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Manifestations and Management of Chronic Insomnia in Adults

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-Based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. This report was requested and funded by the Office of Medical Applications of Research (OMAR), National Institutes of Health (NIH). The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To bring the broadest range of experts into the development of evidence reports and health technology assessments, AHRQ encourages the EPCs to form partnerships and enter into collaborations with other medical and research organizations. The EPCs work with these partner organizations to ensure that the evidence reports and technology assessments they produce will become building blocks for health care quality improvement projects throughout the Nation. The reports undergo peer review prior to their release.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

We welcome comments on this evidence report. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by email to **epc@ahrq.gov.**

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Structured Abstract

Context: Approximately 40 to 70 million Americans are affected by either intermittent or chronic sleep problems, representing approximately 20 percent of the population.

Objectives: To conduct a systematic review of (1) the prevalence, natural history, incidence, risk factors and consequences of chronic insomnia in adults and (2) the efficacy and safety of treatments used in the management of chronic insomnia in adults.

Data Sources: A systematic search of twenty-one electronic databases was conducted. We searched MEDLINE®, EMBASE, CINAHL®, Ovid MEDLINE In-Process & Other Non-Indexed Citations, Ovid OLDMEDLINE®, PsycINFO®, EBM Reviews-Cochrane Central Register of Controlled Trials, International Pharmaceutical Abstracts, AMED (Allied and Complementary Medicine), HealthSTAR/Ovid Healthstar, EBM Reviews-Cochrane Database of Systematic Reviews (CDSR), ACP Journal Club (ACPJC), Database of Abstracts of Reviews of Effects (DARE), Science Citation Index Expanded™, Biological Abstracts, Cochrane Complementary Medicine Field Registry, CAB Abstracts, SIGLE, OCLC Proceedings First, Dissertation Abstracts, Alt HealthWatch, NLM Gateway and PubMed®.

Study Selection: Cohort, case-control and cross-sectional studies were eligible for questions on manifestations of chronic insomnia. Randomized controlled trials were eligible for the question on management of chronic insomnia.

Quality Assessment: One of three instruments was used to assess the quality of studies relevant to the manifestations of chronic insomnia. The Jadad Scale was used to assess the quality of studies relevant to the management of chronic insomnia. The concealment of treatment allocation was also assessed in the latter studies.

Data Analysis: Data were analyzed both qualitatively and quantitatively. The Random Effects Model was used for quantitative analyses.

Main Results: The interquartile range of prevalence of chronic insomnia varied from 8.5-24.3 percent across high quality studies of general populations, to 19.8-53.7 percent across moderate quality studies of outpatient populations, to 27.8-43.0 percent across moderate quality studies of clinical populations. Sleep onset latency (SOL) was significantly decreased by benzodiazepines (Mean Difference (MD): -16.5, 95% Confidence Interval (CI): [-20.5, -12.5]), non-benzodiazepines (MD: -18.1, 95% CI: [-22.5, -13.7]), antidepressants (MD: -7.4, 95% CI: [-10.5, -4.4]) and melatonin (MD: -8.3, 95% CI: [-14.5, -2.0]). All of the preceding interventions, except melatonin, had a significantly higher risk of harm compared to placebo: benzodiazepines (Risk Difference [RD]: 0.15, 95% CI: [0.10, 0.20]), non-benzodiazepines (RD 0.05, 95% CI: [0.01, 0.09]), antidepressants (RD: 0.09, 95% CI: [0.01, 0.18]) and melatonin (RD: 0.09, 95% CI: [-0.11, 0.29]). Wakefulness after sleep onset (WASO) was not significantly reduced by melatonin (MD: -9.7, 95% CI: [-33.6, 14.3]). SOL was significantly decreased by relaxation therapy with short-term treatment (less than 4 weeks) (MD: -22.0, 95% CI: [-41.0, -2.9]); however, WASO was not significantly reduced by relaxation therapy (MD: -1.6, 95% CI: [-14.1,

10.8]). WASO was significantly decreased by cognitive/behavioral therapy (MD: -18.2, 95% CI: [-30.4, -6.0]); however, SOL was not significantly reduced by cognitive/behavioral therapy (MD: -4.6, 95% CI: -9.8, 0.6).

Main Conclusions

- There is evidence that chronic insomnia is associated with older age, female gender, present or past psychiatric illness and psychological problems, medical conditions and poor general health, increased healthcare utilization, lower quality of life and social relationships, socioeconomic status (marital separation, unemployment, poorer working conditions and lower social status), and decrements in memory, mood and cognitive function.

- There is evidence that benzodiazepines and non-benzodiazepines are effective in the management of chronic insomnia. There is some evidence that antidepressants are effective in the management of chronic insomnia: more research is required in this area. There is evidence that benzodiazepines, non-benzodiazepines and antidepressants pose a risk of harm.

- There is some evidence that melatonin is effective in the management of chronic insomnia in subsets of the chronic insomnia population, and there is no evidence that melatonin poses a risk of harm. However, more research is required in this area, given that the results are based on a small number of studies.

- There is evidence that relaxation therapy and cognitive/behavioral therapy are effective in the management of chronic insomnia in subsets of the chronic insomnia population.

- There is evidence that benzodiazepines have a greater risk of harm than non-benzodiazepines.

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Manifestations and Management of Chronic Insomnia in Adults

Summary

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Prevalence of Insomnia

Insomnia, or inability to sleep, is the most commonly reported sleep problem in the industrialized world.[1] Estimates suggest that between 40 and 70 million Americans are affected by either intermittent or chronic sleep problems, representing approximately 20 percent of the population.[2] The Sleep in America Poll, conducted by the National Sleep Foundation, revealed that almost 50 percent of people surveyed had complaints of frequent insomnia, but only 6 percent were formally diagnosed.[3] Moreover, approximately, 30 to 35 percent of respondents complained of nightly insomnia.[3] The most prevalent symptoms of insomnia, experienced at least a few nights a week by people with insomnia, include waking up feeling unrefreshed (34 percent) and being awake often during the night (32 percent).[3] The symptoms of difficulty falling asleep and waking up too early are less common, but still experienced at least a few nights a week by about one-fourth of adults with insomnia (23 to 24 percent).[3]

Risk Factors for Insomnia

Although some risk factors and etiologies of insomnia have been identified, the nature of the relationships has not been fully elucidated. Some risk factors for insomnia that have emerged from data related to insomnia include female gender[3] and old age.[4] Additional risks factors include less education, unemployment, separation or divorce, and medical illness.[1] Insomnia may be primary or secondary to other sleep problems and may be associated with a number of co-morbidities. An association has been found between insomnia and psychiatric (depression and anxiety) and psychological disorders.[4] There is increasing evidence that chronic insomnia may predispose individuals to the development of psychiatric disorders.[5-6] Persistent insomnia increases the risk of depression, substance abuse, and anxiety disorders. Environmental factors such as irregular sleep schedules, use of caffeine or other stimulants, co-morbid medical conditions, and/or shift work may also predispose vulnerable individuals to insomnia.

Consequences of Insomnia

Insomnia has significant direct and indirect effects on the health and wellness of affected individuals. Insomnia has been correlated with frequent use of medical services,[7-8] chronic health problems, [9-10] increased drug use,[7-8] and perceived poor health,[11] and has been associated with medical problems including heart disease,[12] hypertension,[13] and musculoskeletal problems.[12] The daytime consequences of chronic insomnia often include increased healthcare utilization, increased risk of depression,[14] poor memory, reduced concentration, poor work performance, and perceived or real risk of failure at work.[15] The economic implications of insomnia and

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associated morbidity have been described.[7,3] The direct costs of insomnia (insomnia treatments, healthcare services, hospital and nursing home care) are estimated to be nearly $14 billion.[16-17] The indirect costs of insomnia, such as time lost from work and loss of productivity, are estimated to be nearly $28 billion. A National Sleep Foundation survey found that lost productivity from insomnia alone was over $18 billion.

Management of Insomnia

Management of acute insomnia has traditionally involved pharmacotherapy. The use of such agents is common practice for both acute and chronic insomnia, despite the fact that the Food and Drug Administration (FDA) has approved none of them for chronic insomnia. Another medication, eszopiclone (Lunesta), was recently approved by the FDA for treatment of insomnia, but the duration of use is not explicitly stated. An estimated 0.5 percent of the population takes sedative medications for insomnia for more than 1 year.[3] More than 1 in 10 people (11 percent) report using prescription (6 percent) and/or over-the-counter (OTC) medications (6 percent), at least a few nights a month, to help them sleep, according to a Sleep in America Poll.[3] Individuals reporting symptoms of medical conditions are more likely to take sleep aids, both prescription and OTC medications. For example, 14 percent of people with symptoms of depression report using prescription medication, and 12 percent of people with symptoms of depression report using OTC sleep aids.[3] Medications commonly used to treat insomnia include sedating antidepressants,[18] antihistamines, anticholinergics, benzodiazepines, and non-benzodiazepine hypnotics. A side effect of all hypnotics is to reduce slow wave sleep. Other side effects of concern are possible daytime residual effects related to sedation, rebound insomnia, and tolerance, along with minor side effects specific to each drug class. Many questions and challenges related to pharmacological therapy for chronic insomnia remains, such as the appropriate treatment for different types of primary and secondary insomnia, and the long-term side effects and daytime consequences of pharmacotherapy. The evidence for management of chronic insomnia with pharmacotherapy has not been systematically evaluated.

Cognitive/behavioral therapy has been recognized as a valid and successful treatment approach for insomnia. Cognitive/behavioral therapy can include any combination of sleep restriction, sleep hygiene, stimulus control, paradoxical intention, and cognitive restructuring. Many of these commonly used clinical tools have not undergone rigorous testing to determine their efficacy and long-term safety. The efficacy of these treatments has been evaluated in some studies,[4,19] but differences in the definition of insomnia and outcome measures make it difficult to compare study results.

In summary, insomnia is a common complaint with significant consequences. Significant advancements have been made in sleep research over the past three decades, yet many questions related to the treatment of chronic insomnia remain. Our goal was to review the evidence and state of research in the area of chronic insomnia.

Objectives

The objectives of this report are to conduct a systematic review of (1) the prevalence, natural history, incidence, risk factors, and consequences of chronic insomnia in adults and (2) the efficacy and safety of treatments used in the management of chronic insomnia in adults. A population was considered to suffer from chronic insomnia if the sleep disturbance persisted for at least 4 weeks, regardless of severity of symptoms.

Methods

Literature Search

The research librarian, in collaboration with the TEP (Technical Expert Panel), developed and implemented search strategies designed to identify relevant evidence for key questions of the review. A systematic search of 21 electronic databases was conducted. We searched MEDLINE®, EMBASE, CINAHL®, Ovid MEDLINE® In-Process & Other Non-Indexed Citations, Ovid OLDMEDLINE®, PsycINFO®, EBM Reviews-Cochrane Central Register of Controlled Trials, International Pharmaceutical Abstracts, AMED (Allied and Complementary Medicine) , HealthSTAR/Ovid Healthstar, EBM Reviews-Cochrane Database of Systematic Reviews (CDSR), ACP Journal Club (ACPJC), Database of Abstracts of Reviews of Effects (DARE), Science Citation Index Expanded™, Biological Abstracts, Cochrane Complementary Medicine Field Registry, CAB Abstracts, SIGLE, OCLC Proceedings First, Dissertation Abstracts, Alt HealthWatch, NLM Gateway, and PubMed®. Most of the searches were limited to humans, and no age restrictions were applied to any of the searches.

For Question 1, which relates to the definition, classification, diagnosis, and aetiology of chronic insomnia in adults, we searched for narrative and systematic reviews, book

chapters, diagnostic manuals and standards of practice parameters, and applied English-language restrictions. For Question 2, which relates to the prevalence, natural history, incidence, and risk factors for chronic insomnia in adults, and Question 3, which relates to the consequences, morbidities, co-morbidities and public health burden associated with chronic insomnia in adults, we searched for observational studies, encompassing a range of designs including cross-sectional, case-control, and cohort studies, and applied English-language restrictions. For Question 4, which relates to the treatments for chronic insomnia in adults, and the evidence regarding their safety, efficacy, and effectiveness, we searched for randomized controlled trials, and no language restrictions were applied.

Inclusion Criteria

We did not develop formal inclusion criteria for the question pertaining to the definition, classification, diagnosis, and etiology of chronic insomnia (Question 1), nor for the question pertaining to the future direction of insomnia-related research (Question 5). The former question was answered by providing an overview of the literature, and the latter question was answered by assessing the limitations in the evidence for the other questions of the review.

Inclusion criteria were developed for three questions of the review (Questions 2-4). Question-specific inclusion criteria appear below. In the interest of clarity, questions 2 and 3 will be referred to as the questions on manifestations of chronic insomnia, while question 4 will be referred to as the question on management of chronic insomnia.

2. **What are the prevalence, natural history, incidence, and risk factors for chronic insomnia?** Specific risk factors of interest include age, gender, race/ethnicity, psychiatric illness and psychological problems, medical disease, socioeconomic status, and shift work.

A study was considered to be relevant to the portion of Question 2 pertaining to the prevalence, natural history, and incidence of chronic insomnia, if it met the following criteria:

- The report was written in English
- Participants were at least 15 years old
- It examined chronic insomnia
- It had a cross-sectional or cohort design
- It assessed the prevalence, natural history, or incidence of chronic insomnia

A study was considered to be relevant to the portion of Question 2 pertaining to risk factors for chronic insomnia, *if it met the first three criteria listed above* as well as the following:

- It had a cohort, case-control, or cross-sectional design
- It assessed one of the risk factors of interest

3. **What are the consequences, morbidities, co-morbidities, and public health burden associated with chronic insomnia?** Specific outcomes of interest include healthcare utilization, psychiatric illness, absenteeism, work performance, accidents, falls in the elderly, quality of life and social relationships, memory, cognitive function, mood, and direct and indirect costs.

A study was considered to be relevant to this question of the review, *if it met the first three criteria outlined for Question 2* as well as the following:

- It had a cohort or cross-sectional design
- It assessed one of the consequences of interest

For Questions 2 and 3, a study was considered to examine chronic insomnia if this condition was defined as a sleep disturbance of four weeks or more or the report explicitly mentioned that chronic sleep disturbance was examined.

4. **What treatments are used for the management of chronic insomnia and what is the evidence regarding their safety, efficacy, and effectiveness?** Specific treatments of interest include prescription medication, over-the-counter medication, alcohol, behavioral therapy, combination therapy, and complementary and alternative care.

A study was considered to be relevant to this question of the review, if it met the following criteria:

- The report was written in English
- Participants were at least 15 years old, and the majority were at least 18 years old
- Participants suffered from chronic insomnia
- Participants were randomized to intervention or placebo
- Participants and assessors were blind to treatment received
- It assessed at least one of the following outcomes, listed in order of importance in deriving conclusions of the review:
  - sleep onset latency
  - wakefulness after sleep onset
  - sleep efficiency
  - total sleep time

- sleep quality
- quality of life

Sleep onset latency was defined as the amount of time between the participant laying down to sleep and the onset of sleep; wakefulness after sleep onset was defined as the amount of time spent awake in bed following the attainment of sleep; sleep efficiency was defined as the amount of time spent asleep as a percentage of the total time spent in bed; and total sleep time was defined as the total time spent asleep while in bed. Sleep onset latency and wakefulness after sleep onset were given the highest priority in deriving conclusions from the review, since they were considered the best indices of sleep initiation and sleep maintenance, respectively. However, subgroup analyses were conducted only on data relevant to sleep onset latency, since this outcome was the most highly reported outcome across studies.

If the majority of participants met one of the following criteria, the study population was considered to suffer from chronic insomnia:

- Participants suffered from a sleep disturbance of four weeks or more.
- Participants were described as having a chronic/long-standing/persistent sleep disturbance.
- Participants were selected from a sleep disorders clinic.

In the case of combination therapy, the combined treatment could be compared to either placebo or single treatment.

We acknowledged the fact that double-blinding is often not feasible in studies of psychological treatments by not requiring double-blinding in these studies for inclusion in the review. The placebo treatment for relaxation therapy and cognitive/behavioral therapy was minimal treatment, such as sleep hygiene recommendations or minimal instruction. We required that the placebo resemble the intervention of the study except that it was known to produce either no effect or only a minimal effect.

Study Selection

In the first stage of study selection, two reviewers screened the titles and abstracts of all potentially relevant articles, independently. Each reviewer noted the titles and abstracts that were potentially relevant to the review, and these articles were retrieved. In the second stage of study selection, two reviewers appraised the potentially relevant articles, independently, using pre-determined, question-specific, inclusion criteria. Disagreements between reviewers were resolved by discussion and consensus. The rate of disagreement between reviewers and the primary reason for exclusion of potentially relevant articles were noted.

Data Extraction

Data relevant to study design, population, interventions, and outcomes were extracted from studies, as appropriate, using standardized data extraction forms. A trained reviewer extracted relevant data, and a second reviewer verified the data extracted for accuracy and completeness.

Assessment of Study Quality

The quality of studies relevant to the questions on manifestations of chronic insomnia was assessed using one of three instruments; studies on prevalence and incidence were assessed using a scale designed specifically for this purpose.[20] All other studies relevant to manifestations of chronic insomnia were assessed using one of two Newcastle-Ottawa scales (unpublished), each scale specific to either cohort or case-control studies.

The quality of studies relevant to management of chronic insomnia was assessed using the Jadad scale.[21] The concealment of allocation of participants to treatment groups was also assessed.[22]

Data Analysis

Data relevant to manifestations of chronic insomnia were analyzed qualitatively, while data relevant to management of chronic insomnia were analyzed quantitatively.

Manifestations of Chronic Insomnia

For the questions on prevalence, natural history, incidence, risk factors, and consequences of chronic insomnia, data relevant to each variable were analyzed separately, except for data relevant to potential risk factors and potential consequences of chronic insomnia, which were analyzed together as associated factors of chronic insomnia. The data were synthesized to provide a description of the methods and results of the studies relevant to a given variable.

Management of Chronic Insomnia

For continuous outcomes (e.g., sleep onset latency and sleep efficiency), studies were combined using a mean difference (MD), with the exception of sleep quality and quality of life, where studies were combined using a standardized mean difference (SMD). Dichotomous outcomes (i.e., safety outcomes) were combined using a risk difference (RD). A

number needed to harm (NNH) was also reported for any safety outcomes that were found to be statistically significant. The Inverse Variance Method[23] was used to weight the studies. An efficacy estimate, with corresponding 95% confidence interval, was computed for each outcome. All meta-analyses were performed using a Random Effects Model.[24]

For some outcomes (sleep onset latency and number of adverse events), treatment categories were compared indirectly, via their relationship to placebo. Differences of differences with 95% confidence intervals (CI) were computed.

