved over baseline at weeks 4 and 8 |
| Ishak, 2012   | Low           | CBT (unspecified) placebo, no treatment, usual care Total sample: 209 | 1            | SF-36; CIS-20; GHQ; PANAS; FACT-G | **Significant improvements** in sleep efficiency at both 3 and 6-month follow-up (**p<0.01**) |
| Author, Year | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|--------------|---------------|------------------------------|--------------|--------------------|---------------------------------------------------------------|
| Wang, 2005   | Moderate      | CBT - stimulus control; sleep restriction; cognitive therapy; sleep hygiene education; sleep scheduling control; Quasi desensitization; self-monitoring control; sleep hygiene recommendations; waiting-list control | 4            | sleep diary/log polysomnography structured interview | 4 of 4 studies found improvement in sleep efficiency compared to control; only 2 of 4 were statistically significant |
| Taylor, 2014 | Critically Low| CBT - stimulus control, sleep restriction, relaxation therapy, cognitive therapy; image rehearsal therapy; medication withdrawal: NR wait list, usual care, sleep hygiene, placebo control: NR | 13           | sleep diaries     | Mean effect size [95% CI; p-value]: 0.758 [0.557, 0.958; p<0.01] CBT-I results in significant improvement in sleep efficiency in patients with co-morbid psychiatric disorders, medium to large effects were homogeneous across studies |
| Venables, 2014| Critically Low| group CBT: 660 No comparator (pre- post-intervention) | 8            | NR                 | 8 of 8 studies obtained improvements in sleep quality, results demonstrate that group delivered CBT sessions may be slightly more effective than individual sessions |
|              |               | professionally administered CBT: 615 No comparator (pre- post-intervention) | 8            | actigraphy sleep diary | 8 of 8 studies found a significant improvement in sleep efficiency (p-values not reported) |
| Ho, 2015     | Low           | Multi-component CBT - stimulus control, sleep restriction, sleep hygiene, relaxation and/or cognitive therapy: NR waiting-list control; routine care or no treatment: NR | 7            | sleep diary       | Hedges g [95% CI]: 0.79 [0.2, 1.4] I-squared: 92% |
| Okajima, 2011| Critically Low| Multi-component CBT - sleep hygiene education; sleep restriction; | 8            | sleep diary       | Cohen’s d [95% CI]: 0.43 [0.25, 0.59] I-squared: NR |
| Author, Year Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-----------------------------|---------------|------------------------------|--------------|-------------------|---------------------------------------------------------------|
| Trauer, 2015 Meta-analysis  | Moderate      | Multi-component CBT - cognitive therapy, stimulus control, sleep restriction, relaxation, sleep hygiene: NR | 17           | Sleep diary       | Mean difference [95% CI]: 9.91 [8.09, 11.73] I-squared: 47.1% |
| Zachariae, 2016 Meta-analysis | Moderate      | Multi-component CBT - stimulus control, sleep hygiene, cognitive therapy, sleep restriction, relaxation techniques: NR | 10           | NR                | Hedges g [95% CI]: 0.58 [0.36, 0.81] I-squared: 68.4% |
| Howell, 2014 Systematic Review | Moderate      | Multi-component CBT - sleep hygiene, sleep restriction, stimulus control, cognitive restructuring, and relaxation therapies usual care, wait-list control, healthy eating and nutrition, sleep education and hygiene only, no treatment | 1            | SF-36             | Sleep efficiency increased in all studies post CBT intervention (p<0.01) |

stimulus control; cognitive therapy; relaxation; paradoxical intention: NR
wait-list control, placebo; sleep hygiene education; control(unspecified); treatment as usual: NR

Cohen’s $d$ [95% CI]: 0.78 [0.27, 1.17] I-squared: NR

Mean difference [95% CI]: 9.91 [8.09, 11.73] I-squared: 47.1%

Hedges $g$ [95% CI]: 0.58 [0.36, 0.81] I-squared: 68.4%

Sleep efficiency increased in all studies post CBT intervention (p<0.01)
| Author, Year | AMSTAR type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|--------------|-------------|---------------|------------------------------|--------------|--------------------|---------------------------------------------------------------|
| McCurry, 2007 | Systematic Review | Critically Low | Multi-component CBT - sleep hygiene, relaxation, sleep compression, cognitive behavioural therapy, stimulus control delayed treatment, wait-list control, placebo; stress management: | 3 | sleep logs | CBT group had **significant improvement** in sleep efficiency compared to stress management |
| van Straten, 2009 | Meta-analysis | Moderate | self-help CBT: stimulus-control; sleep restriction; cognitive therapy; sleep hygiene; relaxation; in-bed exercises: NR | 3 | sleep diary | Cohen’s $d$ [95% CI]: $-0.29 [-0.65, 0.06]$ I-squared: 22.4% |
| Seyffert, 2016 | Meta-analysis | Low | Internet-based CBT - sleep education, stimulus control, sleep restriction, relaxation, sleep hygiene, cognitive techniques: NR | 2 | Sleep diary | Mean difference [95% CI]: $-1.21 [-49.0, 46.6]$ I-squared: 59.7% |
| Wang, 2005 | Systematic Review | Moderate | CBT - stimulus control; sleep restriction; sleep hygiene education CBT + relaxation therapy | 1 | polysomnography sleep log | Change in outcome: CBT: 77.8%→85.5%; relaxation: 77.8%→78.1% |
| McCurry, 2007 | Systematic Review | Critically Low | CBT + Temazepam CBT | 1 | polysomnography sleep logs | The combination of CBT + temazepam was **significantly more effective** than placebo |
| **Insomnia Severity Index** | | | | | | |
| Brasure, 2015 | Meta-analysis | High | sham treatment/ placebo, wait-list control, no treatment, or sleep hygiene/sleep education): 173 | 5 | ISI | Mean difference [95% CI]: $-5.15 [-7.13, -3.16]$ I-squared: 67% |
| Author, Year          | AMSTAR rating | Intervention and sample size                                                                 | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA)                  |
|-----------------------|---------------|---------------------------------------------------------------------------------------------|--------------|--------------------|---------------------------------------------------------------------------------|
| Cheng, 2012           | Low           | CBT - sleep hygiene; stimulus control; relaxation training; sleep restriction; cognitive restructuring; NR | 2            | ISI                | Standardized mean difference [95% CI]: -0.86 [-1.18, -0.53] I-squared: 0%       |
| Ho, 2016              | Low           | CBT - image rehearsal therapy; exposure, re-scripting and relaxation therapy; mind-body bridging; behavioural sleep intervention: NR | 5            | ISI                | Standardized mean difference [95% CI]: -1.15 [-1.81, -0.49] I-squared: 77%      |
| Johnson, 2016         | Moderate      | CBT-I with both cognitive and behavioral components: NR                                        | 4            | ISI                | Cohen’s $d$ [95% CI]: 0.547 [0.37 to 0.73] I-squared: 0%                        |
| Navarro-Bravo, 2015   | Moderate      | CBT - sleep restriction, stimulus control, sleep education/hygiene: NR                          | 4            | ISI                | Cohen’s $d$ [95% CI]: -0.7 [-1.1, -0.22] Chi square: 11.54; 0.009              |
| Seyffert, 2016        | Low           | CBT - sleep education, stimulus control, sleep restriction, relaxation, sleep hygiene, cognitive techniques: NR | 4            | Sleep diary        | Mean difference [95% CI]: -3.74 [-7.10, -0.39] I-squared: 90%                 |
| Author, Year Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-----------------------------|---------------|------------------------------|--------------|--------------------|---------------------------------------------------------------|
| van Straten, 2007           | Low           | CBT - relaxation; sleep restriction; stimulus control; paradoxical intention; identifying and challenging dysfunctional thoughts: NR | 38           | ISI                | Hedges g [95% CI]: 0.98 [0.82, 1.15] I-squared: 74% |
|                             |               | waitlist control; no treatment; placebo; psycho-education: NR |              |                    |                                                                |
| Ye, 2016                    | Moderate      | CBT - sleep hygiene education; cognitive restructuring; stimulus control; sleep restriction; relaxation therapy; hierarchy development; imagery training; scheduled pseudo desensitization; breathing control: 828 | 11           | sleep diary (ISI)  | Mean difference [95% CI]: -5.88 [-7.46, -4.29] I-squared: NR |
|                             |               | wait-list control, treatment as usual; internet + email; internet + telephone; internet-based control: 827 |              |                    |                                                                |
| Bogdanov, 2017              | Low           | CBT (unspecified) Control (unspecified): NR | 2            | ISI                | Significant improvement compared to control (p<0.01); no clinically meaningful improvement |
|                             |               | CBT (unspecified) usual treatment; waitlist crossover; waitlist control; control; usual treatment | 1            | NR                 | Change in outcome: CBT vs placebo -0.37 [0.10 to 0.84] |
|                             |               | Total sample: 72 |              |                    |                                                                |
|                             |               | CBT: 10 Pre/post intervention; no comparator | 1            | ISI                | Change in outcome: Pre-/post scores 2.67 [1.37-3.73] Treatment significantly improved ISI scores |
|                             |               |                              |              |                    |                                                                |
|                             |               |                              |              |                    |                                                                |
| Ishak, 2012                 | Low           | CBT placebo, no treatment, unspecified, usual care | 1            | ISI                | intervention group had reduced insomnia scores at 12-month follow-up when compared with placebo (p<0.01) |
| Author, Year Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-----------------------------|---------------|-----------------------------|--------------|-------------------|-------------------------------------------------------------|
| Venables, 2014 Systematic Review | Critically Low | group CBT: 660 | 8 | ISI | Change in outcome (average decrease [%]): 53.1; 39.9; 63.9 (p<0.05) 3 of 8 studies had a significant decrease in ISI scores |
| | | No comparison | | | |
| | professionally administered CBT: 132 | | 5 | ISI | Change in outcome (average decrease [%]): 58.2; 53.1; 63.9; 27.4; 39.9 (p=NR) 5 of 5 studies found a reduction in ISI scores |
| | No comparison | self-help CBT: 328 | 4 | ISI | Change in outcome (average decrease [%]): 45.2; 44.5; 52; 56.2 (p=NR) 4 of 4 studies found a non-significant decrease in ISI Scores |
| Zachariae, 2016 Meta-analysis | Moderate | Multi-component CBT - stimulus control, sleep hygiene, cognitive therapy, sleep restriction, relaxation techniques: NR | 8 | ISI | Hedges g [95% CI]: 1.09 [0.74, 1.45] I-squared: 82.8% |
| Howell, 2014 Systematic Review | Moderate | Multi-component CBT - sleep hygiene, sleep restriction, stimulus control, cognitive restructuring, and relaxation therapies usual care, wait-list control, healthy eating and nutrition, sleep education and hygiene only, no treatment: NR | 4 | ISI | Overall significant improvement in ISI after CBT intervention |
| Yang, 2014 Meta-analysis | Moderate | CBT + relaxation - CBT; sleep hygiene; relaxation CD: 56 Sleep hygiene education; treatment as usual: 56 | 2 | habitual sleep efficiency in Pittsburgh sleep quality index | Standardized mean difference [95% CI]: -0.43 [-1.68, 0.83] I-squared: 86% |
| Author, Year | Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|--------------|----------------|---------------|-----------------------------|--------------|-------------------|-------------------------------------------------------------|
| Seyffert, 2016 Meta-analysis | Low | Self-help CBT - sleep education, stimulus control, sleep restriction, relaxation, sleep hygiene, cognitive techniques: NR | 2 | Sleep diary | Mean difference [95% CI]: 1.07 [-6.23, 8.38] I-squared: 0% |
| | | In-person CBT: NR | | | |
| Ballesio, 2017 Meta-analysis | High | CBT-I Group: 302 sleep hygiene, wait-list control, pharmacological, placebo, psychological: 226 | 6 | fatigue symptom inventory, multidimensional fatigue symptom inventory, Flinders fatigue scale, multidimensional fatigue inventory, Krupp fatigue scale | Cohen’s d [95% CI]: 0.35 [-0.16, 0.86] I-squared: 76.5% |
| | | CBT-I Individual: 238 placebo, sleep hygiene, wait-list control, psychological, CBT-I self-help: 160 | 7 | multi-dimensional fatigue inventory, fatigue severity scale, chronic respiratory disease questionnaire-fatigue scale, piper fatigue scale | Cohen’s d [95% CI]: 0.45 [0.07, 0.83] I-squared: 76.5% |
| | | CBT-I Self-help: 665 sleep hygiene, wait-list control, pharmacological: 433 | 7 | fatigue severity scale, multi-dimensional fatigue inventory, daytime fatigue scale, multidimensional fatigue symptoms inventory-short form | Cohen’s d [95% CI]: 0.36 [-0.15, 0.88] I-squared: 76.5% |
| Tang, 2015 Meta-analysis | Moderate | CBT-I - psychoeducation, sleep hygiene, stimulus control, sleep restriction, cognitive therapy, and relaxation: 380 waitlist, treatment as usual; sleep hygiene advice; healthy eating control; nutrition control: 341 | 6 | multidimensional fatigue inventory (MFI); fatigue symptom inventory (FSI); general fatigue scale (GFS); multidimensional fatigue symptom inventory-short form (MFSI-SF); | Standardized mean difference [95% CI]: 0.38 [0.08, 0.69] I-squared: 71% |
| Dickerson, 2014 Systematic Review | High | CBT (unspecified): 12 No comparator (pre- post-intervention) | 1 | NR | Change in outcome: Pre-/post scores (95% CI) -0.82 [-1.87, -0.16] Fatigue improved by week 8 |
| Author, Year            | AMSTAR rating | Intervention and sample size                                                                                                                                                                                                 | # of studies | Measurement method                      | Pooled Estimates (MA) or Narrative Results (from SR with no MA)                                                                 |
|------------------------|---------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|----------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Howell, 2014 Systematic Review | Moderate      | Multi-component CBT - sleep hygiene, sleep restriction, stimulus control, cognitive restructuring, and relaxation therapies; usual care, wait-list control, healthy eating and nutrition, sleep education and hygiene only, no treatment | 3            | Sleep diary                            | Fatigue had **significant improvement** in all studies post CBT intervention                                                   |
| Yang, 2014 Meta-analysis | Moderate      | CBT + relaxation - CBT; sleep hygiene; relaxation CD: 50; Sleep hygiene education; treatment as usual: 48                                                                                                                      | 2            | subjective fatigue questionnaire       | **Standardized mean difference [95% CI]**: 0.77 [0.36, 1.18] I-squared: 0%                                                       |
| **Health-related Quality of Life** |              |                                                                                                                                                                                                                     |              |                                        |                                                                                                                             |
| Brooks, 2014 Systematic Review | Low           | CBT-I: 7; No comparator (pre- post-intervention)                                                                                                                                                                      | 1            | daily sleep diaries, ISI               | **Improvements in quality of life measure (p-values not reported)**                                                        |
| Dickerson, 2014 Systematic Review | High          | CBT (unspecified); usual treatment; waitlist crossover; waitlist control; control; usual treatment                                                                                                                                 | 1            | FACT-B                                 | **Change in outcome:** CBT vs placebo 0.37 [-0.11 to 0.83]                                                                |
|                                                                     |               |                                                                                                                                                                                                                     |              | Global QOL                             | **Change in outcome:** -1.09 [-1.98 to -0.011] Increase in global and cognitive dimensions of quality of life at 8 weeks follow-up |
| Ishak, 2012 Systematic Review | Low           | CBT (unspecified); Placebo; no treatment; unspecified; usual care                                                                                                                                                   | 4            | SF-36; CIS-20; GHQ; PANAS; FACT-G     | **Significant improvement** in physical, emotional and mental health QoL was found in all studies                         |
| Author, Year     | AMSTAR rating | Intervention and sample size                                                                                                                                                                                                 | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA)                  |
|-----------------|---------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|--------------------|---------------------------------------------------------------------------------|
| Howell, 2014 Systematic Review                     | Moderate      | Multi-component CBT - sleep hygiene, sleep restriction, stimulus control, cognitive restructuring, and relaxation therapies usual care, wait-list control, healthy eating and nutrition, sleep education and hygiene only, no treatment | 1            | NR                 | Significant improvement since baseline after CBT intervention (p-values not reported) |
|                 |               | Total sample: 81                                                                                                                                                                                                                                                                         |              |                    |                                                                                  |
| Ishak, 2012 Systematic Review                      | Low           | CBT (individual): psychoeducation, sleep hygiene, stimulus control, sleep restriction, relaxation exercises, cognitive restructuring CBT (group): psychoeducation, sleep hygiene, stimulus control, sleep restriction, relaxation exercises, cognitive restructuring | 1            | SF-36 SIP          | Both groups demonstrated significant improvement in quality of life compared to baseline (p=0.025) |
| Author, Year | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|--------------|---------------|------------------------------|--------------|-------------------|---------------------------------------------------------------|
| **Sleep onset latency** | | | | | |
| Brasure, 2015 | High | Sleep restriction: 68 wait-list control, no treatment, or sleep hygiene/sleep education: 73 | 2 | subjective report | Mean difference [95% CI]: -11.38 [-27.74, 4.99] I-squared: 87% |
| Miller, 2014 | High | Sleep restriction therapy: 98 wait-list control; sleep hygiene instructions: 94 | 4 | sleep diary; actigraphy | Change in outcome (effect size; SD): intervention [pre-post]: -19.34 minutes (0.64; 0.37); control [pre-post]: -3.64 minutes (0.06; 0.36) Sleep restriction arm: sleep latency decreased in all studies, the weighted effect size was medium (0.64) |
| Buscemi, 2005 | High | Relaxation Training (autogenic, breathing process, EMG feedback); Relaxation exercises (group, hypnotic, progressive): 199 Placebo: 185 | 13 | sleep diary | Mean difference [95% CI]: -14.56 [-29.33, 0.20] I-squared: 96.1% |
| Brasure, 2015 | High | Multicomponent Behavioral Interventions or Brief Behavioral Therapy: 70 Information control or placebo: 76 | 3 | subjective report | Mean difference [95% CI]: **-10.43 [-16.31, -4.55]** I-squared: 0% |
| Study                        | Systematic Review | Evidence Level | Multifactor intervention: stimulus control, relaxation response, sleep education | Change in outcome (p-value): | Stimulus control: | Patients achieving SOL $\leq$ 20 mins: | Both groups had a statistically and clinically significant change in mean sleep onset latency; significantly greater proportion of patients receiving multifactor intervention achieved 'good sleeper status' (SOL $\leq$ 20 mins) |
|-----------------------------|-------------------|----------------|---------------------------------------------------------------------------------|-------------------------------|------------------|--------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Wang, 2005                  | Moderate          | Total sample: 18 | Sleep diary                                                                      | Multifactor intervention: 77.3$\rightarrow$17.5 mins ($p<0.001$); stimulus control: 74.9$\rightarrow$28 mins ($p<0.001$) |                   | Multifactor: 6/9; Stimulus control: 2/9 ($p<0.05$ between groups) |                                                                                                                                                    |
| Total Sleep Time            |                   |                |                                                                                |                               |                  |                                      |                                                                                                                                                    |
| Brasure, 2015               | High              | Sleep restriction: 68 wait-list control, no treatment, or sleep hygiene/sleep education: 73 | 2 subjective report            | Mean difference [95% CI]: -17.57 [-102.36, 67.21] I-squared: 93% |                  |                                      |                                                                                                                                                    |
| McCurry, 2007               | Critically Low    | Sleep restriction (nap sleep restriction therapy; sleep compression; sleep compression guidance and sleep hygiene) | 1 actigraphy                  | Sleep restriction more effective than either nap restriction or control on actigraphic total sleep time |                  |                                      |                                                                                                                                                    |
| Miller, 2014                | High              | Sleep restriction therapy: 98 wait-list control; sleep hygiene instructions: 94 | 4 sleep diary; actigraphy      | Change in outcome [effect size (SD)]: intervention [pre-post] 17.06 minutes (0.30; 0.31); control [pre-post] 6.13 minutes (0.01; 0.40) Secondary pre-to-post measures of sleep diary variables were also compared at post-treatment to baseline levels. This revealed a small non-significant increase in total sleep time (ES=0.3) |                  |                                      |                                                                                                                                                    |
| Brasure, 2015               | High              | Relaxation Therapy: 39 passive control: 38 | 2 subjective report            | Mean difference [95% CI]: 10.23 [-19.64, 40.11] I-squared: 29% |                  |                                      |                                                                                                                                                    |
| Study Author & Year | Level of Evidence | Intervention | Control | Change in Outcome | Methodology |
|---------------------|-------------------|--------------|---------|------------------|-------------|
| Miller, 2014        | High              | Sleep restriction therapy: 82 wait-list control; sleep hygiene instructions: 78 | Sleep diary actigraphy | Change in outcome [effect size (SD)]: intervention [pre-post]: -42.17 min, [1.36 (0.42)] control: [pre-post] -11.30 min [0.01 (0.55)] Reductions for wake after sleep onset were found in three studies; the weighted effect size in the intervention was large (1.36) |
| Buscemi, 2005       | High              | Relaxation Training (autogenic, breathing process, EMG feedback); Relaxation exercises (group, hypnotic, progressive): 60 Placebo: 57 | Sleep diary | Mean difference [95% CI]: -1.61 [-14.05, 10.82] I-squared: 20% |
| Brasure, 2015       | High              | Multicomponent Behavioral Interventions or Brief Behavioral Therapy: 70 patients Information control or placebo: 76 patients | Subjective report | Mean difference [95% CI]: -14.9 [-22.66, -7.14] I-squared: 0% |
| Sleep Quality       |                   |              |         |                  |             |
| Hwang, 2016         | Critically Low    | Behavioural therapy; Brief behavioral treatment: NR Control (unspecified): NR | PSQI | Standardized mean difference [95% CI]: 1.90 [0.04, 2.94] I-squared: 96.27% |
| Bogdanov, 2017      | Low               | Problem solving therapy sleep education only Total sample: 356 | PSQI | Significant improvement compared to control at 6-month but not 12-month follow-up (p=0.003, 6 months; p=0.88, 12 months) Change in outcome (effect size: SD): intervention [pre-post] 2.77→2.90 (0.3; NA); control [pre-post]: 2.57→2.58 (0.03; NA) Sleep quality ratings were only reported in one study and were found to increase (ES=0.3) |
| Miller, 2014        | High              | Sleep restriction therapy: 44 wait-list control; sleep hygiene instructions: 50 | Sleep diary | |
| Brooks, 2014        | Low               | Progressive relaxation training: 37 Control: NR | Sleep diary | Treatment group had significant difference in sleep quality pre- and post-treatment |
| Hellström, 2011     | Moderate          | mental imagery usual care Total sample: 36 | VSH-sleep scale | Effects of relaxation on sleep quality were small and did not reach significance |
| Source                  | Strength | Rating | Intervention Details                                                                 | Outcome Measures                                                                 | Result of Intervention Study                                                                 |
|------------------------|----------|--------|--------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|
| Tamrat, 2013           | Low      |        | Relaxation techniques; audiotape guided imagery; relaxation tapes usual care solitary activity; baseline | Total sample: 211                                                               | In summary, there is low strength of evidence that studies of relaxation techniques improve sleep quality |
| Seda, 2015             | Low      |        | Imagery rehearsal therapy (IRT): NR                                                   | CBT (stimulus control and sleep restriction therapy) + Imagery rehearsal therapy (IRT): NR | Cohen’s d (95% CI): IRT post-treatment: 0.50 (0.16 to 0.84) IRT+CBT post-treatment: 1.32 (0.68 to 1.96) Q-statistic (p-value): 4.75 (p=0.03) |
| Sleep Satisfaction     |          |        | Sleep restriction (nap sleep restriction therapy; sleep compression; sleep compression guidance and sleep hygiene) | placebo; waiting list Total sample: 125                                           | sleep compression guidance in combination with sleep education delivered via a standardized video resulted in greater post-test sleep satisfaction scores compared to placebo |
| McCurry, 2007          | Critically Low |        | Sleep restriction (nap sleep restriction therapy; sleep compression; sleep compression guidance and sleep hygiene) | placebo; waiting list Total sample: 125                                           | Sleep restriction therapy was found to be significantly more beneficial than a sleep hygiene/placebo control |
| Sleep Efficiency       | Critically Low |        | Sleep restriction (nap sleep restriction therapy; sleep compression; sleep compression guidance and sleep hygiene) | sleep logs                                                                       | Change in outcome (effect size; SD): intervention [pre-post]: 16.28% (1.50; 0.35); Control [pre-post]: 4.59% (0.04; 0.23) Sleep efficiency increased in three studies; the effect size for sleep efficiency the intervention was large |
| Miller, 2014           | High     |        | sleep restriction therapy: 82 wait-list control; sleep hygiene instructions: 78      | sleep diary actigraphy                                                              |                                                                                             |
| Fatigue Severity       | High     |        | BT Group: 24                                                                        | Placebo: 50                                                                      | Cohen’s d [95% CI]: 0.09 [-0.61 to 0.79] I-squared: 76.5%                                                                 |
| Author, Year | Meta-analysis | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|--------------|---------------|---------------|-------------------------------|--------------|-------------------|---------------------------------------------------------------|
| Sleep onset latency | | | | | | |
| Gong, 2016 | Low | mindfulness based stress reduction; mindfulness meditation; mindfulness based therapy for insomnia | 2 | sleep diary | standardized mean difference [95% CI]: \(-0.53 [-0.97, -0.09]\) I-squared: 0% |
| | | wait list control; sleep hygiene education; self-monitoring condition | | | |
| Total sample: 83 | | | | | | |
| Total Sleep Time | | | | | | |
| Gong, 2016 | Low | mindfulness based stress reduction; mindfulness meditation; mindfulness based therapy for insomnia | 2 | sleep diary | standardized mean difference [95% CI]: 0.28 [-0.24, 0.80] I-squared: 0% |
| | | wait list control; sleep hygiene education; self-monitoring condition | | | |
| Total sample: 58 | | | | | | |
| Sleep Quality | | | | | | |
| Gong, 2016 | Low | mindfulness based stress reduction; mindfulness meditation; mindfulness based therapy for insomnia | 2 | sleep diary | standardized mean difference [95% CI]: \(0.68 [0.24, 1.13]\) I-squared: 0% |
| | | wait list control; sleep hygiene education; self-monitoring condition | | | |
| Total sample: 83 | Total sample: 109 | | 2 | PSQI | standardized mean difference [95% CI]: \(-1.09 [-1.50, 0.69]\) I-squared: 0% |
| Study                         | Criticality | Low | Intervention | Comparator | Measurements | Pre-intervention | Post-intervention | Effect Size | I-squared |
|-------------------------------|-------------|-----|--------------|------------|--------------|-------------------|-------------------|-------------|-----------|
| Venables, 2014 Systematic Review | Critically Low | 1   | mindfulness based stress reduction; mind-body bridging; mindfulness meditation | No comparator | PSQI | 91% score >5; 51% score >10 | 79% score >5; 27% score >10 |
| Gong, 2016 Meta-analysis      | Low         | 2   | mindfulness based stress reduction; mindfulness meditation; mindfulness based therapy for insomnia | wait list control; sleep hygiene education; self-monitoring condition | sleep diary | standardized mean difference [95% CI]: 0.85 [-0.31, 1.40] | I-squared: 0% |
| Venables, 2014 Systematic Review | Critically Low | 3   | mindfulness based stress reduction; mind-body bridging; mindfulness meditation | No comparator | NR | 2 trials showed significant improvement in SE; 1 trial showed no significant improvement |
| Author, Year | Synthesis type | AMSTAR rating | Intervention and sample size | # of studies | Measurement method | Pooled Estimates (MA) or Narrative Results (from SR with no MA) |
|-------------|----------------|---------------|-------------------------------|-------------|-------------------|---------------------------------------------------------------|
| **Sleep onset latency** | | | | | | |
| Chiesa, 2009 | Systematic Review | Low | Pharmacotherapy (general) and Mindfulness based cognitive therapy; mindfulness based stress reduction: 14 No comparator (pre- post- intervention) | 1 | NR | Median sleep latency reduced from 30 minutes to 26 minutes per night |
| **Total Sleep Time** | | | | | | |
| Buscemi, 2005 | Meta-analysis | High | Triazolam; temazepam and CBT: 27 Placebo: 25 | 2 | sleep diary | Mean difference [95% CI]: 23.2 [-2.3, 48.8] I-squared: 0% |
| Chiesa, 2009 | Systematic Review | Low | Pharmacotherapy (general) and Mindfulness based cognitive therapy; mindfulness based stress reduction: 30 No comparator (pre- post- intervention) | 2 | NR | 1 trial showed and average increase of 1 hour total sleep time; 1 trial showed significant improvement in measures of sleep quantity that persisted at 6 and 12 months |
| **Sleep Quality** | | | | | | |
| Chiesa, 2009 | Systematic Review | Low | Pharmacotherapy (general) and Mindfulness based cognitive therapy; mindfulness based stress reduction: 14 No comparator (pre- post- intervention) | 1 | NR | Measures of sleep quality improved significantly post-treatment, improvements were maintained at 6 and 12 months; levels of mindfulness were shown to correlate with quality of sleep |
Appendix F: Tables of primary studies by treatment comparison for outcomes with more than one included SR or SR+MA