All estimates of efficacy were assessed for heterogeneity using the I-squared statistic.[25] For our primary outcome (sleep onset latency), heterogeneity was explored in subgroup and sensitivity analyses using a number of variables (treatment, presence/absence of psychiatric illness, length of treatment, age, gender and study quality). Deeks' chi-square statistic[26] was used to test for significant heterogeneity reduction in partitioned subgroups.

We tested for publication bias visually using the Funnel Plot[27] and quantitatively using the Rank Correlation Test,[28] the Graphical Test,[29] and the Trim and Fill Method.[30]

Main Results

Prevalence of Chronic Insomnia

In general populations: Interquartile Range (IQR): 8.5-24.3 percent. There was evidence of an association between female gender and chronic insomnia.

- In clinical populations: IQR: 27.8-43.0 percent.
- In outpatients of general practice: IQR: 19.8-53.7 percent.
- The majority of studies were either of moderate or high quality.

Natural History of Chronic Insomnia

- Only one study provided evidence on natural history of chronic insomnia: the remission rate was 13.1 percent after a 4-month followup period in a population suffering from insomnia for 1 month or more.
- The study was of moderate quality.

Incidence of Chronic Insomnia

- No studies were identified that provided evidence on incidence of chronic insomnia.

Factors Associated with Chronic Insomnia

Potential Risk Factors

- **Age.** Eleven studies found evidence of an association between age and chronic insomnia, whereas seven studies found no evidence of an association between these variables. Of the studies that found an association, all, except one,[31] found evidence that chronic insomnia is associated with older age.
- **Gender.** Eleven studies found evidence of an association between gender and chronic insomnia, while seven studies found no evidence of an association between these variables. All of the studies that found evidence of an association between gender and chronic insomnia, found evidence that chronic insomnia is associated with female gender.
- **Race/ethnicity.** Two studies found evidence of an association between ethnicity and chronic insomnia,[32-33] while one study found no evidence of an association between these variables.[34] Bixler et al. found evidence that chronic insomnia is associated with being a non-Caucasian minority, and Riedel et al. found evidence that chronic insomnia is associated with being White.
- **Psychiatric illness and psychological problems.** Thirty-eight studies found evidence of an association between present or past psychiatric illness or psychological problems and chronic insomnia. Seven studies did not find evidence of an association between these variables.
- **Medical conditions.** Twelve studies found evidence of an association between medical conditions or poor general health and chronic insomnia, while one study[35] did not find evidence of an association between these variables.
- **Socioeconomic status.** Six studies found evidence of an association between socioeconomic status and chronic insomnia. Nine studies did not find evidence of an association between these variables.
- **Shift work.** Only 2 studies provided evidence regarding the relationship between shift-work and chronic insomnia.[31,36] The study by Kageyama et al. provided evidence that chronic insomnia is associated with three or less night shifts per month within the preceding three months in hospital nurses. The study by Martikainen et al. found no evidence of an association between shift work and chronic insomnia.

Potential Consequences

- **Healthcare utilization.** Five studies provided evidence of an association between increased healthcare utilization and chronic insomnia. One study did not find evidence of an association between chronic insomnia and undergoing medical treatment in hospital nurses.[31]
- **Absenteeism and work performance.** Only two studies provided evidence regarding the relationship between work performance or absenteeism and chronic insomnia;[37-38] both studies found evidence of an association between chronic insomnia and absenteeism. The study by Zammit et al. also found evidence of an association between chronic insomnia and impaired work performance.
- **Quality of life and quality of social relationships.** Five studies examined the relationship between either quality of life (from a global perspective) or quality of social relationships and chronic insomnia. All studies found evidence of an association between chronic insomnia and either lower quality of life or lower quality of social relationships; one of these studies found evidence that both quality of life and quality of social relationships are impaired in chronic insomniacs.[39]
- **Memory, cognitive function, and mood.** Fifteen studies found evidence of an association between decrements in memory, mood or cognitive function and chronic insomnia. One study[40] found evidence of increased recall of presentations made just before sleep onset in chronic insomniacs. Eleven studies found no evidence of an association between mood, memory, or cognitive function and chronic insomnia.

We did not identify any studies that provided data relevant to the relationship between accidents or falls in the elderly and chronic insomnia or direct and indirect costs of the disorder.

The majority of studies were of either moderate or high quality.

Efficacy and Safety of the Six Main Categories of Interventions Identified in the Literature

The efficacy estimates are provided as mean differences (MDs) in the effect of intervention and placebo on sleep onset latency (SOL) or wakefulness after sleep onset (WASO). The safety estimates are provided as risk differences (RDs) between intervention and placebo.

- **Benzodiazepines.** MD (SOL): -16.5, 95% CI: (-20.5, -12.5); MD (WASO): -23.1, 95% CI: (-35.7, -10.5); RD: 0.15, 95% CI: (0.10, 0.20); number needed to harm was eight.
- **Non-benzodiazepines.** MD (SOL): -18.1, 95% CI: (-22.5, -13.7); MD (WASO): -12.6, 95% CI: (-23.0, -2.3); RD: 0.05, 95% CI: (0.01, 0.09); number needed to harm was 20.
- **Antidepressants.** MD (SOL): -7.4, 95% CI (-10.5, -4.4); MD (WASO): -11.4, 95% CI: (-16.2, -6.6); RD: 0.09, 95% CI (0.01, 0.18); number needed to harm was 12.
- **L-Tryptophan.** MD (SOL): -11.0, 95% CI: (-33.0, 11.1)
- **Melatonin.** MD (SOL): -8.3, 95% CI: (-14.5, -2.0); MD (WASO): -9.7, 95% CI: (-33.6, 14.3); RD: 0.09, 95% CI: (-0.11, 0.29)
- **Valerian.** MD (SOL): -1.3, 95% CI: (-21.4, 18.9); MD (WASO): -8.4, 95% CI: (-15.9, -1.0); RD: -0.06, 95% CI: (-0.48, 0.35)
- **Relaxation therapy**. MD (SOL): -14.6, 95% CI: (-29.3, 0.2); MD (WASO): -1.6, 95% CI: (-14.1, 10.8). No adverse event data was provided.
- **Cognitive/behavioral therapy.** MD (SOL): -4.6, 95% CI: (-9.8, 0.6); MD (WASO): -18.2, 95% CI: (-30.4, -6.0). No adverse event data was provided.

Most studies were of moderate or high quality.

Discussion

Prevalence, Natural History, Incidence, and Factors Associated with Chronic Insomnia

The interquartile range of prevalence varied from 8.5-24.3 percent across high-quality studies of general populations, to 19.8-53.7 percent across moderate-quality studies of outpatient populations, to 27.8-43.0 percent across moderate-quality studies of clinical populations. Therefore, the prevalence estimates for chronic insomnia in outpatient and clinical populations appear to be significantly higher than those for the general population, a finding that is consistent with evidence of an association between chronic insomnia and

medical conditions, poor general health, and increased healthcare utilization.

Only one study provided data on the natural history of chronic insomnia; the remission rate was 13.1 percent after a 4-month followup. More research is necessary to determine the course of chronic insomnia in various populations. We did not identify any studies that provided evidence regarding the incidence of chronic insomnia; more research is needed in this area as well.

We found evidence to suggest that chronic insomnia is associated with older age, female gender, present or past psychiatric illness and psychological problems, medical conditions and poor general health, increased healthcare utilization, lower quality of life and social relationships, socioeconomic status (marital separation, unemployment, poorer working conditions, and lower social status), and decrements in memory, mood, and cognitive function. Some of the factors that are thought to contribute to insomnia in the elderly include multiple medical problems, polypharmacy, and environmental factors such as absence of zeitgebers (time/schedule cues).[11,41] Similarly, factors such as stress, pregnancy, menopause, medical conditions, and complex home life may explain the higher prevalence of insomnia in females.

Efficacy and Safety of Treatments for Chronic Insomnia

The interventions for chronic insomnia that were investigated in included studies may be categorized as either benzodiazepines, non-benzodiazepines, antidepressants, complementary and alternative care (L-tryptophan, melatonin and valerian), relaxation therapy, cognitive/behavioral therapy, barbiturates, hormone therapy, alcohol, low energy emission therapy, and combination therapy. The majority of studies were classified under the first six categories of the preceding list.

The review provides evidence that benzodiazepines and non-benzodiazepines are effective treatments for chronic insomnia. There is some evidence that antidepressants are effective treatments for chronic insomnia, although more research is required in this area. The review provides some evidence that melatonin is effective in subsets of the chronic insomnia population; however, more research is required in this area. There is also evidence that relaxation therapy and cognitive/behavioral therapy are effective treatments in subsets of the chronic insomnia population. There were too few studies of L-tryptophan and valerian to draw conclusions regarding the efficacy of these treatments in the management of chronic insomnia: additional large-scale, randomized trials are needed. Additional large-scale, randomized trials are also needed in the area of relaxation therapy and cognitive/behavioral therapy in the management of chronic insomnia to determine the efficacy of these interventions across subsets of the chronic insomnia population. The reduction in sleep onset latency by benzodiazepines and non-benzodiazepines was significantly greater than that for antidepressants and melatonin, based on indirect comparisons. However, it should be noted that there were significantly fewer studies of antidepressants and melatonin compared to benzodiazepines and non-benzodiazepines, and additional large-scale, randomized trials of the former interventions are needed before firm conclusions can be drawn regarding the relative efficacy of these interventions.

The benzodiazepines, non-benzodiazepines, and antidepressants had a significantly greater risk of harm than placebo, while melatonin did not. There were too few studies of L-tryptophan to draw conclusions regarding the safety of this intervention. Although there was no evidence that valerian poses a risk of harm, this result was based on only three studies of relatively small sample size. Therefore, more studies are needed before firm conclusions can be drawn regarding the safety of valerian. The risk for benzodiazepines was significantly greater than for non-benzodiazepines, based on indirect comparisons. Indeed, benzodiazepine use has been shown to increase the risk of injury in the elderly,[42] and there is pharmacologic evidence that the non-benzodiazepines have a better side-effect profile than the benzodiazepines.[43-44] Studies of relaxation therapy and cognitive/behavioral therapy did not provide adverse event data.

There was substantial heterogeneity in the pooled estimate for SOL for benzodiazepines, non-benzodiazepines, L-tryptophan, valerian, and relaxation therapy. Similarly, there was substantial heterogeneity in the pooled estimate for WASO for benzodiazepines, non-benzodiazepines, melatonin, and cognitive/behavioral therapy. The heterogeneity was often due to differences in the magnitude of the point estimate and confidence interval across studies, rather than differences in the directionality of the effect. The exceptions are for estimates of the efficacy of relaxation therapy with respect to SOL and the efficacy of melatonin with respect to WASO. The heterogeneity in the pooled estimates for SOL was explored in

sensitivity and sub-group analyses. The results indicate that heterogeneity in the pooled estimate for SOL for relaxation therapy is at least partially due to type of relaxation therapy, length of treatment, age and gender distribution of the study population, and study quality.

There was strong evidence of publication bias in the pooled estimates for SOL for the benzodiazepine and non-benzodiazepine categories of intervention. This finding suggests that the true estimate of efficacy is lower than the estimate calculated in the current analysis.

We identified a small sample of studies examining the efficacy of combination treatments in the management of chronic insomnia; some of these studies compared a combination of treatments with placebo, while others compared them with single treatment. Many comparisons did not have data for our primary outcome, sleep onset latency, and the majority of results were non-significant. The latter finding may reflect the low power of these analyses. None of the studies provided data on adverse events. We identified only one study that compared the efficacy of a combined pharmacological and psychological treatment with these treatments administered sequentially. The research agenda for the management of chronic insomnia should include an evaluation of the efficacy and safety of combination treatments and sequential treatments.

Our results relating to relaxation therapy and cognitive/behavioral therapy are somewhat at odds with three meta-analyses reviewing the efficacy of psychological treatments in the management of chronic insomnia.[45-47] The difference in the findings may relate to key differences in the conduct of the reviews. First, we restricted our meta-analysis to a review of placebo-controlled, randomized trials and accounted for placebo effects in our estimations of efficacy. Other meta-analyses have included non-controlled studies, and for these studies, have not accounted for placebo/control effects in their estimation of efficacy. Second, we used clearly defined criteria for chronic insomnia; however, for some studies the criteria for insomnia was not clear. Third, we separated predominantly cognitive/behavioral approaches from predominantly relaxation approaches in management of insomnia, resulting in distinct meta-analyses for each category of intervention. These interventions have been grouped under the broader heading of psychological/non-pharmacological treatments in other reviews.

Conclusions

- There is evidence that the prevalence of chronic insomnia in outpatient and clinical populations is larger than in the general population.
- There is evidence that chronic insomnia is associated with older age, female gender, present or past psychiatric illness and psychological problems, medical conditions and poor general health, increased healthcare utilization, lower quality of life and social relationships, socioeconomic status (marital separation, unemployment, poorer working conditions and lower social status), and decrements in memory, mood, and cognitive function.
- Additional studies are needed to determine the incidence and natural history of chronic insomnia in adults. Similarly, additional studies are needed to explore the relationship between chronic insomnia and race/ethnicity, shift work, absenteeism, work performance, accidents, falls in the elderly, and the direct and indirect costs of the disorder. It is necessary that longitudinal studies be undertaken to explore the risk factors and consequences of chronic insomnia.
- There is evidence that benzodiazepines and non-benzodiazepines are effective in the management of chronic insomnia. There is some evidence that antidepressants are effective in the management of chronic insomnia: more research is required in this area. There is evidence that benzodiazepines, non-benzodiazepines, and antidepressants pose a risk of harm.
- There is some evidence that melatonin is effective in the management of chronic insomnia in subsets of the chronic insomnia population, and there is no evidence that melatonin poses a risk of harm. However, more research is required in this area given that the results are based on a small number of studies. Similarly, additional large-scale, randomized trials are needed to determine the efficacy of melatonin across subsets of the chronic insomnia population. There is insufficient evidence to conclude on the efficacy and safety of L-tryptophan and valerian in the management of chronic insomnia. Additional large-scale, randomized trials are needed in these areas.
- There is evidence that relaxation therapy and cognitive/behavioral therapy are effective in the management of chronic insomnia in subsets of the

chronic insomnia population. Additional large-scale, randomized trials are needed to determine their efficacy across subsets of the chronic insomnia population.

- There is evidence that benzodiazepines have a greater risk of harm than non-benzodiazepines.
- There is insufficient evidence to conclude whether there are differences between the short- and long-term efficacy and safety of the various categories of interventions in the management of chronic insomnia; additional long-term studies are needed.
- There is insufficient evidence regarding the efficacy and safety of combined treatments of pharmacological and psychological interventions, and sequential treatments, in the management of chronic insomnia; additional studies are needed in these areas.

Availability of the Full Report

The full evidence report from which this summary was taken was prepared for the Agency for Healthcare Research and Quality (AHRQ) by the University of Alberta Evidence-based Practice Center, under Contract No. C400000021. It is expected to be available in June 2005. At that time, printed copies may be obtained free of charge from the AHRQ Publications Clearinghouse by calling 800-358-9295. Requesters should ask for Evidence Report/Technology Assessment No. 125, *Manifestations and Management of Chronic Insomnia in Adults.* In addition, Internet users will be able to access the report and this summary online through AHRQ's Web site at www.ahrq.gov.

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Evidence Report

Chapter 1. Introduction

Prevalence of Insomnia

Insomnia, or inability to sleep, is the most commonly reported sleep problem in the industrialized world.[1] Estimates suggest that between 40-70 million Americans are affected by either intermittent or chronic sleep problems, representing approximately 20 percent of the population.[2] The Sleep in America Poll, conducted by the National Sleep Foundation, revealed that almost 50 percent of people surveyed had complaints of frequent insomnia, but only 6 percent were formally diagnosed.[3] Moreover, approximately, 30-35 percent of respondents complained of nightly insomnia.[3] The most prevalent symptoms of insomnia, experienced at least a few nights a week by people with insomnia, include waking up feeling un-refreshed (34 percent) and being awake often during the night (32 percent).[3] The symptoms of difficulty falling asleep and waking up too early are less common, but still experienced at least a few nights a week by about one-fourth of adults with insomnia (23-24 percent).[3] The reported prevalence rates of insomnia vary in epidemiological studies based on the definitions and methods used to define insomnia. Earlier studies report prevalences of 5-35 percent.[1] The prevalence rate decreases to 10-15 percent for severe insomnia, when more stringent criteria are used.[1] The duration of insomnia is often classified as being transient, short-term or chronic. Chronic insomnia implies that insomnia is either persistent or recurrent. Definitions of chronic insomnia vary, ranging from greater than one month to greater than 6 months. Unfortunately, there is no standard definition of chronic insomnia used in studies.

There is emerging evidence that short-term sleep deprivation, under strict experimental conditions, is associated with a variety of adverse physiological and cognitive effects. Decrements in memory, concentration and executive function have been reported. There is also an increased risk of injury and accidents. Physiological effects resulting from sleep deprivation include hypertension, activation of the sympathetic nervous system, altered glucose metabolism and increased inflammatory markers. Sleep deprivation is associated with excessive sleepiness. Acute insomnia, however, may not equate to sleep deprivation. There is no evidence to suggest that patients with insomnia experience similar changes. Furthermore, it is not yet clear from the evidence what the physiological consequences of chronic insomnia are or if there is a process of adaptation that occurs in individuals with chronic insomnia. Thus, further research is needed in the area of chronic insomnia to determine what impact chronic insomnia has on health.

Risk Factors for Insomnia

Although some risk factors and etiologies of insomnia have been identified, the nature of the relationships has not been fully elucidated. Some risk factors for insomnia that have emerged from data related to insomnia include female gender [3] and old age.[4] Additional risks factors include less education, unemployment, separation or divorce and medical illness.[1] Insomnia may be primary or secondary to other sleep problems, and may be associated with a number of co-morbidities. An association has been found between insomnia and psychiatric (depression and anxiety) and psychological disorders.[4] There is increasing evidence that chronic insomnia may predispose individuals to the development of psychiatric disorders.[5-6] Persistent insomnia increases the risk of depression, substance abuse and anxiety disorders. Environmental factors

such as irregular sleep schedules, use of caffeine or other stimulants, co-morbid medical conditions and/or shift-work may also predispose vulnerable individuals to insomnia. We speculate that genetic predisposition to insomnia and environmental factors are likely involved in the development and maintenance of insomnia, and differences in the relative exposure to these influences may explain differences in the manifestation of this disorder among affected individuals.