Table F1. Primary studies across included systematic reviews that examined Benzodiazepines

| Primary Studies | Buscemi, 2005* n = 18 | Sateia, 2017* n = 2 | Soldatos, 1999* n = 28\(^1\) | Kolla, 2011 n = 1 | Swainston Harrison, 2005 n = 1 | Times Cited | Outcome(s) |
|----------------|-----------------------|---------------------|-----------------------------|----------------|-------------------------------|-------------|------------|
| Flurazepam (n=10) |                        |                     |                             |                |                               |             |            |
| Campbell, 1987  | +                     | --                  | --                          | --             | --                            | 1           | SOL        |
| Cohn, 1991      | +                     | --                  | --                          | --             | --                            | 1           | SOL        |
| Fillingim, 1982 | +                     | --                  | --                          | --             | --                            | 1           | SOL        |
| Fleming, 1995   | +                     | --                  | --                          | --             | --                            | 1           | SOL        |
| Hartmann, 1983  | +                     | --                  | --                          | --             | --                            | 1           | SOL        |
| Mamelak, 1987   | +                     | --                  | --                          | --             | --                            | 1           | SOL        |
| Mamelak, 1989   | +                     | --                  | --                          | --             | --                            | 1           | SOL        |
| Mello de Paula, 1984 | +             | --                  | --                          | --             | --                            | 1           | SOL        |
| Miller, 1984    | +                     | --                  | --                          | --             | --                            | SOL         |            |
| Scharf, 1990    | +                     | --                  | --                          | --             | --                            | 1           | SOL        |
| Temazepam (n=8) |                        |                     |                             |                |                               |             |            |
| Beary, 1984     | +                     | --                  | --                          | --             | --                            | 1           | SOL        |
| Fillingim, 1982 | +                     | --                  | --                          | --             | --                            | 1           | SOL        |
| Glass, 2008     | --                    | +                   | --                          | --             | --                            | 1           | SOL, TST, SQ |
| Hindmarch, 1979 | --                    | +                   | --                          | --             | --                            | 1           | SQ         |
| Leppik, 1997    | +                     | --                  | --                          | --             | --                            | 1           | SOL        |
| Tuk, 1997       | +                     | --                  | --                          | --             | --                            | 1           | SOL, WASO  |
| Morin, 1999     | +                     | --                  | --                          | --             | --                            | 1           | WASO       |
| Wu, 2006        | --                    | +                   | --                          | --             | --                            | 1           | SOL, TST   |
| Triazolam (n=38) |                        |                     |                             |                |                               |             |            |
| Adam, 1984      | --                    | --                  | +                           | --             | --                            | --          | SOL, TST   |
| Bergougnan, 1992| --                    | --                  | +                           | --             | --                            | --          | SOL, TST   |
| Borberly and Achermann, 1991 | --      | --                  | +                           | --             | --                            | --          | SOL, TST   |
| Bowen, 1978     | +                     | --                  | --                          | --             | --                            | 1           | SOL        |
| Cluydts, 1986   | --                    | --                  | +                           | --             | --                            | --          | SOL, TST   |
| Cohn, 1983      | +                     | --                  | --                          | --             | --                            | 1           | SOL        |
| Drake(1), 2000  | +                     | --                  | --                          | --             | --                            | 1           | SOL        |
| Drake(2), 2000  | +                     | --                  | --                          | --             | --                            | 1           | SOL        |
| Author(s)            | Year | SOL | TST | WASO | SOL, TST, WASO |
|---------------------|------|-----|-----|------|----------------|
| Fabre, 1997         |      |     |     |      |                |
| Kales, 1976         |      |     |     |      | SOL, TST       |
| Kales, 1986         |      |     |     |      | SOL, TST       |
| Kales, 1991         |      |     |     |      | SOL, TST       |
| Kanno, 1993         |      |     |     |      | SOL, TST       |
| Leppik, 1997        |      |     |     |      | SOL            |
| Mamelak, 1984       |      |     |     |      | SOL, TST       |
| Mamelak, 1990       |      |     |     |      | SOL, TST       |
| Merlotti, 1988      |      |     |     |      | SOL, TST       |
| Mitler, 1984        |      |     |     |      | SOL, TST       |
| Monti, 1994         |      |     |     |      | SOL, TST       |
| Mouret, 1990        |      |     |     |      | SOL, TST       |
| Nicholson and Stone, 1980 | |     |     |      | SOL, TST       |
| Nicholson, 1982     |      |     |     |      | SOL, TST       |
| Ogura, 1980         |      |     |     |      | SOL, TST       |
| Okuma and Honda, 1978 |    |     |     |      | SOL, TST       |
| Pegram, 1980        |      |     |     |      | SOL, TST       |
| Roehrs, 1992        |      |     |     |      | SOL, TST       |
| Roth, 1974          |      |     |     |      | SOL, TST       |
| Roth, 1976          |      |     |     |      | SOL, TST       |
| Roth, 1977          |      |     |     |      | SOL, TST       |
| Saletu, 1994        |      |     |     |      | SOL, TST       |
| Scharf, 1990        |      |     |     |      | SOL, TST       |
| Spinweber and Johnson, 1982 | |     |     |      | SOL, TST       |
| Steens, 1993        |      |     |     |      | SOL, WASO      |
| Stepanski, 1982     |      |     |     |      | SOL, TST       |
| Tiberge, 1988       |      |     |     |      | SOL, TST       |
| Vogel, 1975         |      |     |     |      | SOL, TST       |
| Walsh, 1998         |      |     |     |      | SOL            |
| Ware, 1997          |      |     |     |      | SOL, TST       |

* Systematic review with meta-analysis

1 The authors of the Soldatos, 1999 paper did not clearly report which studies were included in the analyses for each outcome. All of the primary studies in this review are listed here but are not included in times cited count.
| Primary Studies | Brasure, 2015* | Buscemi, 2005* | Sateia, 2017* | Soldatos, 1999*1 | Mayers, 2005 | Mendelson, 2005 | Swainston, Harrison, 2005 | Ishak, 2012 | Cimolai, 2007 | Times Cited | Outcome(s) |
|-----------------|----------------|----------------|--------------|----------------|--------------|----------------|--------------------------|--------------|--------------|-------------|------------|
| Allain, 2001    | --             | +              | --           | --             | --           | --             | --                       | --           | --           | 1           | SOL, WASO  |
| Asnis, 1999     | --             | +              | --           | --             | --           | --             | --                       | --           | --           | 1           | SOL, WASO  |
| Benoit, 1992    | --             | --             | --           | +              | --           | --             | --                       | --           | --           | --          | SOL, TST   |
| Bergougnan, 1992| --             | --             | --           | +              | --           | --             | --                       | --           | --           | --          | SOL, TST   |
| Besset, 1995    | --             | --             | --           | +              | --           | --             | --                       | --           | --           | --          | SOL, TST   |
| De Roeck and Cluydts, 1991 | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | SOL, TST |
| Declerck, 1992  | --             | --             | --           | +              | --           | --             | --                       | --           | --           | --          | SOL, TST   |
| Declerck, 1999  | --             | +              | --           | --             | --           | --             | --                       | --           | --           | 1           | SOL, WASO  |
| Dorsey, 2004    | --             | --             | --           | +              | --           | --             | --                       | --           | --           | 1           | SOL, WASO  |
| Dujardin, 1998  | --             | +              | --           | --             | --           | --             | --                       | --           | --           | 1           | SOL, TST   |
| Elie, 1999      | +              | +              | +            | --             | --           | --             | --                       | --           | --           | 3           | SOL, TST, WASO, SQ |
| Erman, 2008     | --             | --             | --           | +              | --           | --             | --                       | --           | --           | 1           | SOL, TST, WASO, SQ |
| Fleming, 1995   | --             | +              | --           | --             | --           | --             | --                       | --           | --           | 1           | SOL, TST   |
| Fry, 2000       | +              | +              | --           | --             | --           | --             | --                       | --           | --           | 2           | SOL, SQ    |
| Hajak, 2002     | --             | --             | --           | --             | --           | --             | +                       | --           | --           | 1           | QoL        |
| Hermann, 1988   | --             | --             | --           | +              | --           | --             | --                       | --           | --           | --          | SOL, TST   |
| Hermann, 1993   | --             | +              | +            | +              | --           | --             | --                       | --           | --           | 2           | SOL, TST, WASO, SE |
| Jacobs, 2004    | +              | --             | +            | --             | --           | --             | --                       | --           | --           | 2           | SOL, TST   |
| Kanno, 1993b    | --             | --             | --           | +              | --           | --             | --                       | --           | --           | --          | SOL, TST   |
| Koshorec, 1988  | --             | --             | --           | +              | --           | --             | --                       | --           | --           | --          | SOL, TST   |
| Kryger, 1991    | --             | --             | --           | +              | --           | --             | --                       | --           | --           | --          | SOL, TST   |
| Lahmeyer, 1997  | +              | +              | --           | --             | --           | --             | --                       | --           | --           | 2           | SOL, SQ    |
| Leppik, 1997    | --             | +              | --           | --             | --           | --             | --                       | --           | --           | 1           | SOL, TST   |
| Merlotti, 1989  | --             | --             | --           | +              | --           | --             | --                       | --           | --           | --          | SOL, TST   |