Consequences of Insomnia

Insomnia has significant direct and indirect effects on the health and wellness of affected individuals. Insomnia has been correlated with frequent use of medical services,[7-8] chronic health problems,[9-10] increased drug use,[7-8] perceived poor health,[11] and associated with medical problems including heart disease,[12] hypertension[13] and musculoskeletal problems.[12] One study reported associations between insomnia and medical problems, and found that individuals with insomnia were more likely to have hypertension (59 percent), night time heartburn (62 percent) and depression (74 percent).[3] The daytime consequences of chronic insomnia often include increased healthcare utilization, increased risk of depression,[14] poor memory, reduced concentration, poor work performance and perceived or real risk of failure at work.[15] The economic implications of insomnia and associated morbidity have been described.[3;7] The direct costs of insomnia (insomnia treatments, healthcare services, hospital and nursing home care) are estimated to be nearly $14 billion.[16-17] The indirect costs of insomnia, such as time lost from work and loss of productivity, are estimated to be nearly $28 billion. A National Sleep Foundation survey found that lost productivity from insomnia, alone, was over $18 billion. Another estimate of total costs of insomnia has reported amounts totaling almost $100 billion.[18] This estimate is based on a high prevalence of insomnia, in the range of 33 percent, and the costs are related to sleepiness rather than insomnia. The data related to costs of chronic insomnia cannot be fully understood because of the impact insomnia has on many aspects of life. Nevertheless, insomnia, in its various forms, does result in substantial burden for affected individuals.

Management of Insomnia

Management of acute insomnia has traditionally involved pharmacotherapy. The use of such agents is common practice for both acute and chronic insomnia, despite the fact that the Food and Drug Administration (FDA) has approved none of them for chronic insomnia. Another medication, eszopiclone (Lunesta), was recently approved by the FDA for treatment of insomnia, but the duration of use is not explicitly stated. An estimated 0.5 percent of the population takes sedative medications for insomnia for more than one year.[3] More than one in ten people (11 percent) report using prescription (6 percent) and/or over-the-counter (OTC) medications (6 percent), at least a few nights a month, to help them sleep, according to a Sleep in America Poll.[3] Individuals reporting symptoms of medical conditions are more likely to take sleep aids, both prescription and OTC medications. For example, 14 percent of people with symptoms of depression report using prescription medication, and 12 percent of people with symptoms of depression report using OTC sleep aids.[3] Medications commonly used to treat insomnia include sedating antidepressants,[19] antihistamines, anticholinergics, benzodiazepines and non-

benzodiazepine hypnotics. A side effect of all hypnotics is to reduce slow wave sleep. Other side effects of concern are possible daytime residual effects related to sedation, rebound insomnia and tolerance, along with minor side effects specific to each drug class. Many questions and challenges related to pharmacological therapy for chronic insomnia remains, such as the appropriate treatment for different types of primary and secondary insomnia, and the long-term side effects and daytime consequences of pharmacotherapy. The evidence for management of chronic insomnia with pharmacotherapy has not been systematically evaluated.

Cognitive/behavioral therapy has been recognised as a valid and successful treatment approach for insomnia. Cognitive/behavioral therapy can include any combination of sleep restriction, sleep hygiene, stimulus control, paradoxical intention and cognitive restructuring. Brief descriptions of these techniques are provided here.

Sleep restriction therapy involves limiting the amount of time in bed. The affected individual spends only the amount of time in bed that he/she sleeps, thus sleep may be restricted to 6 hours for an insomniac that spends 8 hours in bed. The purpose of the exercise is to improve the sleep efficiency progressively until the desired sleep duration is achieved, without prolonged sleep latency or maintenance insomnia.

Sleep hygiene instructions or education involves addressing environmental factors and health practices that may be counterproductive to sleep. It involves education about sleep patterns and the impact of health habits related to sleep. For example, alcohol consumed in the evening may help sleep onset, but promotes sleep maintenance insomnia during the night as the alcohol level declines.

Stimulus control therapy involves instructions aimed at curtailing sleep maladaptive behaviors and altering sleep-wake schedules. The instructions include: 1) going to bed when sleepy; 2) no other activities, besides sleep and sex, should be undertaken in the bed and bedroom; 3) get out of bed when unable to sleep for 15-20 minutes and return only if sleepy; 4) the daily wake-up time should be the same irrespective of how much sleep was obtained the previous night; 5) no naps allowed during the day.

Paradoxical intention is a technique that involves having the patient with insomnia stay awake, which is the most feared activity. The premise is that performance anxiety related to sleep would be alleviated if the patient stops trying to sleep and instead genuinely attempts to stay awake.

Cognitive restructuring can involve cognitive behavioral therapy targeted at an individual's unique perpetuating factors for insomnia.

Sleep non-suppression involves allowing oneself to think about whatever comes to mind, without any restrictions, as one gets to bed. The mind is allowed to go free, without the individual attempting to control his/her thoughts. This approach is thought to counteract the negative effects of thought suppression that often accompanies insomnia.

Relaxation therapy may or may not be a part of cognitive behavioral therapy. Different forms of relaxation therapy are designed to reduce somatic tension or cognitive arousals. Relaxation therapy may focus on somatic tension such as autogenic training, progressive muscle relaxation, or biofeedback, or may focus on the cognitive component such as intrusive thoughts that prevent sleep.

Many of these commonly used clinical tools have not undergone rigorous testing to determine their efficacy and long-term safety. The efficacy of these treatments has been evaluated in some studies,[4;20] but differences in the definition of insomnia and outcome measures make it difficult to compare study results.

In summary, insomnia is a common complaint with significant consequences. Significant advancements have been made in sleep research over the past three decades, yet many questions related to the treatment of chronic insomnia remain. Our goal was to review the evidence and state of research in the area of chronic insomnia.

Objectives

To conduct a systematic review of (1) the prevalence, natural history, incidence, risk factors and consequences of chronic insomnia in adults and (2) the efficacy and safety of treatments used in the management of chronic insomnia in adults. A population was considered to suffer from chronic insomnia if the sleep disturbance persisted for at least 4 weeks, regardless of severity of symptoms.

Analytic Approach

The analytic framework outlining the approach to the review is depicted in Flow Diagram 1. The specific questions addressed in the review appear below.

Etiology and Population at Risk

The following questions pertain to the clinical definition and etiology of chronic insomnia in adults, as well as the population at risk of the disorder.

1. **How is chronic insomnia defined, diagnosed and classified, and what is known about its etiology?**
2. **What are the prevalence, natural history, incidence, and risk factors for chronic insomnia?** Specific risk factors of interest include:
    - Age
    - Gender
    - Race/ethnicity
    - Psychiatric illness and psychological problems
    - Medical disease
    - Socioeconomic status
    - Shift-work

Consequences, Morbidities, Co-morbidities, and Public Health Burden

The following question pertains to the clinical, social and economic consequences of chronic insomnia in adults.

3. **What are the consequences, morbidities, co-morbidities, and public health burden associated with chronic insomnia?** Specific outcomes of interest include:
    - Healthcare utilization
    - Risk of developing psychiatric disease

- Absenteeism, work performance
- Accidents
- Falls in the elderly
- Quality of life, social relationships
- Memory, cognitive function, mood
- Direct and indirect costs

Treatment

The following question pertains to the benefits and harms of treatments used in the management of chronic insomnia in adults.

4. **What treatments are used in the management of chronic insomnia and what is the evidence regarding their safety, efficacy, and effectiveness?** Specific treatments of interest include:

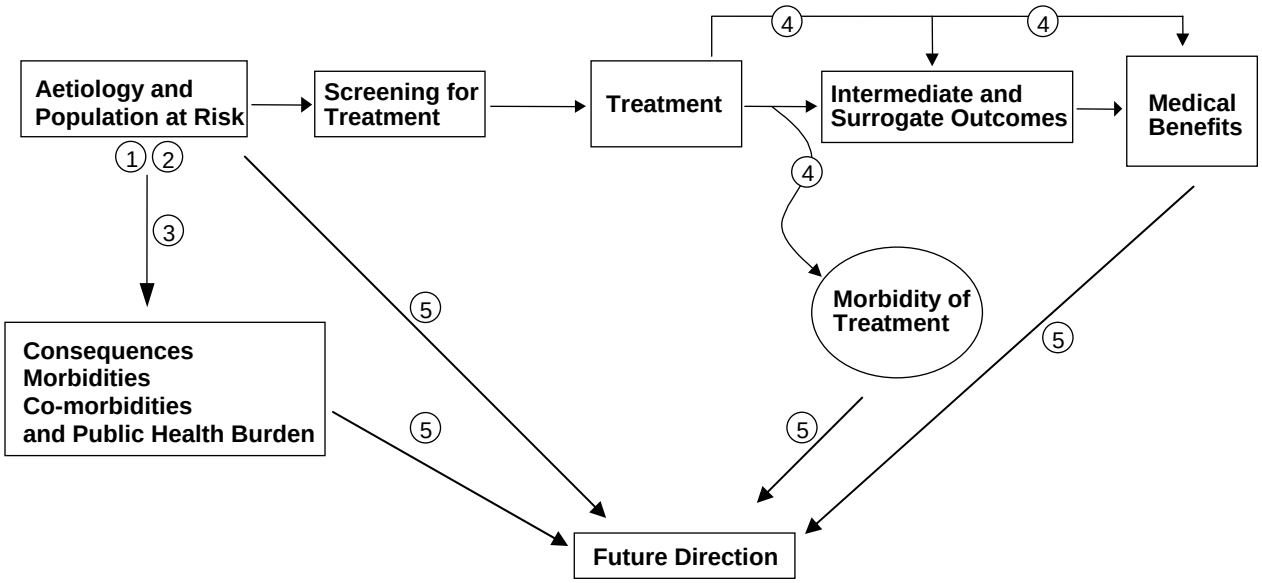
    - Prescription medication
    - Over the counter medication
    - Alcohol
    - Behavioral therapy
    - Combination of therapies
    - Complementary and alternative care

Future Direction

The answer to the following question is based on the evidence for the preceding questions.

5. **What are important future directions for insomnia-related research?**

Flow Diagram 1. Analytic framework



Chapter 2. Methods

Overview

The systematic review involved a number of steps:

- Literature Search
- Development of Inclusion Criteria
- Study Selection
- Data Extraction
- Assessment of Study Quality
- Data Analysis

Literature Search

The research librarian, in collaboration with the TEP (Technical Expert Panel), developed and implemented search strategies designed to identify relevant evidence for key questions of the review. A systematic search of 21 electronic databases was conducted. Table 1 outlines the electronic databases that were searched. Table 2 outlines the subject headings and keywords that were used in the search. Appendix A♦ contains details of the search strategy. Most of the searches were limited to humans, and no age restrictions were applied to any of the searches.

For Question 1, which relates to the definition, classification, diagnosis, and etiology of chronic insomnia in adults, we searched for narrative and systematic reviews, book chapters, diagnostic manuals and standards of practice parameters, and applied English-language restrictions. For Question 2, which relates to the prevalence, natural history, incidence, and risk factors for chronic insomnia in adults, and Question 3, which relates to the consequences, morbidities, co-morbidities and public health burden associated with chronic insomnia in adults, we searched for observational studies, encompassing a range of designs including cross-sectional, case-control, and cohort studies, and applied English-language restrictions. For Question 4, which relates to the treatments for chronic insomnia in adults, and the evidence regarding their safety, efficacy, and effectiveness, we searched for randomized controlled trials, and no language restrictions were applied. We did not apply language restrictions to searches for Question 4, since a portion of this question involves a review of complementary and alternative medicine (CAM), and there is evidence to suggest that studies of some CAM topics are often initially published in non-English languages, and many of these are not published in English.[21] We searched electronic resources that specialize in CAM, including AMED (Allied and Complementary Medicine), Alt HealthWatch, and Cochrane Complementary Medicine Field Registry. In order to systematically search for the different types of studies required for each question, it was useful to refer to: the highly sensitive search strategy for identifying reports of randomized controlled trials in MEDLINE® from the Cochrane Reviewer's Handbook (Appendix 5b)[22]; search strategies for diagnosis, etiology, natural history and morbidities from PDQ Evidence-based Principles and Practice[23]; and the search strategy for systematic reviews in MEDLINE® from the Alberta Research Centre for Child Health Evidence.[24] Searches were also

♦ The Appendices and Evidence Tables cited in this report are provided electronically at http://www.ahrq.gov/clinic/tp/insomntp.htm.

conducted in databases that index grey literature, including SIGLE (System for Information on Grey Literature in Europe), OCLC Proceedings First, Dissertation Abstracts and the NLM Gateway (searched specifically for meeting abstracts).

No hand searching was conducted for this review, given that the key journals pertaining to chronic insomnia, such as *Sleep* and *Sleep Medicine Reviews*, are indexed in MEDLINE.

Development of Inclusion Criteria

We did not develop formal inclusion criteria for the question pertaining to the definition, classification, diagnosis and etiology of chronic insomnia, nor for the question pertaining to the future direction of insomnia-related research. The former question was answered by providing an overview of the literature, and the latter question was answered by assessing the limitations in the evidence for the other questions of the review.

Inclusion criteria were developed for three questions of the review. Question-specific inclusion criteria appear below. The questions have been numbered according the numbering system outlined in the Introduction of this report. In the interest of clarity, questions 2 and 3 will be referred to as the questions on manifestations of chronic insomnia, while question 4 will be referred to as the question on management of chronic insomnia.

2. What are the prevalence, natural history, incidence and risk factors for chronic insomnia? Specific risk factors of interest include age, gender, race/ethnicity, psychiatric illness and psychological problems, medical disease, socioeconomic status and shift-work.

A study was considered to be relevant to the portion of Question 2 pertaining to the prevalence, natural history and incidence of chronic insomnia, if it met the following criteria:

- the report was written in English
- participants were at least 15 years old
- it examined chronic insomnia
- it had a cross-sectional or cohort design
- it assessed the prevalence, natural history or incidence of chronic insomnia

A study was considered to be relevant to the portion of Question 2 pertaining to risk factors for chronic insomnia, if it met the following criteria:

- the report was written in English
- participants were at least 15 years old
- it examined chronic insomnia
- it had a cohort, case-control, or cross-sectional design
- it assessed one of the risk factors of interest

3. What are the consequences, morbidities, co-morbidities, and public health burden associated with chronic insomnia? Specific outcomes of interest include healthcare utilization, psychiatric illness, absenteeism, work performance, accidents, falls in the elderly, quality of life and social relationships, memory, cognitive function, mood, direct and indirect costs.

A study was considered to be relevant to this question of the review, if it met the following criteria:

- the report was written in English
- participants were at least 15 years old
- it examined chronic insomnia
- it had a cohort or cross-sectional design
- it assessed one of the consequences of interest

For Questions 2 and 3, a study was considered to examine chronic insomnia if this condition was defined as a sleep disturbance of four weeks or more, or the report explicitly mentioned that chronic sleep disturbance was examined.

4. **What treatments are used for the management of chronic insomnia and what is the evidence regarding their safety, efficacy, and effectiveness?** Specific treatments of interest include prescription medication, over the counter medication, alcohol, behavioral therapy, combination therapy and complementary and alternative care.

A study was considered to be relevant to this question of the review, if it met the following criteria.

- the report was written in English
- participants were at least 15 years old, and the majority were at least 18 years old
- participants suffered from chronic insomnia
- participants were randomized to intervention or placebo
- participants and assessors were blind to treatment received
- it assessed at least one of the following outcomes, listed in order of importance in deriving conclusions of the review:
    - sleep onset latency
    - wakefulness after sleep onset
    - sleep efficiency
    - total sleep time
    - sleep quality
    - quality of life

Sleep onset latency was defined as the amount of time between the participant laying down to sleep and the onset of sleep; wakefulness after sleep onset was defined as the amount of time spent awake in bed following the attainment of sleep; sleep efficiency was defined as the amount of time spent asleep as a percentage of the total time spent in bed; and total sleep time was defined as the total time spent asleep while in bed. We used broad definitions of sleep outcomes in this review. For example, sleep onset latency could be defined as time to sleep, time to stage 1 sleep, time to stage 2 sleep or latency to persistent sleep. We believe that it was acceptable to combine studies with differing definitions of sleep onset latency in the analysis, since differences in the magnitude of estimations across definitions would be accounted for by subtraction of

placebo effects from treatment effects. Although it could be argued that these definitions are significantly different, the optimal definition of sleep onset latency has not yet been determined. Nonetheless, differences between polysomnography, sleep diary and actigraphy definitions of sleep onset latency were explored indirectly through sub-group analyses.

Sleep onset latency and wakefulness after sleep onset were given the highest priority in deriving conclusions of the review, since they were considered the best indices of sleep initiation and sleep maintenance, respectively. However, sub-group analyses were conducted only on data relevant to sleep onset latency, since this outcome was the most highly reported outcome across studies.

If the majority of participants met one of the following criteria, the study population was considered to suffer from chronic insomnia:

- participants suffered from a sleep disturbance of 4 weeks or more
- participants were described as having a chronic/long-standing/persistent sleep disturbance
- participants were selected from a sleep disorders clinic

The 4-week cut-point for chronic insomnia was considered long enough to eliminate studies involving transient insomnia, and short enough to include studies involving persistent insomnia.

In the case of combination therapy, the combined treatment could be compared to either placebo or single treatment.

We acknowledged the fact that double-blinding is often not feasible in studies of psychological treatments by not requiring double-blinding in these studies for inclusion in the review. The placebo treatment for relaxation therapy and cognitive/behavioral therapy was minimal treatment, such as sleep hygiene recommendations or minimal instruction. We required a placebo control and randomization of participants to intervention groups in order to account for potential confounders in the analysis. That is, we wanted to control for potential improvements in insomnia symptoms that may occur during the natural course of observation, irrespective of treatment effects, and for systematic differences in the experimental and control groups.