| Sopalidem v Placebo (n = 46) |
|-------------------------------|
| Allain, 2001  | -- | + | -- | -- | -- | -- | -- | -- | -- | 1 | SOL, WASO |
| Asnis, 1999   | -- | + | -- | -- | -- | -- | -- | -- | -- | 1 | SOL, WASO |
| Benoit, 1992  | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | SOL, TST |
| Bergougnan, 1992 | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | SOL, TST |
| Besset, 1995  | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | SOL, TST |
| De Roeck and Cluydts, 1991 | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | SOL, TST |
| Declerck, 1992 | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | SOL, TST |
| Declerck, 1999 | -- | + | -- | -- | -- | -- | -- | -- | -- | 1 | SOL, WASO |
| Dorsey, 2004  | -- | -- | -- | + | -- | -- | -- | -- | -- | 1 | SOL, WASO |
| Dujardin, 1998 | -- | + | -- | -- | -- | -- | -- | -- | -- | 1 | SOL, TST |
| Elie, 1999    | + | + | + | -- | -- | -- | -- | -- | -- | 3 | SOL, TST, WASO, SQ |
| Erman, 2008   | -- | -- | -- | + | -- | -- | -- | -- | -- | 1 | SOL, TST, WASO, SQ |
| Fleming, 1995 | -- | + | -- | -- | -- | -- | -- | -- | -- | 1 | SOL, TST |
| Fry, 2000     | + | + | -- | -- | -- | -- | -- | -- | -- | 2 | SOL, SQ |
| Hajak, 2002   | -- | -- | -- | -- | -- | -- | -- | + | -- | 1 | QoL |
| Hermann, 1988 | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | SOL, TST |
| Hermann, 1993 | -- | + | + | + | -- | -- | -- | -- | -- | 2 | SOL, TST, WASO, SE |
| Jacobs, 2004  | + | -- | + | -- | -- | -- | -- | -- | -- | 2 | SOL, TST |
| Kanno, 1993b  | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | SOL, TST |
| Koshorec, 1988 | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | SOL, TST |
| Kryger, 1991  | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | SOL, TST |
| Lahmeyer, 1997 | + | + | -- | -- | -- | -- | -- | -- | -- | 2 | SOL, SQ |
| Leppik, 1997  | -- | + | -- | -- | -- | -- | -- | -- | -- | 1 | SOL, TST |
| Merlotti, 1989 | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | SOL, TST |
| Primary Studies                          | Monti, 1989 | Monti, 1994 | Monti, 1996 | Monti, 2000 | Nicholson and Pascoe, 1986 | Nobuhara, 1992 | Oswald and Adam, 1988 | Perlis, 2004 | Randall, 2012 | Scharf, 1991a | Scharf, 1991b | Scharf, 1991c | Scharf, 1994 | Staner, 2005 | Steens, 1993 | Uchimura, 2012 | Vogel, 1989 | Walsh, 1998 | Walsh, 2000 | Walsh, 2002 | Ware, 1997 | Monti, 1994 |
|----------------------------------------|-------------|-------------|-------------|-------------|---------------------------|----------------|----------------------|-------------|---------------|---------------|---------------|---------------|---------------|-------------|--------------|-------------|---------------|-------------|---------------|
| **Times Cited**                        |             |             |             |             |                           |                |                      |             |               |               |               |               |               |             |              |             |               |             |               |
| **Outcome(s)**                         | SOL, TST    | TST, WASO   | SOL, WASO   | SOL, WASO   | SOL, TST                  | SOL, TST       | SOL, TST             | SOL, TST    | SOL, TST, WASO| SOL, TST, SQ, SE| SOL, TST      | SOL, TST      | SOL, TST, WASO, SQ, SE| SOL, SQ     | SOL, TST | SOL, TST, SQ | SOL, TST | SOL, TST | SOL, TST, WASO, SE|
| **Zolpidem v Triazolam (n = 3)**       |             |             |             |             |                           |                |                      |             |               |               |               |               |               |             |              |             |               |             |               |
| Monti, 1994                           |             |             |             |             |                           |                |                      |             |               |               |               |               |               |             |              |             |               |             |               |
| Primary Studies | Brasure, 2015* n = 8 | Buscemi, 2005* n = 22 | Sateia, 2017* n = 12 | Soldatos, 1999* n = 34 | Mayers, 2005 n = 1 | Mendelson, 2005 n = 1 | Swainston, 2005 n = 2 | Ishak, 2012 n = 3 | Cimolai, 2007 n = 4 | Times Cited | Outcome(s) |
|----------------|----------------------|----------------------|----------------------|------------------------|----------------------|----------------------|----------------------|----------------------|----------------------|-------------|------------|
| Silvestri, 1996 | --                   | --                   | --                   | --                     | --                   | --                   | --                   | --                   | --                   | 1           | WASO, SOL, WASO, SE |
| Ware, 1997      | --                   | --                   | --                   | --                     | --                   | --                   | --                   | --                   | --                   | 1           | WASO, SE |
| **Zolpidem (nightly) v Zolpidem (as needed) (n = 1)** |                     |                      |                      |                       |                      |                      |                      |                      |                      |             |            |
| Hajak, 2002     | --                   | --                   | --                   | --                     | --                   | --                   | --                   | --                   | --                   | --          | 1          |
| **Zopiclone v Placebo (n = 21)** |                     |                      |                      |                       |                      |                      |                      |                      |                      |             |            |
| Billiard, 1989  | --                   | --                   | --                   | +                     | --                   | --                   | --                   | --                   | --                   | --          | SOL, TST |
| Campbell, 1987  | --                   | +                    | --                   | --                     | --                   | --                   | --                   | --                   | --                   | --          | SOL       |
| Chaudoir, 1983  | --                   | +                    | --                   | --                     | --                   | --                   | --                   | --                   | --                   | --          | SOL       |
| Fleming, 1988   | --                   | --                   | +                    | --                     | --                   | --                   | --                   | --                   | --                   | --          | SOL, TST |
| Godtliesen and Dreyfus, 1980 | --             | --                   | --                   | +                     | --                   | --                   | --                   | --                   | --                   | --          | SOL, TST |
| Goldenberg, 1994| --                   | --                   | --                   | --                     | --                   | +                   | --                   | --                   | --                   | --          | SOL       |
| Jobert, 1993    | --                   | --                   | +                    | --                     | --                   | --                   | --                   | --                   | --                   | --          | SOL, TST |
| Kim, 1993       | --                   | --                   | +                    | --                     | --                   | --                   | --                   | --                   | --                   | --          | SOL, TST |
| Lamphere, 1989  | --                   | +                    | --                   | +                     | --                   | --                   | --                   | --                   | --                   | --          | SOL, TST |
| Leger, 1995     | --                   | --                   | --                   | --                     | --                   | +                   | --                   | --                   | --                   | --          | SOL       |
| Lemoine, 1995   | --                   | --                   | --                   | --                     | --                   | --                   | +                   | --                   | --                   | --          | A/D/D     |
| Mamelak, 1982   | --                   | --                   | --                   | +                     | --                   | --                   | --                   | +                   | --                   | --          | SOL, TST, A/D/D |
| Mamelak, 1987   | --                   | +                    | --                   | --                     | --                   | --                   | --                   | --                   | --                   | --          | SOL       |
| Monchesky, 1986 | --                   | +                    | --                   | --                     | --                   | --                   | --                   | --                   | --                   | --          | SOL       |
| Mouret, 1990    | --                   | --                   | +                    | --                     | --                   | --                   | --                   | --                   | --                   | --          | SOL, TST |
| Nicholson and Stone, 1982 | --         | --                   | --                   | +                     | --                   | --                   | --                   | --                   | --                   | --          | SOL, TST |
| Nicholson and Stone, 1987 | --         | --                   | --                   | +                     | --                   | --                   | --                   | --                   | --                   | --          | SOL, TST |
| Pecknold, 1990  | --                   | --                   | --                   | --                     | --                   | --                   | +                   | --                   | --                   | --          | A/D/D     |
| Petre-Quadens, 1982 | --         | --                   | --                   | +                     | --                   | --                   | --                   | --                   | --                   | --          | SOL, TST |
| Ponciano, 1990  | --                   | --                   | --                   | --                     | --                   | --                   | +                   | --                   | --                   | --          | Hangover |
| Tiberge, 1988   | --                   | --                   | --                   | +                     | --                   | --                   | --                   | --                   | --                   | --          | SOL, TST |

*The authors of the Soldatos, 1999 paper did not clearly report which studies were included in the analyses for each outcome. All of the primary studies in this review are listed here and are not included in times cited count.

*systematic review with meta-analysis
### Table F3. Primary studies across included systematic reviews that examined Suvorexant

| Primary Studies (n = 3) | Kishi, 2015* n = 3 | Kuriyama, 2017* n = 3 | Brasure, 2015* n = 2 | Citrome, 2014* n = 3 | Times Cited | Outcome(s) |
|-------------------------|--------------------|-----------------------|----------------------|----------------------|------------|------------|
| Michelson, 2014         | +                  | +                     | --                   | --                   | 1          | SOL, TST, WASO, ISI, Hangover, Injury, A/D/D |
| Herring, 2012           | --                 | +                     | --                   | --                   | --         | SOL, TST, WASO, ISI, Hangover, Injury, A/D/D |
| Herring, 2014†          |                    |                       | +                    | +                    | 3          | SOL, TST, WASO, ISI, Hangover, Injury, A/D/D |
| Suvorexant; 15 and 20mg |                    |                       | +                    | +                    |            |            |
| Suvorexant; 30 and 40mg |                    |                       | +                    | +                    |            |            |

*This publication includes two trials
†only able to ascertain that these three trials were the only ones included in the SR+MA, unable to determine which outcome analyses they contributed to thus they are not counted in the final column
*systematic review with meta-analysis

### Table F4. Primary studies across included systematic reviews that examined antidepressants

| Primary Studies | Brasure, 2015* n = 2 | Buscemi, 2005* n = 5 | Sateia, 2017* n = 5 | Yuan, 2010* n = 4 | Liu, 2017* n = 6 | Kolla, 2011 n = 1 | Mayers, 2005 n = 3 | Vande Griend, 2012 n = 9 | Yeung, 2015 n = NR† | Mendelson, 2005 n = 8 | Times Cited | Outcome(s) |
|-----------------|----------------------|----------------------|---------------------|--------------------|------------------|-------------------|-------------------|---------------------|------------------|----------------|------------|------------|
| Goldberg, 1974  | --                   | --                   | --                  | --                 | --               | --                | --                | --                  | +                | --             | 1          | SOL        |
| Hajak, 1996     | --                   | +                    | --                  | --                 | --               | --                | --                | --                  | --               | --             | 3          | SOL, TST, SQ |
| Hajak, 2000     | --                   | --                   | --                  | --                 | +                | --                | --                | --                  | --               | --             | 1          | TST        |
| Hajak, 2001     | --                   | +                    | --                  | +                  | --               | +                 | +                 | +                  | --               | --             | 5          | SOL, TST, WASO, SQ, SE |
| Krystal, 2010   | +                    | --                   | +                   | --                 | --               | --                | +                 | --                  | --               | --             | 4          | SOL, TST, WASO, SQ, SE |
| Krystal, 2011   | --                   | --                   | +                   | --                 | --               | +                 | --                | --                  | --               | --             | 3          | SOL, TST, WASO, SE |
| Primary Studies       | Brasure, 2015* n = 2 | Buscemi, 2005* n = 5 | Sateia, 2017* n = 5 | Yuan, 2010* n = 4 | Liu, 2017* n = 6 | Kolla, 2011 n = 1 | Mayers, 2005 n = 3 | Vande Griend, 2012 n = 9 | Yeung, 2015 n = NR | Mendelson, 2005 n = 8 | Times Cited | Outcome(s) |
|----------------------|----------------------|----------------------|----------------------|-------------------|-------------------|-------------------|-------------------|----------------------|------------------|------------------|--------------|------------|
| Lankford, 2011       | +                    | --                   | +                    | --                | --                | --                | +                 | --                   | --               | --               | 3            | SOL, TST, WASO |
| Lankford, 2012       | --                   | --                   | +                    | --                | --                | --                | --                | --                   | --               | --               | 1            | SQ          |
| Rodenbeck, 2003      | --                   | +                    | --                   | +                 | --                | --                | --                | --                   | --               | --               | 2            | SOL, TST, WASO, SE |
| Roth, 2007           | --                   | --                   | +                    | +                 | +                 | --                | +                 | --                   | --               | --               | 4            | SOL, TST, WASO, SE |
| Roth, 2010           | --                   | --                   | --                   | --                | --                | --                | +                 | --                   | --               | --               | 1            | SOL, TST, WASO, SE |
| Scharf, 2008         | --                   | --                   | +                    | +                 | +                 | --                | +                 | --                   | --               | --               | 4            | SOL, TST, WASO, SQ, SE |
| Trazodone v Placebo (n = 20) |                     |                      |                      |                   |                   |                   |                   | +                    | --               | --               | 1            | TST, SQ, SE |
| Kaynak, 2004         | --                   | --                   | --                   | --                | --                | --                | --                | --                   | +               | --               | 1            | TST, SQ, SE |
| Blacker, 1988        | --                   | --                   | --                   | --                | --                | --                | --                | --                   | +               | --               | 1            | SQ          |
| Davey, 1988          | --                   | --                   | --                   | --                | --                | --                | --                | --                   | --               | +               | 1            | SQ          |
| Friedmann, 2008       | --                   | --                   | --                   | --                | --                | +                 | --                | --                   | --               | --               | 1            | SQ          |
| Haffmans and Vos, 1999 | --                   | +                    | --                   | --                | --                | --                | --                | --                   | --               | +               | 2            | SOL, TST |
| Le Bon, 2003         | --                   | --                   | --                   | --                | +                 | --                | +                 | --                   | --               | --               | 2            | SOL, TST, WASO, SE |
| Mashiko, 1999        | --                   | --                   | --                   | --                | --                | +                 | --                | --                   | --               | --               | 1            | TST         |
| Montgomery, 1983      | --                   | --                   | --                   | --                | --                | --                | +                 | --                   | --               | --               | 1            | SOL, TST, SQ |
| Moon, 1998           | --                   | --                   | --                   | --                | --                | --                | --                | +                    | --               | --               | 1            | SQ          |
| Mouret, 1988         | --                   | --                   | --                   | --                | --                | --                | --                | +                    | --               | --               | 1            | SOL, TST |
| Nierenberg, 1994     | --                   | --                   | --                   | --                | --                | +                 | --                | --                   | --               | --               | 1            | SOL, TST, SQ |
| Parrino, 1994        | --                   | --                   | --                   | --                | --                | --                | +                 | --                   | --               | --               | 1            | SOL, TST, SQ |
| Roth, 2011           | --                   | --                   | --                   | --                | --                | --                | --                | --                   | --               | --               | 1            | SOL, WASO |
| Saletu-Zyhlarz, 2001 | --                   | --                   | --                   | --                | --                | --                | +                 | --                   | --               | --               | 1            | SOL, TST, SE |
### Primary Studies

| Primary Studies | Brasure, 2015* n = 2 | Buscemi, 2005* n = 5 | Sateia, 2017* n = 5 | Yuan, 2010* n = 4 | Liu, 2017* n = 6 | Kolla, 2011 n = 1 | Mayers, 2005 n = 3 | Vande Griend, 2012 n = 9 | Yeung, 2015 n = NR | Mendelson, 2005 n = 8 | Times Cited | Outcome(s) |
|-----------------|----------------------|----------------------|---------------------|-------------------|------------------|------------------|-------------------|---------------------|----------------|----------------|-------------|------------|
| Saletu-Zyhlarz, 2002 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | + | 1 | TST, SE |
| Scharf and Sachais, 1990 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | + | 1 | SOL, TST, SE |
| Scharf, 1990 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | + | 1 | WASO |
| Stein, 2011 | -- | -- | -- | -- | -- | -- | -- | + | -- | -- | -- | 1 | TST, SE |
| Van Bemmel, 1992 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | + | 1 | SOL, TST, SE |
| Walsh, 1998 | -- | + | -- | -- | -- | -- | + | + | -- | + | + | 4 | SOL, TST, WASO, SQ |

Trazodone v Zolpidem (n = 1)

| Walsh, 1998 | -- | -- | -- | -- | -- | -- | + | + | -- | + | 3 | SOL, TST, WASO |

| ^1 Unable to determine some or all of the primary studies associated with this review |
| ^2 systematic review with meta-analysis |

### Table F5. Primary studies across included systematic reviews that examined anti-psychotics

| Primary Studies | Anderson, 2014 n = 7 | Coe, 2014 n = 2 | Kolla, 2011 n = 1 | Wine, 2009 n = 3 | Times Cited | Outcome(s) |
|-----------------|----------------------|------------------|------------------|------------------|-------------|------------|
| Quetiapine (n = 9) | | | | | | |
| Baune, 2007 | + | -- | -- | -- | 1 | SQ |
| Endicott, 2008 | + | -- | -- | -- | 1 | SQ |
| Juri, 2005 | + | -- | -- | + | 2 | SOL, SQ |
| Martinotti, 2008 | -- | -- | + | -- | 1 | SQ |
| Robert, 2005 | -- | -- | -- | + | 1 | TST, SQ |
| Tassniyom, 2010 | + | + | -- | -- | 2 | SOL, TST |
| Terán, 2008 | + | -- | -- | -- | 1 | SOL, SQ |
| Todder, 2006 | + | -- | -- | -- | 1 | SOL, TST, SQ, SE |
| Wiegand, 2008 | + | + | -- | + | 3 | SOL, TST, SQ, SE |
Table F6. Primary studies across included systematic reviews that examined melatonin

| Primary Studies          | Buscemi, 2004* | Buscemi, 2005* | Ferracini-Oda, 2013* | McCleery, 2016* | Lee, NA, 2015* | Salvia, 2017* | Xu, 2015* | Zhang, 2016* | Bellon, 2006 | Chase, 1997 | Costello, 2014 | Culpepper, 2015 | Vural, 2014 | Times Cited | Outcome(s)          |
|-------------------------|---------------|---------------|----------------------|----------------|---------------|--------------|-----------|--------------|--------------|-------------|----------------|-------------------|--------------|-------------|------------------|
| Almeida, 2003           | --            | --            | --                   | +             | --            | --           | +         | --           | --           | --          | --             | --                | --           | 3           | SOL, TST, SQ, SE |
| Andrade, 2001           | +             | --            | --                   | --            | --            | --           | --        | --           | --           | --          | --             | --                | 1            | 1           | SOL, WASO         |
| Arendt 1986a and 1986b  | --            | --            | --                   | --            | --            | --           | +         | --           | --           | --          | --             | --                | 1            | 1           | SOL, TST, SQ, SE |
| Asaya, 2003             | --            | --            | --                   | --            | --            | +            | +         | --           | --           | --          | --             | --                | 2            | TST         |
| Baskett, 2003           | +             | --            | --                   | +             | --            | --           | --        | --           | --           | +           | --             | --                | 3            | SOL, TST, SQ, SE |
| Dahlitz, 1991           | +             | --            | +                    | --            | --           | --           | --        | +            | --           | --          | --             | --                | 4            | SOL, TST     |
| Dawson, 1998            | +             | +             | +                    | --            | --           | --           | --        | --           | --           | --          | --             | --                | 4            | SOL, TST, WASO, SQ, SE |
| Dowling, 2005           | --            | --            | --                   | --            | --           | +            | --        | --           | --           | --          | --             | --                | 1            | WASO        |
| Dowling, 2008           | --            | --            | +                    | --            | --           | +            | --        | --           | --           | --          | --             | --                | 3            | TST         |
| Eckerberg, 2012         | --            | --            | --                   | +             | --           | --           | --        | --           | --           | --          | --             | --                | 1            | TST         |
| Ellis, 1995             | --            | --            | --                   | --            | +            | --           | --        | --           | --           | --          | --             | --                | 1            | TST, SQ, SE |
| Ellis, 1996             | +             | +             | --                   | --            | --           | --           | --        | +            | --           | --          | --             | --                | 3            | SOL, TST, WASO, SQ, SE |
| Garfunkel, 1995         | +             | +             | --                   | --            | +            | --           | --        | --           | --           | +           | --             | --                | 5            | SOL, TST, WASO, SQ, SE |
| Garfunkel, 1997         | --            | +             | --                   | --            | +            | --           | --        | --           | --           | --          | --             | --                | 2            | SOL, WASO     |
| Garzon, 2009            | --            | --            | +                    | --            | +            | --           | --        | +            | --           | --          | --             | --                | 3            | SQ          |
| Gehman, 2009            | --            | --            | --                   | --            | +            | +            | --        | --           | --           | --          | --             | --                | 2            | TST, WASO, SE |
| Gooneratne, 2012        | --            | --            | --                   | --            | --           | --           | --        | --           | --           | +           | +              | --                | 1            | SQ          |
| Haimov, 1995            | +             | +             | +                    | --            | --           | --           | --        | --           | --           | --          | --             | --                | 4            | SOL, WASO, SQ, SE |
| He, 2005                | --            | --            | --                   | +             | --           | --           | --        | --           | --           | --          | --             | --                | 1            | SOL, TST, SE |
| Hughes, 1998            | --            | --            | --                   | +             | --           | --           | --        | --           | --           | --          | --             | +                 | 2            | SOL, TST, SQ, SE |
| James, 1989             | --            | --            | +                    | --            | --           | --           | --        | --           | --           | --          | --             | --                | 1            | TST         |
| Primary Studies                  | Buscemi, 2004* | Buscemi, 2005* | Ferracoli-Oda, 2013* | McCleery, 2016* | Lee, NA* | Sato, 2017* | Xu, 2015* | Zhang, 2016* | Bellon, 2006 | Chase, 1997 | Costello, 2014 | Culpepper, 2015 | Vural, 2014 | Times Cited | Outcome(s)                     |
|---------------------------------|---------------|---------------|---------------------|----------------|----------|-------------|-----------|-------------|----------------|-------------|----------------|----------------|-------------|-------------|--------------------------------|
| James, 1990                     | +             | +             | +                   | --             | --       | --          | +         | +           | --             | --          | --             | --             | 7           | SOL, TST, WASO, SQ, SE |
| Kayumov, 2001                   | +             | --            | +                   | --             | --       | --          | +         | +           | --             | --          | --             | --             | 3           | SOL, TST, SQ, SE   |
| Kunz, 2010                      | --            | --            | +                   | --             | --       | --          | --       | --          | --             | --          | --             | --             | 1           | SOL, TST, SQ     |
| Lemoine, 2007                   | --            | --            | +                   | --             | +        | --          | --       | +           | --             | --          | +             | --             | 4           | SQ           |
| Lühringer, 2009                 | --            | --            | +                   | --             | +        | --          | --       | --          | +              | --          | --             | --             | 3           | SOL, TST, SQ     |
| MacFarlane, 1991                | --            | --            | --                   | --             | --       | --          | --       | --          | +              | --          | --             | --             | 1           | TST           |
| Medeiros, 2007                  | --            | --            | +                   | --             | --       | --          | +         | --          | --             | --          | --             | --             | 1           | TST, SE        |
| Montes, 2002                    | --            | +             | --                   | --             | --       | --          | --       | --          | --             | --          | --             | --             | 1           | TST           |
| Montes, 2003                    | +             | +             | --                   | --             | --       | --          | --       | --          | --             | --          | --             | --             | 2           | SOL, WASO, SQ, SE |
| Mundey, 2005                    | --            | --            | +                   | --             | --       | --          | --       | --          | --             | --          | --             | --             | 1           | TST, SQ        |
| Nagtegaal, 1995                 | --            | --            | +                   | --             | --       | --          | --       | --          | --             | --          | --             | --             | 1           | SOL           |
| Nagtegaal, 1998                 | --            | --            | --                   | --             | --       | +          | --       | --          | --             | --          | --             | --             | 1           | SOL, TST, SQ, SE |
| Riemersma, 2008a and 2008b      | --            | --            | --                   | --             | --       | +          | --       | --          | --             | --          | --             | --             | 1           | TST, SE        |
| Serfaty, 2002                   | --            | --            | --                   | --             | --       | +          | --       | --          | --             | --          | --             | --             | 2           | TST, SE        |
| Singer, 2003a and 2003b         | --            | --            | --                   | +              | --       | +          | --       | --          | --             | --          | --             | --             | 3           | TST, WASO, SQ, SE |
| Smiths, 2001                    | --            | --            | --                   | +              | --       | --          | --       | --          | --             | --          | --             | --             | 1           | SOL, TST       |
| Smiths, 2003                    | +             | --            | --                   | +              | --       | --          | --       | --          | --             | --          | --             | --             | 2           | SOL, TST       |
| Sugaya, 2007                    | --            | --            | --                   | --             | --       | --          | --       | +          | --             | --          | --             | --             | 1           | QoL           |
| Van Geijlswijk, 2011            | --            | --            | --                   | +              | --       | --          | --       | --          | --             | --          | --             | --             | 1           | SOL           |
| Wade, 2007                      | --            | --            | +                   | +              | --       | --          | --       | --          | --             | --          | +             | --             | 5           | SOL, SQ        |
| Wade, 2011                      | --            | --            | +                   | --             | --       | --          | --       | --          | --             | --          | --             | --             | 2           | SOL, TST, SQ    |
| Wade, 2014                      | --            | --            | --                   | --             | --       | +          | --       | --          | --             | --          | --             | --             | 1           | WASO          |
| Zhdanova, 2001                  | +             | +             | --                   | --             | --       | --          | --       | --          | --             | --          | --             | --             | 4           | SOL, TST,         |
| Primary Studies | Sateia, 2017* | Culpepper, 2015 | Vande Griend, 2012 | Times Cited | Outcome(s) |
|-----------------|---------------|-----------------|-------------------|-------------|------------|
| Glass, 2008     | +             | +               |                   | 3           | SOL, TST, SQ, SE |
| Morin, 2005     | +             | +               |                   | 3           | SOL, TST, SE, ISI |
| Katayose, 2012  | --            | +               | --                | 1           | SOL         |
| Rickels, 1983   | --            | --              | +                 | 1           | SOL, TST    |
| Meuleman, 1987  | --            | --              | +                 | 1           | SOL, TST, WASO |

*Unable to determine some of the primary studies associated with this review
*systematic review with meta-analysis
Table F8. Primary studies across included systematic reviews that compared cognitive behavioural interventions to inactive controls

| Primary Studies (n = 89) | Sleep Onset Latency |
|--------------------------|---------------------|
|                          | Altena, 2008        |
|                          | --                  |
|                          | Arnedt, 2013        |
|                          | +                   |
|                          | Ascher, 1979        |
|                          | --                  |
|                          | Berger, 2009        |
|                          | --                  |
|                          | Blom, 2015a         |
|                          | --                  |
|                          | Blom, 2015b         |
|                          | --                  |
|                          | Bothelius, 2013     |
|                          | +                   |
|                          | Buysse, 2011        |
|                          | --                  |
|                          | Carr-Kaffashan, 1979|
|                          | --                  |
|                          | Chen, 2008          |
|                          | --                  |
|                          | Chen, 2011          |
|                          | --                  |
|                          | Currie, 2000        |
|                          | --                  |
|                          | Currie, 2014        |
|                          | --                  |
|                          | Ho, 2016* n = 4     |
|                          | --                  |
|                          | Ho, 2015* n = 6     |
|                          | --                  |
|                          | Koffel, 2015* n = 6 |
|                          | --                  |
|                          | Krassow, 2015*      |
|                          | --                  |
|                          | van Straten, 2007*  |
|                          | +                   |
|                          | Ye, 2016* n = 15    |
|                          | --                  |
|                          | Yang, 2014* n = 1   |
|                          | --                  |
|                          | Buscemi, 2005* n = 8 |
|                          | +                   |
|                          | Ho, 2015* n = 1     |
|                          | --                  |
|                          | Johnson, 2016* n = 7|
|                          | --                  |
|                          | Trauer, 2015* n = 3 |
|                          | --                  |
|                          | Montgomery, 2003*   |
|                          | --                  |
|                          | Irwin, 2006* n = 1  |
|                          | --                  |
|                          | van Straten, 2009*  |
|                          | +                   |
|                          | Seyfried, 2016* n = 7|
|                          | --                  |
|                          | Ojajärvi, 2011* n = 9|
|                          | --                  |
|                          | Zachariae, 2016* n = 10|
|                          | --                  |
|                          | Howell, 2014 n = 3  |
|                          | --                  |
|                          | McCurry, 2007 n = 1 |
|                          | --                  |
|                          | Brooks, 2014 n = 1  |
|                          | --                  |
|                          | Ishak, 2012 n = 1   |
|                          | --                  |
|                          | Dickerson, 2014 n = 1|
|                          | --                  |
|                          | Venables, 2014 n = 8|
|                          | --                  |