Given that placebo for psychological treatment is variable and not standardized across studies, we restricted our analysis to a particular type of placebo such that our results could be put in some context i.e. the efficacy of psychological treatment could be judged against a particular type of comparator. We required that the placebo resemble the intervention of the study except that it was known to produce either no effect or only a minimal effect. Thus, component controls or attention-placebo were considered appropriate if they were thought to have at most a minimal effect. A waiting-list or measurement control was considered inadequate because no intervention was provided. A pill-placebo was considered inadequate because it did not resemble the experimental intervention, which did not involve administration of a pill.

Study Selection

The research librarian provided three databases containing the titles and abstracts of potentially relevant articles of the review; one database was relevant to the question on the definition and etiology of chronic insomnia, another database was relevant to the questions on manifestations of chronic insomnia, and another database was relevant to the question on management of chronic insomnia. In the first stage of study selection, two reviewers screened the titles and abstracts of all potentially relevant articles, independently. Each reviewer noted the

titles and abstracts that were potentially relevant to the review, and these articles were retrieved. In the second stage of study selection, two reviewers appraised the potentially relevant articles, independently, using pre-determined, question-specific, inclusion criteria. Disagreements between reviewers were resolved by discussion and consensus. The rate of disagreement between reviewers and the primary reason for exclusion of potentially relevant articles were noted.

Assessment of Study Quality

The quality of studies relevant to the questions on manifestations of chronic insomnia was assessed using one of three instruments; studies on prevalence and incidence were assessed using a scale designed specifically for this purpose.[25] This scale assesses bias in sample selection, sampling frame, sample size, outcomes and their assessment, response rate, confidence intervals and sub-group analysis, and sample description. The maximum score is eight. *A priori*, it was established that a score of zero to two would be considered low quality, a score of three to five would be considered moderate quality and a score of six to eight would be considered high quality. All other studies relevant to manifestations of chronic insomnia were assessed using one of two Newcastle-Ottawa scales (unpublished), each scale specific to either cohort or case-control studies. The scale specific to cohort studies assesses bias in the selection of exposed and non-exposed cohorts, ascertainment of exposure, presence of outcomes at the start of the study, comparability of cohorts based on design or analysis, outcome assessment, and length and adequacy of follow-up. The scale specific to case-control studies assesses bias in the definition, selection, comparability, ascertainment of exposure, and non-response rate for both cases and controls, and how these groups compare on these items. The maximum score for the Newcastle-Ottawa scales is nine. *A priori*, it was established that a score of zero to two would be considered low quality, a score of three to five would be considered moderate quality and a score of six to nine would be considered high quality.

The quality of studies relevant to management of chronic insomnia was assessed using the Jadad scale.[26] This scale assesses bias in sample selection, outcome assessment, data analysis, and appropriateness of randomization and blinding methods. The maximum score is five. *A priori*, it was established that a score of zero to one would be considered low quality, a score of two to three would be considered moderate quality and a score of four to five would be considered high quality. The concealment of allocation of participants to treatment groups was also assessed.[27] Allocation was considered adequate, inadequate or unclear.

Appendix B contains the quality assessment tools used in this review.

Data Extraction

The following data were extracted for studies relevant to manifestations of chronic insomnia, as applicable: first author and year of publication, site, objectives, design, time-frame, intended sample size, response and follow-up rates, type of participants, definition of comparison groups, participants' gender, age, and ethnicity, and participants' co-morbid conditions at entry. For the question on prevalence, incidence, natural history and risk factors for chronic insomnia, additional data extracted included setting, sampling frame and method of sampling, data collection method, prevalence, incidence and natural history parameters. We did not identify studies with designs that would support the categorization of outcomes as either risk factors or

consequences of chronic insomnia; therefore, data relevant to potential risk factors and potential consequences of chronic insomnia were extracted, and these outcomes were referred to as associated factors of chronic insomnia.

The following data were extracted for studies relevant to management of chronic insomnia: first author and year of publication, funding source and role of funding organization, design, whether an intent-to-treat analysis was conducted, number of participants enrolled and their distribution by gender, participants' age, number of withdrawals and reasons for withdrawal, duration of insomnia, participants' co-morbid conditions at entry, methods used to assess outcomes, details of the intervention, such as frequency and duration of treatment and timing and route of delivery, number of participants allocated to treatment groups and number analyzed in each group, length of follow-up, patient preference, and data relevant to sleep onset latency, wakefulness after sleep onset, sleep efficiency, total sleep time, sleep quality, quality of life and adverse events. A trained reviewer extracted relevant data, and a second reviewer verified the data extracted for accuracy and completeness.

Appendix B contains data extraction forms for the questions on manifestations and management of chronic insomnia.

The information gathered by data extraction was used to generate Evidence Tables. Appendix C contains these tables.

Data Analysis

Data relevant to manifestations of chronic insomnia were analyzed qualitatively, while data relevant to management of chronic insomnia were analyzed quantitatively.

Manifestations of chronic insomnia. For the questions on prevalence, natural history, incidence, risk factors and consequences of chronic insomnia, data relevant to each variable were analyzed separately, except for data relevant to potential risk factors and potential consequences of chronic insomnia, which were analyzed together as associated factors of chronic insomnia. The key features of all studies providing information on prevalence, natural history, incidence or associated factors of chronic insomnia were summarized in tables, such that data relevant to each variable appeared in a separate table. The information on prevalence was divided into three tables, one for prevalence in the general population, one for prevalence in outpatients of general practice and one for prevalence in clinical populations.

The following information was included in the tables on prevalence: first author and year of publication, study quality, study design, sampling frame, sampling method, response/follow-up rate, method of data collection, type of participants, duration of sleep complaints and definition of cases and comparison groups, gender distribution of sample, age distribution of sample, and prevalence estimates. The following information was included in the table on natural history: first author and year of publication, study quality, study design, time frame for the study, response/follow-up rate, type of participants, duration of sleep complaints, gender distribution of sample, age distribution of sample, and natural history estimates. The following information was included in the table on associated factors for chronic insomnia: author and year of publication, study quality, study design, type of participants, duration of sleep complaints, gender distribution of sample, age distribution of sample, response/follow-up rate, and a qualitative summary of the findings of the study. The qualitative summary of results was derived by consolidating

information available in the results and conclusions of relevant studies. We did not identify information relevant to the incidence of chronic insomnia.

The data provided in the tables were synthesized to provide a description of the methods and results of the studies relevant to a given variable. In the analysis of prevalence of chronic insomnia, a range, median and interquartile range were provided for each population (general, outpatient and clinical), separately for high and moderate quality studies, where appropriate. In the analysis of associated factors of chronic insomnia, the qualitative summary of findings were summarized in terms of the studies that did or did not find an association between chronic insomnia and the various factors of interest.

Management of chronic insomnia. *A priori*, the drug interventions were categorized according to drug class i.e. benzodiazepines, non-benzodiazepines and antidepressants. It was considered acceptable to combine different drugs of the same category in a meta-analysis, based on similar mechanisms of action. For psychological interventions, it was considered acceptable to combine predominantly cognitive approaches in a meta-analysis, and also to combine predominantly relaxation approaches in a meta-analysis; however, it was considered unacceptable to combine these two types of psychological approaches in a meta-analysis, since they were considered too different in their modes of action. Relaxation techniques address somatized tension, and different forms of this type of therapy (progressive relaxation and group relaxation) were considered similar enough to be pooled. However, cognitive therapy addressing the cognitive aspects of insomnia was not thought to be equivalent to relaxation therapy because it targets different aspects of insomnia, and was considered separately. A few interventions (e.g. L-tryptophan, melatonin and valerian) were categorized under the heading of "complementary and alternative care"; however, separate meta-analyses were presented for these interventions. We did not combine these interventions in a meta-analysis, given their distinct modes of action.

For continuous outcomes (i.e. sleep onset latency, sleep efficiency), studies were combined using a Mean Difference (MD), with the exception of sleep quality and quality of life, where studies were combined using a Standardized Mean Difference (SMD). Dichotomous outcomes (i.e. safety outcomes) were combined using a Risk Difference. A number needed to harm (NNH) was also reported for any safety outcomes that were found to be statistically significant. The Inverse Variance Method[28] was used to weight the studies. An efficacy estimate, with corresponding 95% Confidence Interval (CI), was computed for each outcome. For interpreting estimates calculated using the SMD, we used the generalization of 0.2 as small, 0.5 as moderate, and 0.8 as large.[29]

We were usually able to calculate the efficacy estimates for each study exactly (i.e. mean difference, standardized mean difference, risk difference), but occasionally, estimates had to be made by extracting from graphs or using medians. Standard errors of the differences were calculated exactly from available data (i.e. individual patient data or exact *P*-values), whenever possible. For studies with a parallel design, this calculation was usually accomplished with the standard formula for variance of difference of independent variables: $\text{var}(A-B) = \text{var}(A) + \text{var}(B)$. For studies with a crossover design, the standard error was estimated using the formula for variance of difference of dependant variables: $\text{var}(A-B) = \text{var}(A) + \text{var}(B) - 2\rho(\text{var}(A)\text{var}(B))^{½}$ and using a correlation estimate of 0.5. In cases where exact values could not be obtained, standard errors were estimated using conservative *P*-values (i.e. $p < 0.05$), ranges, inter-quartile ranges, and extracting from graphs. As a last resort, an average of standard deviations of other studies was used to impute standard deviations of a study.

For studies with a parallel design, change from baseline data were used if available, otherwise final data were used. For studies with a crossover design, final data were always used. When continuous data were presented for multiple conditions, which we wished to combine, a new mean and standard deviation were computed.

All meta-analyses were performed using a Random Effects Model. Bailey[30] suggests that the Random Effects Model is more appropriate when making recommendations for management and treatment of the next given patient.

For some outcomes (sleep onset latency and number of adverse events), treatment categories were compared indirectly, via their relationship to placebo. Differences of differences with 95% CI were computed. Indirect comparisons were not made between pharmacological and psychological treatments for the following reasons (1) although our inclusion criteria required blinding for drug and complementary and alternative care, this criteria was omitted for psychological treatments (2) the placebo intervention was considered to have no effect for drug and complementary and alternative treatments, while it may have had minimal effect for psychological treatments (3) the pool of participants for psychological interventions was much smaller than for either the benzodiazepines, non-benzodiazepines or antidepressants. Thus, only indirect comparisons between non-psychological intervention categories and between psychological intervention categories were made.

All estimates of efficacy were assessed for heterogeneity using the I-squared statistic.[31] Based on this statistic, heterogeneity for each outcome was classified as negligible ($I^2 = 0$ percent), minimal ($I^2 < 20$ percent), moderate (20 percent $< I^2 < 50$ percent), or substantial ($I^2 >$ 50 percent). This measure of heterogeneity describes the degree of variation in the efficacy estimates among studies. For our primary outcome (sleep onset latency), heterogeneity was explored in sub-group analyses using a number of variables. The following variables were targeted *a priori* and explored in sub-group analyses: treatment sub-group (i.e. type of drug or therapy), presence or absence of psychiatric illness (as defined in the study inclusion criteria), length of treatment (short-term and long-term, defined as less than or equal to 4 weeks and greater than 4 weeks, respectively), age (adult and elderly defined as the majority of patients 15-65 years or greater than 65 years, respectively) and gender (male and female). Method of measurement of sleep outcomes (polysomnography, sleep diary actigraphy) was analyzed post-hoc in a sub-group analysis based on comments from peer reviewers. Study quality (low, moderate and high quality defined as Jadad scores of 0-1, 2-3 and 4-5, respectively) was also explored in a sensitivity analysis. Deeks' chi-square statistic [32] was used to test for significant heterogeneity reduction in partitioned sub-groups.

Publication bias is the publication of studies based on the nature and direction of results. We tested for publication bias visually using the Funnel Plot[33] and quantitatively using the Rank Correlation Test,[34] the Graphical Test,[35] and the Trim and Fill Method.[36]

Table 1. Databases searched

Database	Platform	Dates of Search
MEDLINE®	Ovid Version: rel9.1.0	1966 to September Week 1 2004
EMBASE	Ovid Version: rel9.1.0	1988 to 2004 Week 37
CINAHL	Ovid Version: rel9.1.0	1982 to September Week 2 2004
Ovid MEDLINE In-Process & Other Non-Indexed Citations	Ovid Version: rel9.1.0	September 14, 2004
Ovid OLDMEDLINE(R) ®	Ovid Version: rel9.1.0	1951 to 1965 – Searched September 15, 2004
PsycINFO®	Ovid Version: rel9.1.0	1872 to September Week 1 2004
EBM Reviews - Cochrane Central Register of Controlled Trials	Ovid Version: rel9.1.0	2nd Quarter 2004, Searched September 15, 2004
International Pharmaceutical Abstracts	Ovid Version: rel9.1.0	1970 to August 2004
AMED (Allied and Complementary Medicine)	Ovid Version: rel9.1.0	1985 to September 2004
HealthSTAR/Ovid Healthstar	Ovid Version: rel9.1.0	1975 to August 2004
EBM Reviews – Cochrane Database of Systematic Reviews (CDSR) ; ACP Journal Club (ACPJC) ; Database of Abstracts of Reviews of Effects (DARE)	Ovid Version: rel9.1.0	2nd Quarter 2004 (CDSR); 1991 to March/April 2004 (ACPJC); 2nd Quarter 2004 (DARE); Searched September 15, 2004
Science Citation Index Expanded®	ISI Web of Knowledge	1945-September 2004, Searched September 17, 2004
Biological Abstracts	WebSPIRS from SilverPlatter, Version 4.3	1969-September 17, 2004
Cochrane Complementary Medicine Field Registry	Reference Web Poster 2001, ISI ResearchSoft	1950-September 20, 2004
CAB Abstracts	WebSPIRS from SilverPlatter, Version 4.3	1973-September 18, 2004
SIGLE	FIZ Karlsruhe – Version Interhost 3000	1980-September 18, 2004
OCLC Proceedings First	OCLC FirstSearch	1993-September 18, 2004
Dissertation Abstracts	ProQuest	1980-September 18, 2004
Alt HealthWatch	EBSCOhost	1990-September 18, 2004
NLM Gateway	U.S. National Library of Medicine - http://gateway.nlm.nih.gov/gw/Cmd	1950-September 18, 2004
PubMed	U.S. National Library of Medicine	1950-September 20, 2004

Table 2. Subject headings and keywords used in searches

Terms used for Questions 1-4	Additional Terms used for Question 4
Insomnia	Time zone change
Sleep Initiation and Maintenance Disorders	Jet lag
Sleep onset delay	-------
Sleep onset latency	-------
DIMS	-------
Disorder of initiating and maintaining sleep	-------
Early awakening	-------
Sleeplessness	-------
Agrypnia	-------
Hyposomnia	-------

Chapter 3. Results

Literature Review

The database searches resulted in 16,991 references of potentially relevant articles. One thousand two hundred studies were evaluated for inclusion in the review; 528 studies were potentially relevant to prevalence, natural history, incidence, risk factors and consequences of chronic insomnia, and 672 studies were potentially relevant to efficacy and safety of treatments used in the management of chronic insomnia. The application of inclusion criteria resulted in 79 studies included and 449 studies excluded for the questions on manifestations of chronic insomnia, and 116 studies included and 556 studies excluded for the question on management of chronic insomnia.

The primary reasons for exclusion of studies potentially relevant to manifestations of chronic insomnia were as follows: (1) the study was reported in a language other than English (n=9), (2) the report was a review (n=38), (3) the study was not relevant to the review topic (n=71), (4) the study was a case report (n=9), (5) the study did not have a control group (n=47), (6) the study did not examine an adult population (n=8), (7) the study population did not have chronic insomnia as defined in this report (n=208), (8) the study did not report on any of the outcomes of this review (n=58), and (9) data relevant to the study outcomes were not adequately reported (n=1). The primary reasons for exclusion of studies potentially relevant to the management of chronic insomnia were as follows: (1) the study was reported in a language other than English (n=27), (2) the report was a review/commentary/practice parameter (n=32), (3) the study report was a duplicate publication (n=3), (4) the study did not examine an adult population (n=17), (5) the study population did not suffer from chronic insomnia as defined in this report (n=221), (6) the study was not a randomized controlled trial (n=160), (7) the study did not have a placebo arm (n=48), (8) the study was not double-blind (n=15), (9) the study did not report on any of the outcomes of this review (n=16), and (10) data relevant to the study outcomes were not adequately reported (n=15).

The rate of disagreement between reviewers for inclusion/exclusion of studies was 61/528 (11.6 percent) for the questions on manifestations of chronic insomnia and 53/672 (7.9 percent) for the question on management of chronic insomnia. The primary reason for disagreement between reviewers was oversight of study details, such that reviewers erred on the side of over-inclusion. Therefore, consensus often resulted in exclusion of studies: for the questions on manifestations of chronic insomnia, 18 disagreements resulted in inclusion and 43 disagreements resulted in exclusion, and for the question on management of chronic insomnia, eight disagreements resulted in inclusion and 45 disagreements resulted in exclusion.

Flow Diagram 2 outlines study retrieval and selection for the review.

Data Synthesis

How is chronic insomnia defined, diagnosed and classified, and what is known about its etiology?

There is lack of consensus regarding the “ideal” definition of insomnia and what constitutes chronic insomnia. The threshold of clinically significant sleep disturbance is not established, nor

has the morbidity resulting from insomnia been well studied. It is a matter of debate as to which definition of insomnia encompasses the problem as it would appear in a clinical and/or research setting, and whether the definition of chronic insomnia should be distinct. As a result, many variations in the definition of insomnia exist, especially for research purposes. We reviewed multiple sources to define, diagnose and classify chronic insomnia, including the Principles and Practice of Sleep Medicine textbook,[15] diagnostic manuals (International Classification of Sleep Disorders-Revised (ICSD-R) and Diagnostic and Statistical Manual of Mental Disorders, 4th Ed. (DSM-IV)),[37-38] and standards of practice published by the American Academy of Sleep Medicine.[1;39]

Definition of chronic insomnia

The International Classification of Sleep Disorders Manual. The International Classification of Sleep Disorders Manual is a comprehensive diagnostic manual, which is used as a reference among sleep researchers and physicians for sleep disorders in adults. The manual outlines a highly specific system for diagnosis and classification of insomnia, and includes over 40 diagnoses that may involve a complaint of insomnia. The International Classification of Sleep Disorders defines insomnia as difficulty in initiating and/or maintaining sleep or non-restorative sleep after a habitual sleep episode.[37] The ICSD-R further differentiates insomnia based on severity of symptoms that impact daytime functioning. Mild insomnia is often associated with a feeling of restlessness, irritability, mild anxiety, daytime fatigue and tiredness, without evidence of social or occupational impairment. In contrast, moderate insomnia is accompanied by either mild or moderate impairment of social and occupational functioning. Moderate insomnia is always associated with feelings of restlessness, irritability, anxiety, daytime fatigue and tiredness. Severe insomnia is associated with symptoms similar to moderate insomnia, with severe impairment of social and/or occupational functioning. The duration of the insomnia is usually classified as acute (< 4 weeks), sub-acute (> 4 weeks but < 6 months) or chronic (> 6 months). Investigators have not consistently adhered to this classification scheme to determine severity and duration of insomnia in study populations, thus the definition of insomnia across studies varies. This classification scheme has coding for insomnia secondary to psychiatric conditions, substance abuse as well as medical and sleep disorders. The ICSD-R has been revised, and another edition of the ICSD (ICSD2) is in press for publication. This revised coding manual will replace the current ICSD-R.