Times Cited
| Author(s)                        | Year   | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | + | 1 |
|---------------------------------|--------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|---|---|
| Dirksen,                        | 2008   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Dixon,                          | 2006   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Edinger and Sampson,            | 2003   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Edinger,                        | 2003   | +  |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Edinger,                        | 2007   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Edinger,                        | 2009   | +  |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Epstein and Dirksen,            | 2007   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Epstein,                        | 2012   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Espie,                          | 1989   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Espie,                          | 2001   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Espie,                          | 2006   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Espie,                          | 2007   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Espie,                          | 2008a  |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Espie,                          | 2008b  |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Espie,                          | 2012   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Fiorentino,                     | 2008   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Garland,                        | 2014   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Espie,                          | 2008a  |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Espie,                          | 2008b  |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Espie,                          | 2012   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Fiorentino,                     | 2008   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Garland,                        | 2014   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Espie,                          | 2008   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Espie,                          | 2008a  |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Espie,                          | 2008b  |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Espie,                          | 2012   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Fiorentino,                     | 2008   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Garland,                        | 2014   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Author(s) | Year | Value 1 | Value 2 | Value 3 | Value 4 | Value 5 | Value 6 | Value 7 | Value 8 | Value 9 | Value 10 | Value 11 | Value 12 | Value 13 | Value 14 | Value 15 | Value 16 | Value 17 | Value 18 | Value 19 | Value 20 | Value 21 | Value 22 | Value 23 | Value 24 |
|-----------|------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|--------|
| Harvey,   | 2003 |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 1      |
| Ho,       | 2014 |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 3      |
| Holqvist, | 2014 |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 1      |
| Irwin,    | 2014 |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 1      |
| Jacobs,   | 2004 |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 2      |
| Jernelov, | 2012 |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 1      |
| Jungquist,| 2010 |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 1      |
| Kaldo,    | 2015 |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 1      |
| Lacks,    | 1983b|         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 2      |
| Lancee,   | 2012 |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 3      |
| Lancee,   | 2013a|         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 1      |
| Lancee,   | 2013b|         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 1      |
| Lancee,   | 2015 |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 1      |
| Lichstein | 2001 |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 3      |
| Lick,     | 1977 |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 1      |
| Lovato,   | 2014 |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 1      |
| Mack,     | 2013 |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 1      |
| Margolies | 2013 |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 1      |
| Matthews, | 2010 |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 1      |
| Matthews, | 2014 |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 1      |
| Author          | Year | Value 1 | Value 2 | Value 3 | Value 4 | Value 5 | Value 6 | Value 7 | Value 8 | Value 9 | Value 10 | Value 11 | Value 12 | Value 13 | Value 14 |
|-----------------|------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|
| McCrae, 2007    |      |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Mimeault, 1999  |      |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Morawetz, 1989  |      |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Morin, 1988     |      |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Morin, 1993     |      |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Nicassio, 1974  |      |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Nicassio, 1982  |      |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Pallesen, 2003  |      |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Pillai, 2015    |      |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Puder, 1983     |      |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Quesnel, 2003   |      |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Raymond, 2010   |      |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Riedel, 1995    |      |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Ritterband, 2009 |      |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Ritterband, 2012 |      |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Rybarczyk, 2002 |      |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Rybarczyk, 2005 |      |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Sanavio, 1990   |      |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Savard, 2005    |      |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Author            | Year | References |
|-------------------|------|------------|
| Savard            | 2014 | 1          |
| Smith             | 2015 | 1          |
| Soeffing          | 2008 | 1          |
| Stanton           | 1989 | 2          |
| Strom             | 2004 | 5          |
| Suzuki            | 2008 | 1          |
| Talbot            | 2014 | 1          |
| Tang              | 2012 | 1          |
| Taylor            | 2014 | 1          |
| Thiart            | 2015 |            |
| Turner            | 1979 | 1          |
| Turner            | 1982 | 1          |
| Ulmer             | 2011 | 1          |
| Van Straten       | 2009 | 1          |
| Van Straten       | 2014 | 4          |
| Vincent           | 2009 | 5          |
| Vitiello          | 2009 | 1          |
| Waters            | 2003 | 2          |
| Primary Studies | Woolfolk, 1983 | Wu, 2006 | Brasure, 2015* n=15 | Cheng, 2012* n=4 | Ho, 2016* n=4 | Koffel, 2015* n=6 | Navarro-Bravo, 2015* n=8 | van Straaten, 2007* n=10 | Ye, 2016* n=15 | Dickerson, 2014 | Venables, 2014* n=8 | Ho, 2015* n=8^2 | Irwin, 2006* n=15 | Montgomery, 2003* n=4 | Okajima, 2011* n=^2 | Seyffert, 2016* n=8 | Trauer, 2015* n=16 | van Straaten, 2009* n=8 | Zachariae, 2016* n=10 | Howell, 2014* n=2 | Wang, 2005* n=2 |
|-----------------|----------------|----------|---------------------|-----------------|----------------|------------------|-------------------------|------------------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
| Times Cited     | 1              | 2        |                     |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Arnedt, 2013    | +              | +        |                     |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Barsevick, 2010 | --             | --       |                     |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Berger, 2009    | --             | --       |                     |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Blom, 2015a     | --             | --       |                     |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Blom, 2015b     | --             | --       |                     |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Bothelius, 2013 | --             | --       |                     |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Buysse, 2011    | --             | --       |                     |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Chen, 2001      | --             | --       | +                   |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Currie, 2000    | --             | --       | +                   |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Davidson, 2001  | --             | --       |                     |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Dirksen, 2008   | --             | --       |                     |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Edinger and Sampson, 2003 | --     | --       | +                   |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Edinger, 2001   | +              | --       |                     |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Edinger, 2003   | +              | --       |                     |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Edinger, 2007   | --             | --       |                     |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Edinger, 2009   | +              | --       |                     |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Epstein and Dirksen, 2007 | --   | --       | +                   |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Epstein, 2012   | --             | --       | +                   |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Espie, 2001     | --             | --       | +                   |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Espie, 2003     | --             | --       | --                  |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Espie, 2006     | --             | --       |                     |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Espie, 2007     | +              | --       | +                   |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Espie, 2008a    | --             | --       | +                   |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Espie, 2008b    | --             | --       |                     |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Espie, 2012     | +              | --       | --                  |                 |                 |                  |                         |                        |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Author, Year | Code 1 | Code 2 | Code 3 | Code 4 | Code 5 | Code 6 | Code 7 | Code 8 | Code 9 | Code 10 | Code 11 | Code 12 | Code 13 | Code 14 | Code 15 | Code 16 | Code 17 | Code 18 | Code 19 | Code 20 | Code 21 | Code 22 |
|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Fiorentino, 2008 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| Ho, 2014 | -- | -- | -- | -- | -- | + | -- | -- | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | 3 |
| Holmqvist, 2014 | -- | -- | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| Jacobs, 2004 | + | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 2 |
| Jernelov, 2012 | + | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| Kaldo, 2015 | -- | -- | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 2 |
| Lancee, 2012 | -- | -- | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| Lancee, 2013a | -- | -- | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 3 |
| Lancee, 2013b | -- | -- | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| Lancee, 2015 | -- | -- | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| Lichstein, 2001 | -- | -- | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 2 |
| Lick, 1977 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| Lovato, 2014 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| Mack, 2013 | -- | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| Margolies, 2013 | -- | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| Matthews, 2010 | -- | -- | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| McCrae, 2007 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| Mimeault, 1999 | + | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 2 |
| Morawetz, 1989 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| Morin, 1988 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | 2 |
| Morin, 1993 | -- | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | 4 |
| Morin, 1999 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | 4 |
| Pallesen, 2003 | -- | -- | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| Pillai, 2015 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| Quesnel, 2003 | -- | -- | -- | -- | -- | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| Raymond, 2010 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| Riedel, 1995 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| Ritterband, 2009 | + | + | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 5 |
| Ritterband, 2012 | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | 3 |
| Rybarczyk, 2002 | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 2 |
| Rybarczyk, 2005 | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| Savard, 2005 | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 3 |
| Savard, 2013 | -- | -- | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| Siervesten, 2006 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| Soeffing, 2008 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| Strom, 2004 | + | + | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| Suzuki, 2008 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| Primary Studies n = 70 | Braeure, 2015* n = 11 | Cheng, 2012* n = 4 | Ho, 2016* n = 4 | Koffel, 2015* n = 6 | Navarro-Bravo, 2015* n = 7 | van Straten, 2007* n = 10^2 | Ye, 2016* n = 11 | Dickerson, 2014 n = 1 | Vennables, 2014 n = 8 | Wang, 2005 n = 3 | Busseni, 2015* n = 10^2 | Ho, 2015* n = 6 | Irwin, 2016* n = 15 | Johnson, 2016* n = 7 | Okajima, 2011* n = 6^2 | Trauer, 2015* n = 14 | Montgomery, 2003* n = 4 | Seyler, 2016* n = 6 | van Straten, 2009* n = 6 | Zachariae, 2016* n = 7 | Howell, 2014 n = 2 | McCurry, 2007 n = 1 |
|------------------------|---------------------|------------------|----------------|-------------------|--------------------------|------------------------|----------------|-----------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Wake After Sleep Onset | Arndt, 2013 | + | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | 1 |
| | Berger, 2009 | - | - | - | - | - | - | - | + | - | - | - | - | - | - | - | - | - | - | - | - | - | 1 |
| | Bothelius, 2013 | + | - | - | - | - | - | - | - | - | - | - | - | - | - | - | + | - | - | - | - | - | 2 |
| | Buysse, 2011 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | + | - | 1 |
| | Currie, 2000 | - | - | - | + | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | 2 |
| | Currie, 2004 | - | - | - | - | - | - | - | + | - | - | - | - | - | - | - | - | - | - | - | - | - | 1 |
| | Davies, 1986 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | 2 |
| | Dirksen, 2008 | - | - | - | - | - | - | - | + | - | - | - | - | - | - | - | - | - | - | - | - | - | 1 |
| Reference                          | Data Points | 2003 | 2001 | 2003 | 2003 | 2007 | 2009 | 2007 | 2007 | 2008a | 2008b | 2012 | 2012 | 2008 | 2008 | 2014 | 2014 | 1988 |
|-----------------------------------|-------------|------|------|------|------|------|------|------|------|-------|-------|------|------|------|------|------|------|
| Edinger and Sampson, 2003         | --          | --   | --   | --   | --   | --   | --   | +    | --   | --    | --    | +    | --   | --   | --   | +    | --   | 2    |
| Edinger, 2001                     | --          | --   | --   | --   | --   | --   | --   | +    | --   | +     | --    | +    | --   | --   | --   | +    | --   | 4    |
| Edinger, 2003                     | +           | --   | --   | --   | --   | --   | --   | +    | --   | +     | --    | --   | --   | --   | --   | +    | --   | 3    |
| Edinger, 2007                     | --          | --   | --   | --   | --   | --   | --   | +    | --   | --    | --    | --   | +    | --   | --   | --   | --   | 1    |
| Edinger, 2009                     | +           | --   | --   | --   | --   | --   | --   | --   | --   | --    | --    | --   | --   | +    | --   | --   | +    | 2    |
| Epstein and Dirksen, 2007         | --          | --   | --   | --   | --   | +    | --   | -    | --   | --    | --    | --   | +    | --   | --   | --   | --   | 4    |
| Espie, 2001                       | --          | --   | --   | --   | --   | +    | --   | --   | --   | --    | --    | --   | --   | --   | --   | --   | --   | 2    |
| Espie, 2006                       | --          | --   | --   | --   | --   | +    | --   | --   | --   | --    | --    | --   | --   | --   | --   | --   | --   | 1    |
| Espie, 2007                       | +           | --   | --   | --   | --   | +    | --   | --   | --   | --    | --    | --   | +    | --   | --   | +    | --   | 4    |
| Espie, 2008a                      | --          | --   | --   | --   | --   | +    | --   | --   | --   | --    | --    | --   | --   | +    | --   | --   | --   | 4    |
| Espie, 2008b                      | --          | --   | --   | --   | --   | +    | --   | --   | --   | --    | --    | --   | --   | +    | --   | --   | --   | 1    |
| Espie, 2012                       | +           | --   | --   | --   | --   | +    | --   | --   | --   | --    | --    | --   | +    | --   | +    | +    | --   | 4    |
| Esptein, 2012                     | --          | --   | --   | --   | +    | --   | --   | --   | --   | --    | --    | --   | --   | +    | --   | --   | --   | 1    |
| Fiorentino, 2008                   | --          | --   | --   | --   | --   | +    | --   | --   | --   | --    | --    | --   | --   | --   | --   | --   | --   | 1    |
| Garland, 2014                     | --          | --   | --   | --   | --   | --   | +    | --   | --   | --    | --    | --   | --   | --   | +    | --   | --   | 1    |
| Ho, 2014                          | --          | --   | --   | --   | --   | +    | --   | --   | --   | --    | --    | --   | +    | --   | --   | +    | --   | 3    |
| Hoelscher and Edinger, 1988       | --          | --   | --   | --   | --   | --   | --   | --   | --   | --    | --    | --   | --   | --   | --   | +    | 1    |
| Author(s)          | Years   | Table Data |
|-------------------|---------|------------|
| Holmqvist, 2014   |         | -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- 1 |
| Irwin, 2014       |         | + -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- 1 |
| Jernelov, 2012    |         | + -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- 1 |
| Jungquist, 2010   |         | + -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- 1 |
| Lacks, 1983       |         | -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- 2 |
| Lancee, 2012      |         | -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- 3 |
| Lancee, 2013a     |         | -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- 1 |
| Lancee, 2013b     |         | -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- 1 |
| Lancee, 2015      |         | -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- 1 |
| Lichstein, 2001   |         | + -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- 3 |
| Lick, 1977        |         | + -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- 1 |
| Lovato, 2014      |         | + -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- 1 |
| Mack, 2013        |         | -- -- + -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- 1 |
| Margolies, 2013   |         | -- -- + -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- 1 |
| Matthews, 2010    |         | -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- 1 |
| Matthews, 2014    |         | + -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- 1 |
| McCrae, 2007      |         | -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- 1 |
| Mimeault, 1999    |         | + -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- 1 |
| Morawetz, 1989    |         | + -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- 1 |
| Morin, 1988       |         | + -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- -- 1 |
| Morin, 1993 | + | - | - | + | - | - | - | - | - | - | - | - | + | - | - | - | - | - | + | 6 |
| Morin, 1999 | + | - | - | - | + | - | - | - | - | - | - | + | - | - | + | - | - | - | - | - | - | 6 |
| Pallesen, 2003 | - | - | - | - | - | - | - | + | - | - | - | - | - | - | - | - | + | - | - | - | - | 1 |
| Quesnel, 2003 | - | - | - | - | - | - | - | + | - | - | - | - | - | - | - | - | - | - | - | - | 1 |
| Raymond, 2010 | - | - | - | - | - | - | - | + | - | - | - | - | - | - | - | - | - | - | - | - | 1 |
| Riedel, 1995 | - | - | - | - | - | - | - | + | - | - | - | - | - | - | - | - | - | - | - | - | 1 |
| Ritterband, 2009 | + | + | - | - | - | - | - | + | - | - | - | - | - | - | - | - | - | - | - | - | 5 |
| Ritterband, 2012 | - | + | - | - | - | - | - | + | - | - | - | - | - | - | - | - | - | - | - | - | 4 |
| Rybarczyk, 2002 | - | - | - | + | - | - | - | - | - | - | - | + | - | - | - | - | - | - | - | - | 3 |
| Rybarczyk, 2005 | + | - | - | - | + | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | 3 |
| Sanavio, 1990 | - | - | - | - | - | - | - | + | - | - | - | - | - | - | - | - | - | - | - | - | 1 |
| Savard, 2005 | - | - | - | - | + | - | - | - | - | - | - | + | - | - | - | - | - | - | - | - | 4 |
| Savard, 2014 | - | - | - | - | - | - | - | + | - | - | - | - | - | - | - | - | - | - | - | - | 1 |
| Smith, 2015 | + | - | - | - | - | - | - | + | - | - | - | - | - | - | - | - | - | - | - | - | 1 |
| Soeffing, 2008 | - | - | - | - | - | - | - | + | - | - | - | - | - | - | - | - | - | - | - | - | 1 |
| Strom, 2004 | + | + | - | - | - | - | - | + | - | - | - | - | - | - | - | - | - | - | - | - | 5 |
| Talbot, 2014 | - | - | - | - | - | - | - | + | - | - | - | - | - | - | - | - | - | - | - | - | 1 |
| Tang, 2012 | + | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | 1 |
| Taylor, 2014 | - | - | - | - | - | - | - | + | - | - | - | - | - | - | - | - | - | - | - | - | 1 |
| Turner, 1979 | - | - | - | - | - | - | - | + | - | - | - | - | - | - | - | - | - | - | - | - | 1 |
| Primary Studies | Sleep Quality |
|-----------------|---------------|
| n = 47          |               |
| Turner, 1982    |               |
| Ulmer, 2011     |               |
| Vincent, 2009   |               |
| Vitiello, 2009  |               |
| Waters, 2003    |               |