International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10). The World Health Organization-supported definition for nonorganic insomnia is a condition of unsatisfactory quantity and/or quality of sleep, which persists for a considerable period of time, including difficulty falling asleep, difficulty staying asleep, or early final wakening. It also states that insomnia is a common symptom of many mental and physical disorders, and should be classified here in addition to the basic disorder only if it dominates the clinical picture. The duration of insomnia is not specified.

Diagnostic and Statistical Manual of Mental Disorders. In contrast to the definition of insomnia in the ICSD-R, in the DSM-IV, insomnia is not subcategorized, but rather referred to as primary insomnia,[38] implying that insomnia is not caused or significantly influenced by a psychiatric disorder. Insomnia caused or associated with psychiatric illness is classified separately. The

duration of insomnia is listed as being longer than one month. Chronic insomnia is not defined in the DSM nosology.

American Academy of Sleep Medicine: Standards of Practice. The standards of practice published by the American Academy of Sleep Medicine defines insomnia as a complaint of unsatisfactory sleep, which may involve difficulty initiating sleep, frequent or lengthy awakenings, early awakening, inadequate total sleep time or poor quality of sleep, impacting daytime functioning.[1] The daytime dysfunction may include any of the following: change in alertness, energy, cognitive function, behavior or emotional state. This definition of insomnia allows for subjective diagnosis in a clinical setting based on the patients' history, without the aid of polysomnography. Although short-term insomnia is generally considered to last less than three months, the time frame for chronic insomnia is not explicitly stated in the standards of practice statement.

Classification of insomnia

The International Classification of Sleep Disorders Manual. A clinically relevant classification of insomnia is outlined in the ICSD-R, 2001.[37] According to the ICSD-R, the different categories of insomnia include: psychophysiological insomnia, sleep state misperception, idiopathic insomnia, as well as insomnia secondary to other medical conditions or sleep disorders. Acute and chronic insomnia are not classified separately; however, insomnia is considered to be chronic if the symptoms last for more than six months. A brief overview of the ICSD-R categories follows:

A. Psychophysiological insomnia, also known as conditioned or learned insomnia, is a disorder of somatized tension and learned sleep preventing associations that result in a complaint of insomnia and associated decreased functioning during wakefulness.[37] Continued problems in somatized tension and maladaptive learned sleep-preventing associations can worsen insomnia, creating a vicious cycle by perpetuating the initial problem. One must search for precipitating, predisposing and perpetuating factors for insomnia. A hallmark of this diagnosis is the individual's fixation with his/her sleep problem. This diagnosis cannot be made in the context of other medical or psychiatric disorders. Associated features include perceived decrement in daytime mood and functioning, without overt sleepiness. The true prevalence of psychophysiological insomnia in the general population is not known, although approximately 15 percent of patients referred to a sleep disorders clinic suffer from this type of insomnia.[37] Diagnostic criteria for psychophysiological insomnia include:

    a) A combination of a complaint of insomnia and a complaint of decreased functioning during wakefulness.
    b) Indications of learned sleep-preventing associations such as trying too hard to sleep, or increased arousal in the bedroom (concern and worry about sleep).
    c) Evidence of somatized tension.
    d) Polysomnography may show increased sleep latency, reduced sleep efficiency and increased number and/or duration of awakenings during the sleep period.
    e) No other medical condition accounts for the sleep disturbance.

The diagnosis of psychophysiological insomnia requires that criteria a) and b) are satisfied.

B. Sleep state misperception, or pseudo insomnia, is a subjective complaint of problems initiating or maintaining sleep without objective findings to support the complaint. There is no psychopathology per se associated with this disorder. The afflicted individual honestly has complaints of insomnia and decreased daytime functioning, without objective data to support the claim. Although the exact prevalence of this disorder is not known, this group accounts for approximately 5 percent of individuals with complaints of insomnia. Diagnostic criteria for sleep state misperception include:

    a) complaint of insomnia.
    b) sleep quality and quantity are normal.
    c) polysomnography shows normal sleep latency, sleep duration and awakenings during the sleep period.

The diagnosis of sleep state misperception requires that criteria a) and b) are satisfied.

C. Idiopathic Insomnia is defined as a life-long inability to obtain adequate sleep and may be related to abnormalities in the neurological systems affecting the sleep-wake cycle. The exact prevalence of this disorder is not known, but it is thought to be rare. Diagnostic criteria for idiopathic insomnia include:

    a) Complaint of insomnia with decreased functioning.
    b) Insomnia is life-long and may begin in early childhood.
    c) Insomnia is relentless and does not vary.
    d) Polysomnography shows increased sleep latency, decreased sleep efficiency and multiple awakenings during the night.
    e) No other medical illness or disease explains the early onset of insomnia.

The diagnosis of idiopathic insomnia requires that criteria a), b), and d) are satisfied.

Proposed classification for insomnia. A more recent article considers a novel method for classifying insomnia for research purposes.[40] The authors propose research diagnostic criteria for Insomnia Disorder, Primary Insomnia, Insomnia due to a Mental Disorder, Paradoxical Insomnia and Psychophysiological Insomnia. The main differences between this classification scheme and that of ICDS-R, 2001, is that the criteria are more precise and the duration of symptoms must be more than one month for all categories. This classification scheme does not define a subcategory of chronic insomnia. This classification scheme was developed to allow for clear categorization of insomniacs within a study population, and thus avoid the study of a heterogeneous population. Based on a review of the literature, acute, situational or transient insomnia is considered to be different from chronic insomnia. It is not clear whether there are distinct differences in the nature of insomnia that lasts for more than 1 month, but less than 6 months versus insomnia lasting for more than 6 months.

Diagnosis and assessment of insomnia. Different evaluation methods have evolved to identify individuals with insomnia. Diagnosis of insomnia is made in the context of a clinical history based on any of the aforementioned criteria or definitions. There are semi-structured or structured interviews available for diagnosing insomnia [i.e., Insomnia Interview Schedule and Duke Structured Sleep Inventory (the latter is currently being evaluated in a large-scale study)]. Sleep diaries/logs, sleep histories, actigraphy, ambulatory monitoring, and in-home polysomnography are often used to assess sleep parameters. The most commonly used measure for evaluation of insomnia is self-reported questionnaires. The use of objective tools, such as polysomnography or multiple sleep latency tests for the diagnosis of insomnia are not recommended.[41-43] Sleep diaries are essential for identifying sleep onset and sleep maintenance difficulties; however, the reporting of sleep onset latency by diary is subjective. Scientists have tried to evaluate more objective measures for measuring sleep disturbances in patients with insomnia, but currently available tools have limitations (polysomnography and unattended home studies), and are most commonly used to diagnose sleep disorders other than insomnia. Moreover, these methods are cumbersome and costly. Actigraph monitors are small watch-like devices that are worn on the wrist and are used to record movement; they can be useful adjuncts for gathering data from individuals with sleep complaints; however, these devices are not indicated for the routine diagnosis of any sleep disorder.[39] There is currently no biomarker of insomnia, which makes objective diagnosis of insomnia more difficult. Research in the area of insomnia has recently been directed towards identifying specific hormones or neurotransmitters that may be involved in this disorder.[15] Various research groups are studying the link between specific electroencephalogram findings and insomnia. A less commonly used diagnostic tool for insomnia, position emission tomography imaging, has been used to evaluate brain metabolism and its role in insomnia.[44] Insomnia is a clinical diagnosis and the lack of a research model for insomnia makes it difficult to target appropriate therapy for this disorder and evaluate treatment outcomes.

Etiology of insomnia. Despite significant advances in sleep medicine over the past 50 years, much less is known about the cause of insomnia, its natural history, and its consequences than the treatments available for insomnia. Recent studies have demonstrated an increased metabolic rate in patients with insomnia,[45] suggesting that sleep difficulties may at least partially have a physiological basis. It is also speculated that patients with insomnia are more aroused than people without insomnia;[46] however, this theory is difficult to prove, given that the neurotransmitters involved in arousal are unknown. Advances in molecular genetics have shed light on the potential role of genetics in sleep disorders. Indeed, a familial etiology of this disorder has been postulated. A recent study concluded that more than 33 percent of patients with insomnia had a family history of insomnia.[47] A similar study estimated a family history of insomnia among first-degree relatives of people suffering from insomnia to be 48.8 percent, compared to 23.5 percent among first-degree relatives of people who did not suffer from insomnia.[48] The familial aggregates of insomnia have led researchers to investigate the genetic basis of insomnia, but no specific gene has been implicated.

Certain populations, including the elderly, psychiatric patients, and those suffering from chronic pain are known to have more chronic sleep maintenance problems.[1;49] A strong link has been found between insomnia and depression.[50] The directionality of the association has not been fully elucidated, but the association appears to be strong.[1]

Environmental factors, such as irregular sleep schedules, use of caffeine or other stimulants, co-morbid medical conditions, and/or shift-work may also predispose vulnerable individuals to insomnia.[1] Genetic predisposition, in addition to environmental factors, are likely involved in the development and maintenance of insomnia, and differences in the relative exposure to these influences may explain differences in the manifestation of this disorder across affected individuals.

What are the prevalence, natural history, incidence and risk factors for chronic insomnia?

What are the consequences, morbidities, co-morbidities and public health burden associated with chronic insomnia?

Prevalence. A description of key features of studies relevant to prevalence of chronic insomnia is provided in Tables 3a (prevalence in general population), 3b (prevalence in outpatients of general practice) and 3c (prevalence in clinical populations), and additional information on each study is provided in Evidence Table C-1♦. The evidence provided in Tables 3a, b and c is summarized here.

Forty-one studies provided evidence regarding the prevalence of chronic insomnia in adults; 38/41 studies were cross-sectional studies, one study was a cross-sectional case-control study and compared the prevalence of chronic insomnia in bipolar subjects and healthy controls,[51] one study had both cross-sectional and case-control components,[52] and one study had both cross-sectional and cohort components.[53] Seventeen studies were considered of high quality, 19 studies were considered of moderate quality and five studies were considered of low quality.

Twenty-four studies described the sampling frame; most studies used census data, phone lists or patients presenting to a health clinic. Thirty-four studies described the sampling method; 21 studies used a random method, while the majority of the remaining studies used a non-random method, and a minority of studies investigated entire populations. Twenty-seven studies provided a response or follow-up rate. The rate ranged from 25-100 percent; slightly more than half of the studies had a rate greater than 80 percent. All studies except one [54] clearly described the method of data collection; 19 studies used self-reported questionnaires, 12 studies used face-to-face interviews and 10 studies used phone interviews. One of these studies [55] used both self-reported questionnaires and phone interviews. Of the studies that described the method of data collection, slightly more than half used a validated method. The criteria used to establish the duration of chronic insomnia ranged from one month to one year; most of the studies required that participants suffer from insomnia symptoms for at least one month. Most studies reported the gender distribution of the population; the majority of studies used mixed gender populations and a minority of studies used all-female populations. All studies provided an estimate of the age of the population; the age of the populations ranged from 18 to 98 years, based on studies that provided a range.

Twenty-six studies investigated general populations (Table 3a), eight studies investigated populations of outpatients from general practice (Table 3b), and eight studies investigated clinical populations (Table 3c). For high quality studies investigating general populations, the

♦ The Appendices and Evidence Tables cited in this report are provided electronically at http://www.ahrq.gov/clinic/tp/insomntp.htm.

prevalence of chronic insomnia ranged from 5-45 percent, and the median was 17.6 percent. The interquartile range was 8.5-24.3 percent. For moderate quality studies investigating general populations, the prevalence of chronic insomnia ranged from 7.5-42.5 percent, and the median was 15.3. The interquartile range was 11.2-29.2 percent.

We did not identify any high quality studies investigating the prevalence of chronic insomnia in outpatients of general practice. For moderate quality studies investigating this population, the prevalence of chronic insomnia ranged from 11.7-63.7 percent, and the median was 38.4 percent. The interquartile range was 19.8-53.7 percent.

We identified only one high quality study investigating clinical populations, and it compared the prevalence of chronic insomnia in patients with Bipolar I disorder and a non-psychiatric population.[56] One hundred percent of participants in the psychiatric group reported a long-standing sleep disturbance, while 21 percent of participants in the non-psychiatric group reported such a disorder. For moderate quality studies investigating clinical populations, the prevalence of chronic insomnia ranged from 26-51.3 percent, with a median of 33.5 percent. The interquartile range was 27.8-43 percent. The disorders of the clinical populations investigated were Parkinson's Disease, brain injury, diabetes, stroke, Bipolar I disorder, migraines, blood disorders and metastatic breast cancer.

Natural history. A description of key features of the study relevant to natural history is provided in Table 4, and additional information on this study is provided in Evidence Table C-1. The evidence provided in Table 4 is summarized here.

Only one study was identified that provided evidence regarding the natural history of chronic insomnia,[53] and it was of moderate quality. In this prospective cohort study, the participants consisted of outpatients from general hospitals with sleep complaints lasting for at least one month. The population was of mixed gender and had an age range of 18-65 years. At a four-month follow-up, the prevalence of chronic insomnia was reduced from 100 percent to 86.9 percent, providing a remission rate of 13.1 percent. The follow-up rate was 42.2 percent.

Incidence. We did not identify any studies that provided evidence on the incidence of chronic insomnia in adults.

Associated factors. The majority of studies identified did not have designs that would support the categorization of an associated factor of chronic insomnia as either a risk factor or consequence of the disorder, such as longitudinal cohort studies. Most studies that examined the risk factors and consequences of interest were either of a cross-sectional or cross-sectional case-control design. Thus, we do not report on risk factors and consequences of chronic insomnia per se, rather we report on associated factors. For simplicity, we separate the results relevant to the various factors according to their categorization in the relevant question of the review, such that potential risk factors are reported separately from potential consequences.

A description of key features of the studies relevant to associated factors is provided in Table 5, and additional information for each study is provided in Evidence Table C-1. The evidence provided in Table 5 is summarized here.

Sixty-seven studies provided evidence regarding the association between various factors and chronic insomnia in adults; 30/67 studies were cross-sectional studies and 37/67 studies were cross-sectional case-control studies. The cross-sectional case-control studies compared chronic insomniacs (cases) and normal sleepers (control) on various factors to determine whether these

factors are associated with chronic insomnia. Similarly, the cross-sectional studies examined the relationship of various factors and chronic insomnia by comparing chronic insomniacs and normal sleepers within a given population. Twenty-three studies were considered of high quality, 30 studies were considered of moderate quality and 14 studies were considered of low quality.

The criteria for chronic insomnia varied widely across studies and it was explicitly reported for most studies. The duration of sleep disturbance required to meet the criteria for chronic insomnia ranged from one month to 5 years, although the majority of studies required symptoms to be present for one or 6 months. Most studies reported the gender distribution of the population; the majority of populations were of mixed gender, and a minority of populations were all-female. The age of participants was reported for most studies, and ranged from 18 to 98 years, based on studies that provided a range. A number of studies (37/67) did not report the response/follow-up rate for the study. Of those that reported the response/follow-up rate, it ranged from 37.6-100 percent. The majority of studies had a rate of 80 percent or more.

Potential risk factors

Age. Eleven studies found evidence of an association between age and chronic insomnia, while seven studies found no evidence of an association between these variables. Of the studies that found an association, all, except one,[57] found evidence that chronic insomnia is associated with older age. Kageyama et al. found evidence that chronic insomnia is associated with age 24 years or less.

Gender. Eleven studies found evidence of an association between gender and chronic insomnia, while seven studies found no evidence of an association between these variables. All of the studies that found evidence of an association between gender and chronic insomnia, found evidence that chronic insomnia is associated with female gender.

Race/ethnicity. Two studies found evidence of an association between ethnicity and chronic insomnia,[58-59] while one study found no evidence of an association between these variables.[60] Bixler et al. found evidence that chronic insomnia is associated with being a non-Caucasian minority, and Riedel et al. found evidence that chronic insomnia is associated with being White.

Psychiatric illness and psychological problems. Thirty-eight studies found evidence of an association between present or past psychiatric illness or psychological problems and chronic insomnia. Cumulatively, chronic insomnia was found to be associated with anxiety, depression, tension, loneliness, neuroticism, worry, rumination, psychological distress, nervousness, obsessive compulsiveness, maladaptive perfectionism, impulsivity, phobia, paranoid ideation, psychoticism and hypochondrial concerns. Seven studies did not find evidence of an association between one or more of the following conditions and chronic insomnia: neurological problems, anxiety, depression, tension and confusion.

Medical conditions. Twelve studies found evidence of an association between medical conditions or poor general health and chronic insomnia, while one study[57] did not find evidence of an association between these variables.

Socioeconomic status. Six studies found evidence of an association between socioeconomic status and chronic insomnia. Cumulatively, chronic insomnia was found to be associated with marital separation, divorce or death of a spouse, unemployment, exposure to poorer working conditions and lower social status. Moreover, chronic insomnia was found to be associated with both lower and higher education. Nine studies did not find evidence of an association between one or more of the following factors and chronic insomnia: education, employment and marital status.

Shift-work. Only two studies provided evidence regarding the relationship between shift-work and chronic insomnia.[57-61] The study by Kageyama et al. provided evidence that chronic insomnia is associated with three or less night shifts per month within the preceding three months in hospital nurses. The study by Martikainen et al. found no evidence of an association between shift-work and chronic insomnia.

Potential consequences

Healthcare utilization. Five studies provided evidence of an association between increased healthcare utilization and chronic insomnia. Cumulatively, chronic insomnia was found to be associated with hospitalization, visits to neurology and psychiatric departments and undergoing medical treatment. One study did not find evidence of an association between chronic insomnia and undergoing medical treatment in hospital nurses.[57]

Absenteeism and work performance. Only two studies provided evidence regarding the relationship between work performance or absenteeism and chronic insomnia;[62-63] both studies found evidence of an association between chronic insomnia and absenteeism. The study by Zammit et al. also found evidence of an association between chronic insomnia and impaired work performance.

Quality of life and quality of social relationships. Five studies examined the relationship between either quality of life or quality of social relationships and chronic insomnia. All studies found evidence of an association between chronic insomnia and either lower quality of life or lower quality of social relationships; one of these studies found evidence that both quality of life and quality of social relationships are impaired in chronic insomniacs.[64] Lower quality of social relationships was reported as receiving less support from colleagues and conflicts with relatives.

Memory, cognitive function and mood. Fifteen studies found evidence of an association between decrements in memory, mood or cognitive function and chronic insomnia. Cumulatively, the measures of cognitive function were cognitive fatigue, sensory acuity, perceptual/motor skills, reaction time, psychosocial function, concentration, psychomotor function, attention, alertness, mental acuity, reasoning, problem-solving ability and mental reactivity. One study[65] found evidence of increased recall of presentations made just before sleep onset in chronic insomniacs. Eleven studies found no evidence of an association between mood, memory or cognitive function and chronic insomnia. Cumulatively, the measures of cognitive function were vigilance, proof-reading, reaction time, motor performance, concentration, divided attention, recent memory, audio/verbal patterns, psychomotor function, words heard and repeated, free recall, alertness and concentration.

We did not identify any studies that provided data relevant to the relationship between accidents or falls in the elderly and chronic insomnia, nor did we find evidence on the direct and indirect costs associated with the disorder.

What treatments are used for the management of chronic insomnia in adults and what is the evidence regarding their safety, efficacy and effectiveness?

One hundred and sixteen studies were relevant to the management of chronic insomnia; 34 studies were considered of high quality, 68 studies were considered of moderate quality and 14 studies were considered of low quality. All studies were described as randomized, while only 91 studies were described as double-blind. Seventy-eight studies provided a description of withdrawals and dropouts. Only nine studies described an appropriate method to generate the sequence of randomization, and 41 studies described an appropriate method of double-blinding. All other studies did not describe the method to generate the sequence of randomization, or the method of double-blinding. Only nine studies had adequate concealment of treatment allocation; for the remaining 107 studies, the adequacy of concealment was unclear. One hundred and four studies reported on sleep onset latency and only 33 studies reported on wakefulness after sleep onset, the outcomes of highest priority in this review. Regarding the other outcomes of interest in this review, 33 studies reported on sleep efficiency, 71 studies reported on total sleep time, 66 studies reported on sleep quality and only one study reported on quality of life.

Only 51 studies provided information on source of funding; 38 studies received private funding, 10 studies received government funding, two studies received academic funding, and one study received foundation funding. The majority of studies did not provide information on the role of the funding organization; however, only two out of 38 studies that reported receiving private funding explicitly stated that the funding organization was involved in data analysis and/or research design and selection of investigators.

The majority of studies had a parallel design. For studies in which there was a discrepancy between the number of participants enrolled and analyzed, it was often unclear whether an intent-to-treat analysis had been conducted. The majority of studies used sleep diary to assess sleep outcomes, and a number used both sleep diary and polysomnography to assess outcomes. Of the 111 studies that reported a treatment length, it ranged from one day to six months, with a median of three weeks. Of the 25 studies that reported a follow-up period, it ranged from one week to three years, with a median of 6 months.

The duration of chronic insomnia suffered by participants ranged from two months to 51 years, based on the 54 studies that provided a range. The age range of the population was 15-95 years, based on the 84 studies that provided a range; only two studies included participants under the age of 18 years old. Of the 111 studies that reported on the gender distribution of the population, 102 studies had a mixed gender population, while five studies had an all-female population and four studies had an all-male population. The inclusion criteria of nine studies were designed to select individuals with a psychiatric illness, including individuals with depression, dysthymic disorder, dementia, schizophrenia, personality disorder, myocolonus, anxiety disorders, Pick's disease, alcoholic psychoses, Huntington chorea, and cerebral laceration and contusion.

The studies were categorized according to intervention: benzodiazepines (n=51), non-benzodiazepines (n=36), antidepressants (n=7), complementary and alternative care (n=14),

relaxation therapy (n=15), cognitive/behavioral therapy (n=18), alcohol (n=1), barbiturates (n=2), hormones (n=1) and LEET therapy (n=1). Complementary and alternative care had two studies on L-tryptophan, 8 studies on melatonin and 4 studies on valerian. A number of studies fell under the general category of combination treatment (n=8). A given study could be relevant to more than one category. The number of participants analyzed in the efficacy analysis (sleep onset latency only) was as follows: benzodiazepines (n=1858), non-benzodiazepines (n=4169), antidepressants (n=298), L-tryptophan (n=47), melatonin (n=103), valerian (n=51), relaxation therapy (n=384), cognitive/behavioral therapy (n=276), alcohol (n=11), barbiturates (n=93), hormones (n=49) and LEET therapy (n=97). The number of participants analyzed in the safety analysis was as follows: benzodiazepines (n=3800), non-benzodiazepines (n=5485), antidepressants (n=288), complementary and alternative care (n=87), relaxation therapy (n=0), cognitive/behavioral therapy (n=0), alcohol (n=0), barbiturates (n=48), hormones (n=0) and LEET therapy (n=0).

Benzodiazepines

Sleep onset latency. Meta-analysis of the 32 studies that compared the effects of benzodiazepines and placebo on sleep onset latency (SOL) showed a statistically significant, albeit modest, difference of 16.5 minutes in favour of benzodiazepines (Figure 1). While there was substantial heterogeneity among the studies, all but two studies had a point estimate that favoured benzodiazepines. The heterogeneity was due more to different estimates of how effective the drugs were than as to whether or not they were superior to placebo. The study estimates ranged from about 65 minutes improvement in SOL to no difference.

Table 6 lists all of the sub-group analyses conducted for sleep onset latency. Nine different types of benzodiazepines were examined by the studies. With the exception of nitrazolam (which had a significantly higher estimate than all other drugs except flunitrazepam, flurazepam, and triazolam, but was examined by only one study) all drug types had SOL estimates between 24 and 10 minutes. The four studies that examined patients with a psychiatric illness showed a mean SOL difference of about 26 minutes, 10 minutes more than the remainder of the studies that had patients without a psychiatric illness (not statistically significant). The two studies that had results for long-term treatment showed a nearly identical estimate to those with results for short-term treatment. Similarly, age had little impact on SOL, with a 19-minute difference for elderly patients compared to a 15-minute difference for adult patients. There were only three studies that examined solely male patients and only one study that examined solely female patients. These studies were not very different from each other or the remaining studies. Finally, subdividing the studies by method of measurement of outcomes showed that those studies that used a sleep diary to measure SOL had a significantly greater efficacy estimate than those that used polysomnography (about 18 minutes compared to 7 minutes). The sub-groups of drug type, psychiatric illness, age and method of measurement had a Deeks' chi-square *P*-value less than 0.05, indicating that heterogeneity was significantly reduced by the sub-group.

Analysis of the studies by quality revealed that the high quality studies showed a slightly stronger estimate of SOL difference (19 minutes) than the moderate quality studies (14 minutes) (there were no low quality studies). Although the difference is not statistically significant, Deeks' chi-square shows that this sub-grouping significantly reduced heterogeneity.

Although both Begg's (*P*-value = 0.81) and Duval's (no studies added) tests indicated no publication bias non-parametrically, Egger's test (p-value < 0.001) showed significant

asymmetry in the funnel plot. This finding is also confirmed by a visual inspection of the funnel plot (Figure 2). The finding may indicate that the efficacy estimate given by the meta-analysis may in fact overestimate true efficacy, due to possible unpublished studies with non-significant results.

Wakefulness after sleep onset. Only eight benzodiazepine studies reported data on wakefulness after sleep onset (WASO). They revealed an average 23-minute improvement in WASO in the benzodiazepine patients as compared to the placebo patients (Figure 3). This result was statistically significant. Although there was substantial heterogeneity in this estimate, seven of the eight studies showed a point estimate that favoured treatment.

Other efficacy outcomes. Three other estimates of efficacy were measured, and the results can be viewed in Table 7. All outcomes showed statistically significant results that favoured benzodiazepines over placebo. Benzodiazepines increased sleep efficiency over placebo by an average of 6.3 percent and increased total sleep time by an average of 39 minutes. Sleep quality also showed a large difference between the groups with the benzodiazepines group having a standard mean difference (SMD) that was 0.8 standard deviations larger than placebo. Heterogeneity was negligible for sleep efficiency, substantial for total sleep time, and moderate for sleep quality.

Safety. The benzodiazepines showed a significantly greater proportion of adverse events than did placebo, although the meta-analysis showed substantial heterogeneity (Table 7). The risk difference estimates had a range of (0.01, 0.30) and an interquartile range of (0.08, 0.22) across interventions. The pooled risk-difference of 0.15 translates into a number needed to harm of seven patients (95% CI: 5, 10).

The most commonly reported adverse events of benzodiazepine use were somnolence (n=27 studies), headache (n=18), dizziness (n=16), nausea (n=11) and fatigue (n=11). There were no reports of falls, injury or death.

Non-benzodiazepines

Sleep onset latency. Twenty-nine studies on non-benzodiazepines showed a statistically significant difference of about 18 minutes in sleep onset latency compared to placebo (Figure 4). This difference is similar to the one reported for benzodiazepines. Again, similar to benzodiazepines, there was substantial heterogeneity among the studies, but all studies had a point estimate that favoured non-benzodiazepines. The study estimates ranged from about 67 minutes improvement to 4 minutes improvement in SOL.

The results for the sub-group analyses for sleep onset latency can be viewed in Table 8. Four different types of non-benzodiazepines were examined by the studies. The four different drugs examined ranged in their efficacy from a 31-minute improvement (zopiclone) to a 13-minute improvement (zolpidem). Deeks' chi-square test showed that this sub-grouping resulted in a significant reduction in heterogeneity. All of the other sub-groups examined did not show significant reductions in heterogeneity. For psychiatric illness, only one study had patients with such an illness, and that study showed a significantly shorter improvement in SOL. For length of treatment, the short-term and long-term studies had nearly identical improvements, as did the studies for adult and elderly patients. For gender, there was one study that examined an all-male

population and one study that examined an all-female population. Although the results differed from the overall average (less effective for males and much more effective for females), there was not enough data to draw any firm conclusions (no statistically significant differences). Finally, the studies that used polysomnography to estimate sleep onset latency were not different from those that used a sleep diary.

The high quality studies had an SOL estimate (30 minutes) that was significantly greater than the estimate for moderate quality studies (14 minutes) (there were no low quality studies), as was the case with the benzodiazepines. However, this sub-grouping did not significantly reduce heterogeneity.

Only Duval's test (no studies added in the trim and fill) showed no evidence of publication bias. Begg's (*P*-value = 0.01) and Egger's (*P*-value = 0.01) tests both showed evidence of funnel plot asymmetry, as did a visual examination of the plot (Figure 5). This finding suggests a possible overestimation of the efficacy in terms of SOL of non-benzodiazepines in our meta-analysis.

Wakefulness after sleep onset. Nine studies reported on WASO comparing non-benzodiazepines to placebo. The studies found that non-benzodiazepines decreased WASO by an average of about 13 minutes, which was statistically significant. Heterogeneity was substantial, caused mostly by one study, whose estimate was very different from the others (Figure 6).

Other efficacy outcomes. Four other estimates of efficacy were measured, and their results can be viewed in Table 9. All outcomes showed statistically significant results that favoured non-benzodiazepines over placebo. Sleep efficiency was increased in non-benzodiazepines by about 6 percent, while total sleep time was increased by about 28 minutes. Both sleep quality and quality of life showed moderate improvements in non-benzodiazepines compared to placebo with SMDs of 0.48 and 0.45, respectively. Heterogeneity was negligible for sleep efficiency, moderate for total sleep time, and substantial for sleep quality.

Safety. The non-benzodiazepines showed a significantly greater proportion of adverse events than did placebo, although the meta-analysis showed substantial heterogeneity (Table 9). The risk-difference had a range of (0.00, 0.15) and an interquartile range of (0.05, 0.08) across interventions. The pooled risk-difference of 0.05 translates into a number needed to harm of 20 patients (95% CI: 11, 100).

The most commonly reported adverse events of non-benzodiazepine use were headache (n=16 studies), dizziness (n=14), nausea (n=13) and somnolence (n=13). Accidental injury was reported in only one study, although there was no difference in the frequency of this event between experimental and control groups.

Antidepressants

Sleep onset latency. There were six studies that examined the effect of antidepressants (doxepin, pivagabine, trazodone and trimipramine) on sleep onset latency. They showed a small but statistically significant difference of about 7 minutes in sleep onset latency compared to placebo (Figure 7). The heterogeneity in this estimate was minimal and all six studies had an estimate that favoured the drug. The study estimates ranged from about 17 minutes improvement in SOL to no difference.

The results of sub-group analyses for sleep onset latency can be viewed in Table 10. All six studies were of mixed gender and featured only adults, so no sub-group analysis on gender or age was performed. Of the comparisons that were made, none significantly reduced heterogeneity, despite some marked differences in point estimates. This finding was mainly due to the low number of studies: most categories had a sub-group of only one study and method of measurement had a sub-group of only two studies. None of the differences in point estimates were statistically significant.

The one high quality study had an SOL estimate (17 minutes) that was higher than the estimate for the moderate quality studies (7 minutes) (there were no low quality studies). This sub-grouping did not significantly reduce heterogeneity, and the difference between estimates was not significant.

Since only six studies were included in this analysis, there were too few studies to perform any meaningful tests of publication bias.

Wakefulness after sleep onset. Three studies reported on WASO comparing antidepressants (doxepin and trazodone) to placebo. The studies found that antidepressants decreased WASO by an average of about 11 minutes, which was statistically significant. Heterogeneity was negligible (Figure 8).

Other efficacy outcomes. Three other estimates of efficacy were measured (no studies included an analysis of quality of life), and their results can be viewed in Table 11. All outcomes showed statistically significant results that favoured antidepressants over placebo. Sleep efficiency was increased in the antidepressant group by about 13.8 percent, while total sleep time was increased by about 53.1 minutes. Sleep quality showed a moderate increase for antidepressants of about 0.63 on the SMD scale. Heterogeneity was negligible for sleep efficiency and substantial for both total sleep time and sleep quality.

Safety. The antidepressants showed a significantly greater proportion of adverse events than placebo, and the meta-analysis showed negligible heterogeneity (Table 11). The risk-difference had a range of (-0.07, 0.13) and an interquartile range of (0.01, 0.11). The pooled risk-difference of 0.09 translates into a number needed to harm of 11 patients (95% CI: 6, 100).

The most commonly reported adverse events with antidepressant use were somnolence (n=4), headache (n=3), dizziness (n=3), and nausea (n=3). There were no reports of falls, injury or death.

Complementary and alternative care

There were three different types of complementary and alternative therapies observed in our included studies: L-tryptophan, melatonin, and valerian. These three substances were considered too different clinically to combine, and thus their results will be considered separately.

<u>L-tryptophan</u>

Sleep onset latency. Only two studies reported data for l-trytophan versus placebo and the results for sleep onset latency can be seen in Figure 9. The two studies showed an average reduction in SOL of 11 minutes, but the result was not significant, and the heterogeneity between the two

studies was substantial. There were too few studies to do any meaningful tests for publication bias. No other outcomes of interest were reported for L-tryptophan (Table 12). The two studies used different methods to measure sleep onset latency. The study that used polysomnography showed a significant effect of L-tryptophan (-20.1 minutes; 95% CI: -33.6, -6.6), while the study that used sleep diary did not (2.9 minutes; 95% CI: -21.6, 27.4). However, the difference between the two studies was not statistically significant.

Melatonin

Sleep onset latency. There were 8 studies on melatonin that examined sleep onset latency. Similar to the antidepressants, this category of intervention showed a small but statistically significant difference of about 8 minutes in sleep onset latency compared to placebo (Figure 9). The heterogeneity in this estimate was moderate, and all but two of the studies had an estimate that favoured the drug. The study estimates ranged from about 20 minutes improvement in SOL to 10 minutes detriment. When the eight studies were grouped by method of measurement, some differences in efficacy estimates were observed among the groups. The estimate for polysomnography (-3.6 minutes; 95% CI: -8.8, 1.6) was significantly different from the estimate for actigraphy (-16.7 minutes; 95% CI: -25.0, -8.3). Neither estimate was significantly different from the estimate for sleep diary (5.1 minutes; 95% CI: -20.0, 30.2).

No publication bias was immediately apparent from the funnel plot (Figure 10), and both Begg's test (*P*-value = 0.90) and Egger's test (*P*-value = 0.21) did not show significant asymmetry. However, Duval's trim and fill test did add one study to the meta-analysis and slightly increased the efficacy estimate (-8.7 minutes; 95% CI: -14.9, -2.5).

Wakefulness after sleep onset. Five studies reported on WASO comparing melatonin to placebo. The studies found that melatonin decreased WASO by an average of about 10 minutes, but this difference was not statistically significant. Heterogeneity was substantial, with two studies indicating a significant effect in favour of melatonin, while the other three studies all had estimates on the side of the null favouring placebo (Figure 11).

Other efficacy outcomes. Three other estimates of efficacy were measured for melatonin versus placebo (no studies included an analysis of quality of life), and their results can be viewed in Table 13. None of the three outcomes showed statistically significant results. The point estimates for sleep efficiency and total sleep time were 3 percent and 6 minutes, respectively. Sleep quality had a small efficacy difference of 0.3 standard deviations. Heterogeneity was substantial for both sleep efficiency and total sleep time, while it was negligible for sleep quality.

Safety. The melatonin studies did not show any significant difference in number of adverse events versus placebo (Table 13), with an estimated risk difference of 0.09. Heterogeneity among studies was moderate.