| Brasure, 2015* n = 6 | Ho, 2016* n = 6 | Kofkel, 2015* n = 5 | Navarro-Bravo, 2015* n = 5 | van Straten, 2007* n = 4 | Bogdanov, 2017 n = 1 | Venables, 2014 n = 2 | Bussemi, 2005* n = 2 | Yang, 2014* n = 3 | Ho, 2015* n = 4 | Irwin, 2006* n = 7 | Okajima, 2011* n = 2 | Tang, 2015* n = 11 | van Straten, 2009 n = 7 | Zacharie, 2016* n = 8 | Howell, 2014 n = 2 | McCurry, 2007 n = 4 | Times Cited |
|---------------------|-----------------|-------------------|-------------------------|----------------------|----------------|----------------|----------------|----------------|----------------|----------------|-----------------|----------------|----------------|-----------------|----------------|----------------|--------------|
| Arnedt, 2013        | + -- -- -- -- -- | -- -- -- -- -- -- | -- -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | 1 |
| Barsevick, 2010     | -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | 1 |
| Berger, 2009        | -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | 1 |
| Bjorvatn, 2011      | + -- -- -- -- -- | -- -- -- -- -- -- | -- -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | 3 |
| Chen, 2008          | -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | 1 |
| Chen, 2011          | -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | 2 |
| Currie, 2000        | -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | 3 |
| Davis, 2007         | -- + -- -- -- -- | -- -- -- -- -- -- | -- -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | 1 |
| Davis, 2011         | -- + -- -- -- -- | -- -- -- -- -- -- | -- -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | 1 |
| Edinger, 2001       | -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | 1 |
| Edinger, 2003       | -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | 1 |
| Edinger, 2005       | -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | 1 |
| Edinger, 2009       | + -- -- -- -- -- | -- -- -- -- -- -- | -- -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | 1 |
| Epstein and Dinksen, 2007 | -- -- + -- -- -- | -- -- -- -- -- -- | -- -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | 1 |
| Espie, 2007         | + -- + -- -- -- | -- -- -- -- -- -- | -- -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | 3 |
| Espie, 2008         | -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | 1 |
| Espie, 2012         | -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | 1 |
| Fiorentino, 2008    | -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- -- -- -- -- -- | -- -- -- -- -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | -- -- | 1 |
| Author              | Year | Score |
|---------------------|------|-------|
| Fiorentino, 2009    |      |       |
| Garland, 2014       |      |       |
| Ho, 2014            |      |       |
| Jungquist, 2010     |      |       |
| Krakow, 2001       |      |       |
| Lichstein, 2000    |      |       |
| Lichstein, 2001    |      |       |
| Lick, 1977          |      |       |
| Lu, 2016            |      |       |
| Mack, 2013          |      |       |
| Margolies, 2013     |      |       |
| Martínez, 2014      |      |       |
| McCurry, 1998       |      |       |
| Mimeault, 1999      |      |       |
| Miro, 2011          |      |       |
| Rambod, 2013        |      |       |
| Riedel, 1995        |      |       |
| Ritterband, 2009    |      |       |
| Ritterband, 2012    |      |       |
| Rybarczyk, 2002     |      |       |
| Rybarczyk, 2005     |      |       |
| Savard, 2005        |      |       |
| Strom, 2004         |      |       |
| Suzuki, 2008        |      |       |
| Turner, 1979        |      |       |
| Turner, 1982        |      |       |
| Ulmer, 2011         |      |       |
| Van Straten, 2014   |      |       |
| Vincent, 2009       |      |       |
| Primary Studies                     | Sleep Efficiency |
|-----------------------------------|------------------|
| Cheng, 2012* n = 4                |                  |
| Ho, 2016* n = 5                   |                  |
| Koffel, 2015* n = 6               |                  |
| Navarro-Bravo, 2015* n = 8        |                  |
| van Straten, 2007* n = 10^2       |                  |
| Ye, 2016* n = 15                  |                  |
| Bodeun, 2017 n = 1                |                  |
| Brooks, 2014 n = 3                |                  |
| Dickerson, 2014 n = 1             |                  |
| Ishak, 2012 n = 1                 |                  |
| Wang, 2006 n = 4                  |                  |
| Venables, 2014 n = 12             |                  |
| Yang, 2014* n = 2                 |                  |
| Ho, 2015* n = 7                   |                  |
| Irwin, 2006* n = 8                |                  |
| Johnson, 2003* n = 3              |                  |
| Okajima, 2011* n = 10^2           |                  |
| Seyffert, 2016* n = 4             |                  |
| Trauer, 2015* n = 17              |                  |
| van Straten, 2009* n = 7^2        |                  |
| Zachariae, 2016* n = 11           |                  |
| Howell, 2014 n = 3                |                  |
| Taylor, 2014 n = 13               |                  |
| McCurry, 2007 n = 3               |                  |
| Altena, 2008                      |                  |
| Arnedt, 2007                      |                  |
| Arnedt, 2011                      |                  |
| Berger, 2009                      |                  |
| Blom, 2015a                       |                  |
| Blom, 2015b                       |                  |
| Bootzin and Stevens, 2005         |                  |
| Bothelius, 2013                   |                  |
| Buysse, 2011                      |                  |
| Chen, 2008                        |                  |
| Chen, 2011                        |                  |
| Currie, 2000                      |                  |
| Author(s)          | Year | Values | | Values | | Values | | Values | | Values | | Values | | Values | | Values | | Values | | Values | | Values | | Values | | Values | | Values | | Values | | Values | | Values | | Values | | Values | | Values | | Values |
|-------------------|------|--------|---|--------|---|--------|---|--------|---|--------|---|--------|---|--------|---|--------|---|--------|---|--------|---|--------|---|--------|---|--------|---|--------|---|--------|---|--------|---|--------|---|--------|---|--------|---|--------|"
| Year        | Study Details       | Design Features | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 |
|------------|---------------------|-----------------|------|------|------|------|------|------|------|------|
| Ho, 2014   | --                  | --              | +    | --    | --    | --    | --    | --    | --    | --    |
| Holmqvist, | --                  | --              | --   | +     | --    | --    | --    | --    | --    | --    |
| 2014       |                     |                 |      |       |       |       |       |       |       |       |
| Jacobs,    | --                  | --              | --   | --    | --    | --    | --    | --    | --    | --    |
| 2004       |                     |                 |      |       |       |       |       |       |       |       |
| Kaldo,     | --                  | --              | --   | +     | --    | --    | --    | --    | --    | --    |
| 2015       |                     |                 |      |       |       |       |       |       |       |       |
| Lancee,    | --                  | --              | --   | --    | --    | --    | --    | --    | --    | --    |
| 2012       |                     |                 |      |       |       |       |       |       |       |       |
| Lancee,    | --                  | --              | --   | +     | --    | --    | --    | --    | --    | --    |
| 2013a      |                     |                 |      |       |       |       |       |       |       |       |
| Lancee,    | --                  | --              | --   | --    | --    | --    | --    | --    | --    | --    |
| 2013b      |                     |                 |      |       |       |       |       |       |       |       |
| Lancee,    | --                  | --              | --   | +     | --    | --    | --    | --    | --    | --    |
| 2015       |                     |                 |      |       |       |       |       |       |       |       |
| Lichstein, | --                  | --              | --   | --    | --    | --    | --    | --    | --    | --    |
| 1999       |                     |                 |      |       |       |       |       |       |       |       |
| Lichstein, | --                  | --              | --   | --    | --    | --    | --    | --    | --    | --    |
| 2001       |                     |                 |      |       |       |       |       |       |       |       |
| Lichstein, | --                  | --              | --   | --    | --    | --    | --    | --    | --    | --    |
| 2013       |                     |                 |      |       |       |       |       |       |       |       |
| Lovato,    | --                  | --              | --   | --    | --    | --    | --    | --    | --    | --    |
| 2014       |                     |                 |      |       |       |       |       |       |       |       |
| Mack,      | --                  | --              | +    | --    | --    | --    | --    | --    | --    | --    |
| 2013       |                     |                 |      |       |       |       |       |       |       |       |
| Manber,    | --                  | --              | --   | --    | --    | --    | --    | --    | --    | --    |
| 2008       |                     |                 |      |       |       |       |       |       |       |       |
| Margolies, | --                  | --              | +    | --    | --    | --    | --    | --    | --    | --    |
| 2013       |                     |                 |      |       |       |       |       |       |       |       |
| Matthews,  | --                  | --              | --   | --    | --    | --    | --    | --    | --    | --    |
| 2010       |                     |                 |      |       |       |       |       |       |       |       |
| Matthews,  | --                  | --              | --   | --    | --    | --    | --    | --    | --    | --    |
| 2014       |                     |                 |      |       |       |       |       |       |       |       |
| McCrae,    | --                  | --              | --   | --    | --    | --    | --    | --    | --    | --    |
| 2007       |                     |                 |      |       |       |       |       |       |       |       |
| Mimeault   | --                  | --              | --   | --    | --    | --    | --    | --    | --    | --    |
| and Morin, |                     |                 |      |       |       |       |       |       |       |       |
| 1999       |                     |                 |      |       |       |       |       |       |       |       |
| Author(s)                  | Year | Category | Gender | Infant | Toddler | Child | Adolescent | Adult | Chronic | Emotional | Physical | Total |
|---------------------------|------|----------|--------|--------|---------|-------|-------------|-------|---------|-----------|----------|-------|
| Morin, 1993               |      |          |        |        |         |       |             |       |         |           |          |   4    |
| Morin, 1999               |      |          |        |        |         |       |             |       |         |           |          |   4    |
| Morin, 2004               |      |          |        |        |         |       |             |       |         |           |          |   1    |
| Morin, 2012               |      |          |        |        |         |       |             |       |         |           |          |   1    |
| Okajima, 2013             |      |          |        |        |         |       |             |       |         |           |          |   1    |
| Raymond and Morin, 2007   |      |          |        |        |         |       |             |       |         |           |          |   1    |
| Pallesen, 2003            |      |          |        |        |         |       |             |       |         |           |          |   1    |
| Quesnel, 2003             |      |          |        |        |         |       |             |       |         |           |          |   1    |
| Quesnel, 2003             |      |          |        |        |         |       |             |       |         |           |          |   1    |
| Rambod, 2013              |      |          |        |        |         |       |             |       |         |           |          |   1    |
| Raymond, 2010             |      |          |        |        |         |       |             |       |         |           |          |   1    |
| Riedel, 1995              |      |          |        |        |         |       |             |       |         |           |          |   1    |
| Ritterband, 2009          |      |          |        |        |         |       |             |       |         |           |          |   4    |
| Ritterband, 2012          |      |          |        |        |         |       |             |       |         |           |          |   5    |
| Rybarczyk, 2002           |      |          |        |        |         |       |             |       |         |           |          |   3    |
| Rybarczyk, 2005           |      |          |        |        |         |       |             |       |         |           |          |   1    |
| Savard, 2005              |      |          |        |        |         |       |             |       |         |           |          |   4    |
| Savard, 2014              |      |          |        |        |         |       |             |       |         |           |          |   1    |
| Sivertsen, 2006           |      |          |        |        |         |       |             |       |         |           |          |   1    |
| Author       | Year | Data Quality | Notes |
|-------------|------|--------------|-------|
| Soeffing    | 2008 | -            | +     |
| Strom       | 2004 | +            | -     |
| Suzuki      | 2008 | -            | -     |
| Talbot      | 2014 | -            | +     |
| Taylor      | 2012 | -            | -     |
| Taylor      | 2014 | -            | +     |
| Thiart      | 2015 | -            | +     |
| Ulmer       | 2011 | -            | +     |
| Ustinov     | 2013 | -            | +     |
| Van Straten | 2013 | -            | +     |
| Van Straten | 2014 | -            | +     |
| Vincent     | 2009 | +            | -     |
| Vitiello    | 2009 | -            | +     |
| Wagley      | 2013 | -            | +     |
| Wu          | 2006 | -            | +     |
| Primary Studies | Brause, 2015* n = 9 | Cheng, 2012* n = 2 | Ho, 2016* n = 5 | Navarro-Bravo, 2015* n = 4 | van Straten, 2007* n = 38 | Ye, 2016* n = 11 | Bogdanov, 2017 n = 2 | Dickerson, 2014 n = 2 | Ishak, 2012 n = 1 | Venables, 2014 n = 10 | Johnson, 2016* n = 4 | Seyffert, 2016* n = 4 | Zachariae, 2016* n = 8 | Howell, 2014 n = 4 | Times Cited |
|-----------------|---------------------|-------------------|-----------------|-----------------------------|---------------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|-----------|
| Arnedt, 2013    | +                   | --                 | --              | --                          | --                        | --                   | --                   | --                   | --                   | --                   | --                   | --                   | --                   | 1         |
| Bothelius, 2013 | +                   | --                 | --              | --                          | --                        | --                   | --                   | --                   | --                   | --                   | --                   | --                   | --                   | 1         |
| Byles, 2003     | --                  | --                 | --              | --                          | --                        | --                   | --                   | --                   | +                    | --                   | --                   | --                   | --                   | 1         |
| Casault, 2011   | --                  | --                 | --              | --                          | --                        | --                   | --                   | --                   | +                    | --                   | --                   | --                   | --                   | 1         |
| Dirksen and Epstein, 2008 | -- | -- | -- | -- | -- | -- | -- | -- | + | -- | + | -- | -- | -- | 2 |
| Dirksen, 2008   | --                  | --                 | --              | --                          | --                        | --                   | --                   | --                   | +                    | --                   | --                   | --                   | --                   | 2         |
| Epstein and Dirksen, 2007 | -- | -- | -- | + | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | 1 |
| Epstein, 2012   | --                  | --                 | --              | --                          | --                        | --                   | --                   | --                   | --                   | --                   | --                   | --                   | --                   | 1         |
| Espie, 2012     | --                  | --                 | --              | --                          | +                        | --                   | --                   | --                   | --                   | --                   | +                    | --                   | --                   | 2         |
| Fiorentino, 2008 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | + | -- | -- | -- | 1 |
| Fiorentino, 2009 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | + | 1 |
| Garland, 2014   | --                  | --                 | --              | --                          | --                        | --                   | --                   | --                   | +                    | --                   | --                   | --                   | --                   | 2         |
| Ho, 2014        | --                  | --                 | --              | --                          | --                        | --                   | --                   | --                   | +                    | --                   | +                    | --                   | --                   | 3         |
| Holmqvist, 2014 | --                  | --                 | --              | --                          | --                        | --                   | --                   | --                   | --                   | --                   | --                   | --                   | --                   | 1         |
| Jernelov, 2013  | +                   | --                 | --              | --                          | --                        | --                   | --                   | --                   | --                   | --                   | --                   | --                   | --                   | 1         |
| Jungquist, 2010 | +                   | --                 | --              | --                          | --                        | --                   | --                   | --                   | --                   | --                   | --                   | --                   | --                   | 1         |
| Kaldo, 2015     | --                  | --                 | --              | --                          | --                        | --                   | --                   | --                   | --                   | --                   | --                   | --                   | --                   | 1         |
| Lancee 2015     | --                  | --                 | --              | --                          | +                        | --                   | --                   | --                   | --                   | --                   | --                   | --                   | --                   | 1         |
| Lancee, 2012    | --                  | --                 | --              | --                          | +                        | --                   | --                   | --                   | --                   | --                   | --                   | --                   | --                   | 1         |
| Lancee, 2013a   | --                  | --                 | --              | --                          | +                        | --                   | --                   | --                   | --                   | --                   | --                   | --                   | --                   | 1         |
| Lancee, 2013b   | --                  | --                 | --              | --                          | +                        | --                   | --                   | --                   | --                   | --                   | --                   | --                   | --                   | 1         |
| Lu, 2016        | --                  | --                 | --              | --                          | --                        | +                    | --                   | --                   | --                   | --                   | --                   | --                   | --                   | 1         |
| Mack, 2013      | --                  | +                  | --              | --                          | --                        | --                   | --                   | --                   | --                   | --                   | --                   | --                   | --                   | 1         |
| Margolis, 2013  | --                  | +                  | --              | --                          | --                        | --                   | --                   | --                   | --                   | --                   | --                   | --                   | --                   | 1         |
| Matthews, 2014  | --                  | --                 | --              | --                          | +                        | --                   | --                   | --                   | --                   | --                   | --                   | --                   | --                   | 2         |
| Ouellet and     | --                  | --                 | --              | --                          | --                        | --                   | --                   | --                   | --                   | --                   | --                   | --                   | --                   | 1         |

**Insomnia Severity Index (ISI)**
| Primary Studies n = 26 | Ballesio, 2017* n = 20 | Dickerson, 2014 n = 1 | Yang, 2014* n = 2 | Tang, 2015* n = 6 | Howell, 2014 n = 2 | Times Cited |
|------------------------|-------------------------|-----------------------|------------------|------------------|-------------------|-------------|
| Morin, 2007            | +                       | --                    | --               | --               | --                | 1           |
| Pigeon, 2012           | --                      | --                    | --               | --               | --                | 1           |
| Pillai, 2015           | --                      | --                    | --               | --               | --                | 1           |
| Quesnel, 2003          | --                      | --                    | --               | --               | +                 | 2           |
| Raymond, 2010          | --                      | --                    | --               | +                | --                | 1           |
| Ritterband, 2009       | +                       | +                     | --               | --               | --                | 4           |
| Ritterband, 2011       | --                      | --                    | --               | --               | --                | 1           |
| Ritterband, 2012       | --                      | --                    | +                | --               | --                | 3           |
| Rybarczyk, 2005        | --                      | --                    | +                | --               | --                | 1           |
| Savard, 2005           | --                      | --                    | +                | --               | +                 | 4           |
| Savard, 2011           | --                      | --                    | --               | --               | --                | 1           |
| Savard, 2013           | --                      | --                    | --               | --               | +                 | 1           |
| Savard, 2014           | --                      | --                    | --               | --               | --                | 1           |
| Smith, 2015            | +                       | --                    | --               | --               | --                | 2           |
| Strom, 2004            | --                      | --                    | --               | +                | --                | 1           |
| Talbot, 2014           | --                      | +                     | --               | --               | --                | 1           |
| Tang, 2012             | +                       | --                    | --               | --               | --                | 1           |
| Thiart, 2015           | --                      | --                    | --               | --               | +                 | 2           |
| Ulmer, 2011            | --                      | +                     | --               | --               | --                | 1           |
| Ustino, 2013           | --                      | +                     | --               | --               | --                | 1           |
| Vincent, 2009          | --                      | +                     | --               | --               | +                 | 5           |

| Fatigue Severity |
|-------------------|
| Arendt, 2011      | +                 |
| Barsevick, 2010   | --                |
| Berger, 2009      | --                |
| Chen, 2008        | +                 |
| Chen, 2011        | +                 |
| Davidson, 2001    | +                 |
| Dirksen, 2008     | +                 |
| Primary Studies | Brooks, 2014 \(n = 7\) | Dickerson, 2014 \(n = 2\) | Ishak, 2012 \(n = 4\) | Howell, 2014 \(n = 1\) | Times Cited |
|-----------------|-------------------------|-------------------------|-------------------------|-------------------------|--------------|
| Espie, 2008     | +                       | --                      | --                      | +                       | +            | 2            |
| Ho, 2014        | +                       | --                      | --                      | --                      | --           | --           |
| Irwin, 2014     | +                       | --                      | --                      | --                      | --           | --           |
| Jernelov, 2012  | +                       | --                      | --                      | --                      | --           | --           |
| Kapella, 2011   | +                       | --                      | --                      | --                      | --           | --           |
| Lichstein, 2001 | +                       | --                      | --                      | --                      | --           | --           |
| Lovato, 2014    | +                       | --                      | --                      | --                      | --           | --           |
| Martinez, 2013  | +                       | --                      | --                      | --                      | --           | --           |
| Martinez, 2014  | --                      | --                      | --                      | +                       | --           | 1            |
| Matthews, 2014  | +                       | --                      | --                      | --                      | --           | --           |
| Morgan, 2012    | +                       | --                      | --                      | --                      | --           | --           |
| Pigeon, 2012    | +                       | --                      | --                      | --                      | --           | --           |
| Rios, 2013      | +                       | --                      | --                      | +                       | --           | 1            |
| Ritterband, 2011| --                      | --                      | --                      | --                      | +            | 1            |
| Ritterband, 2012| +                       | --                      | --                      | +                       | --           | 1            |
| Savard, 2005    | +                       | --                      | --                      | --                      | --           | --           |
| Savard, 2014    | +                       | --                      | --                      | --                      | --           | --           |
| Tang, 2012      | +                       | --                      | --                      | --                      | --           | --           |
| Vincent, 2009   | +                       | --                      | --                      | --                      | --           | --           |

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- Arnedt, 2007: +
- Byles, 2003: --
- Dirksen and: --
Table F9. Primary studies across systematic reviews that compared behavioural interventions to inactive controls

| Primary Studies | Brasure, 2015* | Busemi, 2005* | Hwang, 2016* | Bogdanov, 2017 | Brooks, 2014 | Helleström, 2011 | McCurdy, 2007 | Miller, 2014 | Tamrat, 2013 | Wang, 2005 | Times Cited | Outcome(s) |
|-----------------|----------------|----------------|--------------|----------------|--------------|-----------------|--------------|--------------|-------------|-------------|-------------|------------|
| Alessi, 2005    | --             | --             | +            | --             | --           | --              | --           | --           | --          | 1           | SQ          |
| Bliwise, 1995   | --             | --             | --           | --             | --           | --              | --           | +            | --          | 1           | SOL, TST    |
| Primary Studies                  | Times Cited | Outcome(s)          |
|---------------------------------|-------------|---------------------|
| Buysse, 2011                    | 2           | SOL, WASO, SQ       |
| Carr-Kaffashan, 1979            | 1           | SOL                 |
| Choliz, 1995                    | 1           | SOL                 |
| Edinger, 2001                   | 1           | TST, WASO           |
| Epstein, 2012                   | 2           | SOL, TST, WASO, SQ  |
| Espie, 1989                     | 1           | SOL, TST            |
| Friedman, 2000                  | 2           | SOL, TST, WASO, SE  |
| Germain, 2006                   | 1           | SQ                  |
| Greef and Conradie, 1998        | 1           | SQ                  |
| Haynes, 1974                    | 1           | SOL                 |
| Haynes, 1977                    | 1           | SOL                 |
| Haynes, 1977                    | 1           | SOL                 |
| Hong and Kim, 2009              | 1           | SQ                  |
| Hughes, 1978                    | 1           | SOL                 |
| Jacobs, 1993                    | 1           | SOL                 |
| Lacks, 1983                     | 1           | SOL                 |
| Lareau, 2008                    | 1           | SQ                  |
| Lichstein, 2001                 | 2           | SOL, TST, WASO, SE  |
| McCrae, 2007                    | 1           | SOL, WASO           |
| Curry, 2013                     | 1           | SQ                  |
| McDowell, 1998                  | 1           | SQ                  |
| Mitchell, 1979                  | 1           | SOL                 |
| Nicassio, 1974                  | 1           | SOL                 |
| Richardson, 2003                | 1           | SQ                  |
| Sanavio, 1990                   | 1           | SOL, WASO           |
### Table F10. Primary studies across included systematic reviews that examined mindfulness based interventions

| Primary Studies | Gong, 2016* | Venables, 2014 | Times Cited | Outcome(s) |
|-----------------|-------------|----------------|-------------|------------|
| Black, 2015     | +           | --             | 1           | SQ         |
| Britton, 2012   | +           | --             | 1           | SOL, TST, SQ, SE |
| Carlson, 2005   | --          | +              | 1           | SQ, SE     |
| Lengacher, 2013 | --          | +              | 1           | SE         |
| Ong, 2014       | +           | --             | 1           | TST, SE    |
| Shapiro, 2003   | --          | +              | 1           | SE         |
| Zhang, 2015     | +           | --             | 1           | SOL, SQ    |

*systematic review with meta-analysis

### Table F11. Primary studies across included systematic reviews that compared combination therapy to inactive controls

| Primary Studies (n=4) | Buseemi, 2005* | Chiesa, 2009 | Times Cited | Outcome(s) |
|-----------------------|----------------|--------------|-------------|------------|
|                       | n = 2          | n = 2        |             |            |

*systematic review with meta-analysis
| Author, Year | Rating | Quality | Study Type | Codes |
|-------------|--------|---------|------------|-------|
| Milby, 1993 | +      | --      | 1          | TST   |
| Morin, 1999 | +      | --      | 1          | TST   |
| Heidenreich, 2006 | -- | +      | 1          | SOL, TST |
| Ong, 2008 | -- | +      | 1          | TST, SQ |

*systematic review with meta-analysis