Valerian

Sleep onset latency. There were three studies on valerian that examined sleep onset latency. The studies showed a small average difference between valerian and placebo (1 minute), which was not statistically significant (Figure 9). The heterogeneity in this estimate was substantial with

two studies favouring valerian and the third being well on the side of placebo. The study estimates ranged from about 17 minutes improvement in SOL to 23 minutes detriment. There were too few studies to do any meaningful tests for publication bias. When the studies were grouped by method of measurement, differences among groups were observed. The estimate for polysomnography (9.5 minutes; -11.3, 30.3) was significantly different from the estimate for sleep diary (-16.0 minutes; 95% CI: -29.5, -2.5).

Wakefulness after sleep onset. Only one study reported on WASO comparing melatonin to placebo, but it did find a difference of 8 minutes between the groups, which favoured valerian and was statistically significant (Figure 11).

Other efficacy outcomes. Three other estimates of efficacy were measured for valerian versus placebo (no studies included an analysis of quality of life), and their results can be viewed in Table 14. None of the three outcomes showed statistically significant results. The point estimates for sleep efficiency and sleep onset latency were very small at 0.1 percent and 1 minute, respectively. Sleep quality had a large efficacy difference of 1.38 standard deviations, but, as mentioned, it was not statistically significant. Heterogeneity was negligible for sleep efficiency and substantial for sleep quality.

Safety. The valerian studies did not show any significant difference in number of adverse events versus placebo (Table 14), with an estimated risk difference of -0.06, which actually favoured valerian. Heterogeneity among studies was substantial.

Relaxation therapy

Sleep onset latency. There were 13 studies on relaxation therapy that examined sleep onset latency. Meta-analysis showed a pooled difference of 15 minutes favouring therapy over placebo (Figure 12). This result was not statistically significant. The heterogeneity in this estimate was extremely high (I^2: 96 percent), although all but three of the studies had an estimate that favoured the drug. The study estimates ranged from about 60 minutes improvement in SOL to 14 minutes detriment.

The results for sub-group analyses for sleep onset latency in relaxation therapy can be viewed in Table 15. All 13 studies analysed patients without psychiatric illnesses and used sleep diary to measure SOL, so no sub-group analyses on these variables were performed. The other four sub-groups examined yielded highly significant reductions in heterogeneity. Despite this finding, many of the individual sub-groups had very high heterogeneity. Subdividing by type of relaxation therapy, efficacy estimates ranged from 60 minutes improvement to 5 minutes improvement. Only breathing training, group relaxation, and hypnotic relaxation showed statistically significant efficacy despite each sub-group containing only one trial. The short-term effects of relaxation therapy on SOL proved significantly greater than the long-term effects (22 minutes improvement versus 2 minutes detriment). There was only one study of elderly patients, and it showed no improvement in sleep onset latency compared to the studies on adults, which showed an improvement of 16 minutes. This difference was not significant. Finally, one study had only female participants (there were no studies of all-male populations), and it had a lower efficacy than the remainder of the studies (6 minutes compared to 16 minutes). This difference was non-significant.

The moderate quality studies had a slightly higher (but not significantly higher) efficacy estimate than the low quality studies (18 minutes compared to 9 minutes) (there were no high quality studies). This sub-grouping significantly reduced heterogeneity.

No publication bias was immediately apparent from the funnel plot (Figure 13). Both Egger's test (*P*-value = 0.49) and Duval's trim and fill (no studies added) did not show significant asymmetry. However, Begg's test did show some evidence of asymmetry (*P*-value = 0.004). This finding is somewhat surprising considering that Begg's test is usually the most conservative test (i.e. it is unusual to have a significant Begg *P*-value and a non-significant Egger *P*-value).

Wakefulness after sleep onset. Only three studies reported on WASO comparing relaxation therapy to placebo. Their combined efficacy estimate was very small (-2 minutes) and favoured relaxation therapy (Figure 14). The result was not statistically significant. Heterogeneity was minimal.

Other efficacy outcomes. Three other estimates of efficacy were measured for relaxation therapy versus placebo (no studies included an analysis of quality of life), and their results can be viewed in Table 16. Only total sleep time showed a statistically significant result, with an average improvement in the relaxation group of 23 minutes. Sleep efficiency had an estimate of 0.4 percent, while sleep quality showed a small estimate of 0.4 standard deviations. Neither estimate was statistically significant. Heterogeneity was negligible for sleep efficiency and total sleep time, but was substantial for sleep quality.

Safety. None of the trials of this category reported on adverse events.

Cognitive/behavioral therapy

Sleep onset latency. There were nine studies on cognitive/behavioral therapy (CBT) that examined sleep onset latency. Meta-analysis showed a pooled difference of 5 minutes favouring therapy over placebo (Figure 15). This result was not statistically significant. The heterogeneity in this estimate was minimal, although three of the nine studies had an estimate that favoured placebo. The study estimates ranged from about 30 minutes improvement in SOL to 19 minutes detriment.

The results of sub-group analyses for sleep onset latency in CBT can be viewed in Table 17. All nine studies were of mixed gender, analysed patients without psychiatric illnesses and used sleep diary to measure SOL, so no sub-group analyses on gender, psychiatric illness or method of measurement were performed. Of the three sub-groups examined, none showed significant reduction in heterogeneity. Subdividing by type of intervention, stimulus control and thought non-suppression had slightly higher estimates than multi-component CBT, paradoxical intention, and sleep compression, but the differences were not significant. Similarly, the short-term and long- term differences were comparable. There was only one study that examined elderly participants, and its efficacy estimate was not very different from the adult studies.

The low quality studies had a slightly higher efficacy estimate than the moderate quality studies (8 minutes compared to 1 minute), but the difference was not statistically significant (there were no high quality studies). This sub-grouping did not significantly reduce heterogeneity.

There was no evidence of publication bias. The funnel plot did not appear to be asymmetric (Figure 16), and Begg's (*P*-value = 0.53), Egger's (*P*-value = 0.37) and Duval's (no studies added) tests all confirmed this finding.

Wakefulness after sleep onset. Eight studies reported on WASO comparing CBT to placebo. Their combined efficacy estimate showed that CBT improved WASO by an average of 18 minutes (Figure 17). The result was statistically significant, although heterogeneity was substantial. Despite the high heterogeneity, all but one study showed a result that favoured CBT.

Other efficacy outcomes. Three other estimates of efficacy were measured for CBT versus placebo (no studies included an analysis of quality of life), and their results can be viewed in Table 18. Both sleep efficiency and sleep quality showed statistically significant improvements for CBT over placebo. Sleep efficiency improved by an average of 6 percent, while sleep quality showed an improvement of 0.38 standard deviations. Total sleep time showed no difference. Heterogeneity was negligible for sleep quality, but substantial for both the sleep efficiency and total sleep time estimates.

Safety. None of the CBT trials reported on adverse events.

Indirect comparisons

Efficacy. Table 19 shows the results of the pair-wise indirect comparisons of sleep onset latency for each of the four pharmacological treatment categories: benzodiazepines, non-benzodiazepines, antidepressants, and complementary and alternative care, the latter divided into L-tryptophan, melatonin, and valerian. Both benzodiazepines and non-benzodiazepines proved significantly more efficacious than antidepressants and melatonin. None of the other comparisons showed significant differences. Comparing the two non-pharmacological treatment categories (relaxation therapy and cognitive/behavioral therapy) also showed no significant difference (-10 min.; 95% CI: -25.7, 5.7).

Safety. Table 20 shows the results of indirect comparisons of adverse events for the four main pharmacological treatment categories that provided relevant data: benzodiazepines, non-benzodiazepines, antidepressants and complementary and alternative care, the latter divided into melatonin and valerian (there was no safety data for L-tryptophan). The only significant comparison is that of benzodiazepines and non-benzodiazepines, where the latter treatment category was found to be significantly safer than the former in terms of number of adverse events. Note that despite the fact that valerian had the lowest point estimate, the larger confidence interval prevented a meaningful comparison of its safety relative to the other treatment categories.

Other treatments

There were some studies that examined treatments that did not fall under any of the preceding six treatment categories. They are outlined here.

Barbiturates. There were two trials that examined barbiturates versus placebo. Four different types of barbiturates were examined in the trials: glutethimide, methyprylon, phenobarbitol and secobarbitol.

Only two outcomes (sleep onset latency and adverse events) were analysed in the two trials. The results can be viewed in Table 21. Neither SOL nor number of adverse events differed significantly from placebo in the meta-analyses.

Hormones. One trial examined the efficacy of two different hormones (climodein and estradiol) in women with a diagnosis of insomnia related to post-menopausal syndrome. Four outcomes (sleep onset latency, sleep efficiency, total sleep time, and sleep quality) were examined (Table 22). Sleep efficiency and sleep quality showed a statistically significant improvement (5 percent and 22 minutes respectively) with the hormones, while sleep onset latency and total sleep time showed an improvement that was not significant.

Alcohol. One trial examined the efficacy of ethanol versus placebo. The three outcomes examined (sleep onset latency, WASO, and sleep efficiency) had non-significant differences between treatment and placebo (Table 23). All three efficacy estimates favoured placebo, although the differences were not significant.

Low energy emission therapy. One study compared the effect of low energy emission therapy (LEET) with placebo for insomniacs. The results for the four efficacy (sleep onset latency, WASO, sleep efficiency, and total sleep time) and one safety outcome can be viewed in Table 24. Statistically significant improvements in both sleep efficiency and total sleep time (11 percent and 56 minutes, respectively) were found. The estimates for sleep onset latency and WASO were not significant, but did favour the LEET intervention. There was also no evidence that adverse events were higher for LEET than for placebo.

Combination treatments

This section will outline the results of eight trials that employed various combinations of the above treatments. Unlike all other sections of this review, we did not limit ourselves to comparing these treatments to placebo. All comparisons within the trials were examined. Ten different comparisons resulted and are outline below. The combination therapy in each case is always considered to be the "treatment arm."

Relaxation therapy and cognitive behavioral therapy versus placebo. There were four studies included in a meta-analysis of a combined relaxation therapy and CBT treatment versus placebo. The results for four outcomes (SOL, WASO, total sleep time, and sleep quality) can be viewed in Table 25. Although all estimates favoured treatment, only the result for sleep onset latency proved statistically significant, with an estimated improvement of about 22 minutes. Interestingly, this is nearly identical to the sum of the calculated effect from the meta-analyses of each of these interventions alone.

Relaxation therapy and cognitive behavioral therapy versus relaxation therapy. Two studies compared relaxation therapy and CBT treatment with relaxation therapy alone. Table 26 contains the results for the four reported outcomes (SOL, WASO, total sleep time, and sleep

quality). None of the results were statistically significant with only sleep onset latency favouring the combined treatment. The other three outcomes showed an efficacy estimate that favoured relaxation alone, although as mentioned, none were significant.

Relaxation therapy and cognitive behavioral therapy versus cognitive behavioral therapy. Two studies compared relaxation therapy and CBT treatment with CBT alone. None of the results for the four outcomes (SOL, WASO, total sleep time, and sleep quality) were statistically significant (Table 27). Two of the outcomes (SOL and sleep quality) favoured the combined treatment, while the other two outcomes (WASO and total sleep time) favoured CBT alone.

Relaxation therapy and cognitive behavioral therapy versus benzodiazepine. One study compared relaxation therapy and CBT versus a benzodiazepine. The results for SOL, WASO, and sleep quality can be viewed in Table 28. All three outcomes favoured the benzodiazepine over the combined treatment. The difference was not significant for SOL or WASO, but it was significant for sleep quality (a large difference of about 1.5 SDs).

Benzodiazepine and cognitive behavioral therapy versus placebo. Table 29 lists the results for the four outcomes (SOL, WASO, sleep efficiency, and total sleep time) that were reported in comparisons of benzodiazepine and CBT versus placebo. Two studies were meta-analysed. All four outcomes favoured the combined treatment, and the difference was significant for sleep efficiency (13 percent improvement).

Benzodiazepine and cognitive behavioral therapy versus benzodiazepine. One study compared the combined treatment of a benzodiazepine and CBT versus the benzodiazepine alone. The results for three outcomes (WASO, sleep efficiency and total sleep time) can be viewed in Table 30. The result for sleep efficiency was statistically significant in favour of the combined treatment (7 percent improvement). WASO favoured the combined treatment but not significantly. Total sleep time favoured the benzodiazepine alone, but the difference was not significant.

Benzodiazepine and cognitive behavioral therapy versus cognitive behavioral therapy. The comparison of a benzodiazepine and CBT versus CBT alone was available through one study. The results of the three outcomes (WASO, sleep efficiency, and total sleep time) can be viewed in Table 31. None of the results were significant and all had relatively small efficacy estimates.

Non-benzodiazepine and cognitive behavioral therapy taken in combination versus the same two treatments taken sequentially. One study examined the difference between the effects of a non-benzodiazepine taken simultaneously with CBT versus the same two treatments taken sequentially. The results for the two outcomes examined (sleep efficiency and total sleep time) can be viewed in Table 32. Neither result was significant.

Cognitive behavioral therapy and modafinil versus cognitive behavioral therapy. One study compared CBT combined with the stimulant modafinil versus CBT alone. Results for the three reported outcomes (SOL, WASO, and total sleep time) can be viewed in Table 33. None of the results are significant, and all three efficacy estimates favour CBT alone over the combined treatment.

Cognitive behavioral therapy and modafinil versus modafinil. CBT and modafinil was compared to modafinil alone in one study. The results of the three outcomes examined (SOL, WASO, and total sleep time) can be viewed in Table 34. All outcomes favoured the combined treatment, but none of them were significant.

What are the important future directions for insomnia-related research?

The response to this question appears under "Limitations and Future Research" in the Discussion section of the Evidence Report.

Flow Diagram 2. Study retrieval and selection

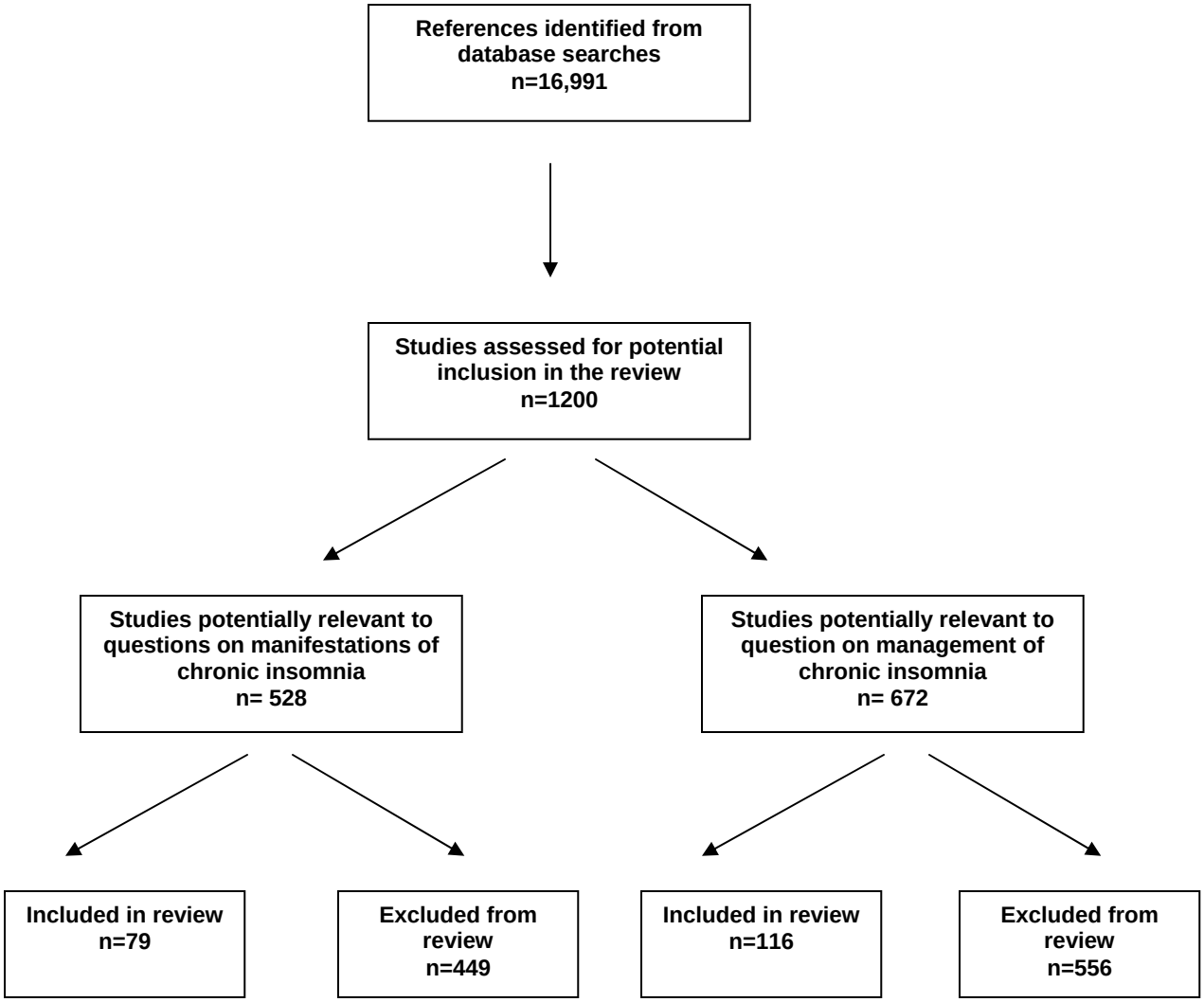


Table 3a. Prevalence of chronic insomnia in adults: general population

Author / Year Quality (score)	Study Design	Sampling Frame / Method	Method Of Data Collection	Participants	Duration of Sleep Complaints, Definition of Cases and Comparison Groups	Gender	Age (years)	Response Rate / Follow-up Rate	Prevalence
Ancoli-Israel, S / 1999 Moderate (3/8)	Cross-sectional	Phone list/ random	Phone interview (non-validated)	General population	Sleep complaints on a frequent basis; population referred to as "chronic" insomniacs.	Not specified	Range: 18-65	51.2%	9% (95%CI: 7.23-10.77)
Bixler, EO / 1979 Moderate (3/8)	Cross-sectional	Census data/ random	Face-to face interview (non-validated)	General population	Current or past sleep disorders; prevalence reported for "long-term" insomniacs.	**Male:** 44% **Female:** 56%	Over 18	Not specified	**Lifetime:** (Current or past insomnia): 42.5% (95%CI: 39.4-45.5). Current chronic insomnia: 32.2% (95%CI: 29.3-35.0).
Bixler, EO / 2002 Moderate (3/8)	Cross-sectional	Phone list/ random	Self-reported Qu (non-validated)	General population	Sleep complaint for at least one year.	**Male:** 42.6% **Female:** 57.4%	Over 20	66.6%	**Point:** (Insomnia during at least 1 year): 7.5% (95%CI: 6.27-8.73).
Broman, JE / 1996 High (6/8)	Cross-sectional	Population register/ random	Self-reported Qu (validated)	General population	Sleep complaints during the last three months.	**Male:** 46.9% **Female:** 53.1%	Range: 20-64	68%	**Three-month:** (Chronic sleep loss): 12% (95%CI: 8.8-15.2).
Hajak, G / 2001 High (6/8) - cross sectional High (7/9) - case control	Cross-sectional and Case-Control (matched)	Census data/ random	Face-to face interview (non-validated)	Cross-sectional: General population Case-control:: **Cases**: severe insomnia **Controls**: normal sleepers	Cross-sectional: Insomnia disorders during the previous month (DSM-III-R and DSM-IV criteria). Severe insomniacs had sleep complaints during the previous month. Case-control: **Cases**: Severe insomniacs as defined above. **Controls**: No sleep complaints.	Cross-sectional: **Male:** 46.8% **Female:** 53.1%	Over 18	Not specified	**One-month:** (Sleep disturbances) 45% (95%CI: 42.7-47.2). (Severe insomnia): 4% (95%CI: 3.2-4.8).

Table 3a. Prevalence of chronic insomnia in adults: general population (continued)

Author / Year Quality (score)	Study Design	Sampling Frame / Method	Method Of Data Collection	Participants	Duration of Sleep Complaints, Definition of Cases and Comparison Groups	Gender	Age (years)	Response Rate / Follow-up Rate	Prevalence
Hetta, J / 1999 Low (0/8)	Cross-sectional	Not specified/ non-random (quota method)	Not clearly specified	General population	Sleep complaints over the past month (DSM-III-R criteria modified).	Not specified	Over 18	25%	**One-month:** 31% (95%CI: 27-35).
Hidalgo, MP / 2002 Moderate (5/8)	Cross-sectional	Not specified	Self-reported Qu (validated)	Medical students	Sleep complaints for at least one month during the past year.	**Male:** 58.2% **Female:** 41.8%	Range: 18-35	Not specified	**One-year:** (Sleep difficulties persisting for at least one month): 26% (95%CI: 21.3-30.6).
Kageyama, T / 1997 Moderate (6/8)	Cross-sectional	Residential registration information/ random sample of some districts, recruitment at block meetings in others	Self-admin Qu (non-validated)	Adult women living in urban areas	Sleep complaints for at least one month (ICD-10 and DSM-IV criteria).	All women	Range: 20-80	Varied between district 51-59%	**Point:** 11.2% (95% CI 10.2, 12.2)
Kageyama, T / 2001 Moderate (5/8)	Cross-sectional	Not specified	Self-admin Qu (non-validated)	Hospital nurses	Sleep complaints for at least one month.	Not specified	Range: 24-59	Not specified	**Point:** 29.2% (95% CI 28.7, 29.7)
Kawada, T / 2003 High (6/8)	Cross-sectional	Map/ Not specified	Self-reported Qu (non-validated)	Women from the general population	Sleep complaint for at least one month (ICD-10 and DSM-IV criteria).	All female	Range: 20-80	50.4%	**Point:** (DSM-IV criteria for at least one month): 8.8% (95%CI: 6.6-10.9).

Table 3a. Prevalence of chronic insomnia in adults: general population (continued)

Author / Year Quality (score)	Study Design	Sampling Frame / Method	Method Of Data Collection	Participants	Duration of Sleep Complaints, Definition of Cases and Comparison Groups	Gender	Age (years)	Response Rate / Follow-up Rate	Prevalence
Leger, D / 2000 High (6/8)	Cross-sectional	Census data/ random	Face-to face interview (non-validated)	General population	Sleep complaint for at least a month (DSM-IV criteria). "Severe insomnia" considered as "chronic insomnia" if sleep complaints were over a four-month period.	**Male:** 47% **Female:** 53%	Over 18	85.2%	**One-month:** (Insomnia) 19% (95%CI: 18.3-19.6). (Severe/chronic insomnia): 9% (95%CI: 8.51-9.49).
Martikainen, K / 2003 Moderate (5/8)	Cross-sectional	Not specified **/** random	Self-reported Qu (non-validated)	General population	Sleep complaints during the previous three months.	**Male:** 42.2% **Female:** 57.8%	Range: 41-55	52.6%	**Three-month:** 14% (95%CI: 11.3-16.7).
Millar, A / 2004 High (6/9)	Cross sectional case-control	Not applicable	Self-reported Qu (validated), sleep laboratory investigations	**Cases:** remitted Bipolar I disorder subjects **Controls:** healthy subjects	**Cases:** DSM-IV criteria for Bipolar I disorder. **Controls:** No psychiatric disorders.	Cases: **Male**: 8 **Female**: 11 Controls: **Male**: 8 **Female**: 11	**Cases:** range: 26-68 **Controls:** range: 27-67	**Cases:** 59.3% (follow-up) **Controls:** Not specified	Percentage of reported longstanding sleep disturbances (Sleep History Questionnaire): **Cases:** 100%. **Controls:** 21% (95%CI: 2.7-39.3).
Ohayon, MM / 2002 High (8/8)	Cross-sectional	Phone list/ random	Phone interview (validated)	General population	Insomnia complaints during the last year (DSM-IV criteria).	**Male:** 48.2% **Female:** 51.8%	Over 15	89.4%	**One-year:** (Insomnia symptoms)**:** 27.6% (95%CI: 26.2-28.9). (Insomnia disorder diagnoses): 7% (95%CI: 6.2-7.7).

Table 3a. Prevalence of chronic insomnia in adults: general population (continued)

Author / Year Quality (score)	Study Design	Sampling Frame / Method	Method Of Data Collection	Participants	Duration of Sleep Complaints, Definition of Cases and Comparison Groups	Gender	Age (years)	Response Rate / Follow-up Rate	Prevalence
Ohayon, MM / 2002 High (8/8)	Cross-sectional	Census data/ random	Phone interview (validated)	General population	Chronic insomnia diagnosed according to DSM-IV criteria.	**Male:** 48.2% **Female:** 51.8%	Over 18	78.2%	**Point:** Insomnia disorder diagnoses: 11.7%
Ohayon, MM / 1997 High (8/8)	Cross-sectional	Census data/ random	Phone interview (validated)	General population	Insomnia complaints for at least one month.	**Male:** 47.9% **Female:** 52.1%	Over 15	80.7%	**Point:** (Insomnia complaints lasting for at least one month): 15.3% (95%CI: 14.36-16.24)
Ohayon, MM / 2003 High (7/8)	Cross-sectional	Census data/ random	Phone interview (validated)	General population	Insomnia complaints for more than six months.	**Male:** 47.9% **Female:** 52.1%	Over 15	78.6%	**Point:** (Chronic insomnia lasting more than six months): 17.6% (95%CI: 16.9-18.21). (Insomnia lasting more than one month): 18.4% (95%CI: 17.78-19.02).
Ohayon, MM / 2000 High (7/8)	Cross-sectional	Census data/ random	Computer-ized phone interview (validated)	General population	Diagnoses of chronic sleep disorders according to DSM-IV criteria.	**Male:** 49.2% **Female:** 50.8%	Range: 19 -24	Not specified	**Point**: 5.4% (95% CI: 4.5, 6.4)
Ohayon, MM / 2001 High (7/8)	Cross-sectional	Census data/ random	Phone interview (validated)	General population	Chronic insomnia defined by both DSM-IV and ICSD criteria.	**Male:** 49.5% **Female:** 50.5%	Range: 19-24	Not specified	**Point**: 8.1% (95% CI: 7.4, 8.8).

Table 3a. Prevalence of chronic insomnia in adults: general population (continued)

Author / Year Quality (score)	Study Design	Sampling Frame / Method	Method Of Data Collection	Participants	Duration of Sleep Complaints, Definition of Cases and Comparison Groups	Gender	Age (years)	Response Rate / Follow-up Rate	Prevalence
Ohayon, MM / 2001 High (8/8)	Cross-sectional	Census data/ random	Telephone interview (validated)	General population	Sleep complaints for at least a month (DSM-IV criteria).	**Male:** 49% **Female:** 51%	Over 15	All countries, except Germany (68.1%) had participation rate of 80% or higher. Overall 81.0%	**Point:** 6.1% (95% CI 5.8, 6.4)
Ohayon, MM / 2002 High (8/8)	Cross-sectional	Phone lists/ random	Telephone interview (validated)	General population	Chronic insomnia diagnosed according to ICSD and DSM-IV criteria.	**Male:** 49.5% **Female:** 50.5%	Range: 15-90	91.4%	**Point:** 5% (95% CI 4.3, 5.7)
Riedel, BW / 2004 High (6/8)	Cross-sectional	Not specified/ random	Self-reported Qu (validated)	General population	Sleep complaints for at least six months (ICSD criteria).	**Male:** 49.3% **Female:** 50.7% - 390/769	Range: 20-98	43.4%	**Point:** 32.1% (95%CI: 28.8-35.3).
Rocha, FL / 2002 High (7/8)	Cross-sectional	Census data/ whole population studied	Face-to-face interview (validated)	Elderly from the general population	Sleep complaints during the last month.	**Male:** 38.9% **Female:** 61.1%	Over 60	87%	**One-month:** (Insomnia): 38.9% (95%CI: 34.6-41.3).
Rocha, FL / 2002 High (7/8)	Cross-sectional	Census data/ random	Face-to-face interview (validated)	General population	Sleep complaints in the last month.	**Male:** 44.3% **Female:** 55.7%	Over 18	87.3%	**One-month:** 35.4% (95%CI: 32.5-38.3).
Taylor, DJ / 2003 High (6/8)	Cross-sectional	Three-digit telephone prefixes/ random digit dialling	Sleep diaries and self-admin Qu	General population	Sleep complaints for at least six months.	**Male:** 49.4% **Female:** 50.6%	Range: 20-98	49%	**Point:** 19.6% (95% CI 16.8, 22.4)

Table 3a. Prevalence of chronic insomnia in adults: general population (continued)

Author / Year Quality (score)	Study Design	Sampling Frame / Method	Method Of Data Collection	Participants	Duration of Sleep Complaints, Definition of Cases and Comparison Groups	Gender	Age (years)	Response Rate / Follow-up Rate	Prevalence
Yeo, BKL / 1996 Moderate (3/8)	Cross-sectional	House registers/ random	Face-to face interview (non-validated)	General population	Sleep complaint for the past year.	**Male:** 50% **Female:** 50%	Range: 15-55	Not specified	**One-year:** 15.3% (95%CI: 13.8-16.73).

Abbreviations: **CI** = confidence interval; **DSM-III-R** = Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised; **DSM-IV** = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; **ICSD** = International Classification of Sleep Disorders; **MSK** = musculoskeletal injury; **Qu =** questionnaire; **rehab** = rehabilitation; **SCI** = spinal cord injury; **TBI** = traumatic brain injury

Table 3b. Prevalence of chronic insomnia in adults: outpatients of general practice

Author / Year Quality (score)	Study Design	Sampling Frame / Method	Method Of Data Collection	Participants	Duration of Sleep Complaints, Definition of Cases and Comparison Groups	Gender	Age (years)	Response Rate / Follow-up Rate	Prevalence
Hohagen, F / 1993 Moderate (4/8)	Cross-sectional	Not specified/ non-random (consecu-tive)	Self-reported Qu (non-validated)	Outpatients from general practices	Insomnia disorders during the last month (DSM-III-R criteria).	**Male:** 44.7% **Female:** 55.3%	Range: 18-65	97.9%.	**Six-month:** (Severe, moderate, and mild insomnia): 45.9% (95%CI: 44-48). (Severe): 18.7% (95%CI: 17.1-20.2).
Hohagen, F / 1994 Moderate (4/8)	Cross-sectional	Not specified / non-random (consecu-tive)	Self-reported Qu (non-validated)	Elderly outpatients from general practices	Sleep complaints (mild, moderate, and severe) for at least one month (DSM-III-R criteria).	**Male:** 28% **Female:** 72%	Over 65	97.5%	**Point:** (All DSM-III-R diagnoses of insomnia): 56.3% (95%CI: 50.9-61.6). (Severe DSM-III-R insomnia diagnosis): 23% (95%: 18.4-27.5).
Hohagen, F / 1994 Moderate (4/8)	Cross-sectional and prospective cohort	Not specified/ non-random (consecu-tive)	Self-reported Qu (non-validated)	Outpatients from general practices	Sleep complaints for at least one month.	Cross-sectional: **Male:** 44.7% **Female:** 55.3% Cohort: **Male**: 60.4%. **Female**: 39.6%	Range: 18-65	Cross-sectional: 97.9% Cohort: 42.2% (follow-up)	**One-month:** Cross-sectional: 31% (95%CI: 29.2-32.8). Cohort (Data after a four-month follow-up period: 86.9% (95%CI: 83.2-90.5). Remission rate: 19%-24% (for insomnia sub-groups).
Ishigooka, J / 1999 Moderate (5/8)	Cross-sectional	Not specified	Self-reported Qu (non-validated)	Outpatients from general hospitals	Long-term insomnia defined as sleep complaints for more than one month.	**Male:** 41.9% **Female:** 58.1%	Range: 15-65	88.3%	**Point:** (Insomnia lasting more than one month): 11.7% (95%CI: 10.9-12.4).

Table 3b. Prevalence of chronic insomnia in adults: outpatients of general practice (continued)

Author / Year Quality (score)	Study Design	Sampling Frame / Method	Method Of Data Collection	Participants	Duration of Sleep Complaints, Definition of Cases and Comparison Groups	Gender	Age (years)	Response Rate / Follow-up Rate	Prevalence
Kappler, C / 2003 Low (2/8)	Cross-sectional	Not specified	Self-reported Qu (non-validated)	Outpatients from general practices	Diagnosis of chronic insomnia (moderate and severe) according to DSM-III-R criteria.	**Male:** 49.9% **Female:** 50.1%	Range: 18-65	37.6%	**Point:** (DSM-III definition of severe/moderate insomnia): 27.3% (95%CI: 24.5-30.1).
Ohayon, MM / 1999 Moderate (5/8)	Cross-sectional	Not specified/ non-random	Face-to-face clinical interview (validated)	Outpatients from general practices	Chronic sleep disorders diagnosed according to DSM-IV criteria.	**Male:** 44.5% **Female:** 55.5%	Over 15	Not specified	**Point:** (Complaint of insomnia symptoms accompanied with sleep dissatisfaction): 16.0% (95%CI: 15.3-16.7).
Scochat, T / 1999 Low (1/8)	Cross-sectional	All patients presenting to participating family medicine clinics/ all asked to participate	Self-administration Qu (non-validated)	Patients consulting their primary care physician	**Normal sleepers**: no sleep complaints; **Occasional insomniacs**: sleep complaints on an occasional basis. **Chronic insomniacs**: sleep complaints on a frequent basis; chronic insomniacs defined as such.	**Male:** 42% **Female:** 58%	Range: 18-87	Not specified	**Point:** 19% (95% CI 14.5, 23.5)
Terzano, MG / 2004 Moderate (4/8)	Cross-sectional	List of general practitioner patients/ non-random	Face-to-face clinical interview (non-validated)	Patients presenting to their general practitioner for medical problems other than sleep disorders	Sleep complaints for at least one month.	**Male:** 39.1% **Female:** 60.9%	Over 18	Not specified	**Point:** (Sleep difficulties persisting for at least one month): 63.7% (95%CI: 62-65).

Abbreviations: **CI** = confidence interval; **DSM-III-R** = Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised; **DSM-IV** = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; **ICSD** = International Classification of Sleep Disorders; **MSK** = musculoskeletal injury; **Qu =** questionnaire; **rehab** = rehabilitation; **SCI** = spinal cord injury; **TBI** = traumatic brain injury

Table 3c. Prevalence of chronic insomnia in adults: clinical population

Author / Year Quality (score)	Study Design	Sampling Frame / Method	Method Of Data Collection	Participants	Duration of Sleep Complaints, Definition of Cases and Comparison Groups	Gender	Age (years)	Response Rate / Follow-up Rate	Prevalence
Braga-Neto, P / 2004 Low (2/8)	Cross-sectional	Not specified/ non-random (consecu-tive)	Face-to-face clinical interview (non-validated)	Patients with Parkinson's Disease	Sleep complaints over the last month.	**Male:** 64% **Female:** 36%	Range: 34-86	Not specified	**One-month:** 53.3% (95%CI: 42.8-63.8).
Fichtenberg, NL / 2002 Moderate (4/8)	Cross-sectional	Patients enrolled in outpatient rehab. clinics/ non-random (consecu-tive)	Self-reported Qu (validated), sleep diaries, clinical interview	Rehabilitation patients (TBI, SCI, MSK)	DSM-IV criteria	TBI**: Male**: 56% **Female**: 44%. SCI: **Male**: 76% **Female**: 24%. MSK: **Male**: 20% **Female**: 80%	**TBI:** mean±SD: 36.5±14.5 **SCI:** mean±SD: 38.2±13.5 **MSK:** mean±SD: 47.3±12.2	100%	**Point**: (By DSM-IV Criteria): 30% (95% CI 27.3, 42.7) of TBI patients.
Han, SY / 2002 Low (2/8)	Cross-sectional	Not specified	Self-reported Qu (non-validated)	Diabetic haemodialy-sis patients	Sleep complaints for at least two months (DSM-IV criteria modified).	**Male:** 61% **Female:** 39%	Range: 27-78	Not specified	**Point:** (Sleep difficulties for at least two months): 68.2% (95%CI: 58.2-78.2).
Leppavuori, A / 2002 Moderate (4/8)	Cross-sectional	Not specified / non-random (consecu-tive)	Face-to-face clinical interview (validated)	Stroke patients	Insomnia complaints for at least one month (DSM-IV criteria).	**Male:** 50.9% **Female:** 49.1%	Range: 55-85	Not specified	**Point:** (DSM-IV criteria of insomnia): 37.6% (95%CI: 31.9-43.3). (Insomnia complaints): 56.7% (95%CI: 50.9-62.5).

Table 3c. Prevalence of chronic insomnia in adults: clinical population (continued)

Author / Year Quality (score)	Study Design	Sampling Frame / Method	Method Of Data Collection	Participants	Duration of Sleep Complaints, Definition of Cases and Comparison Groups	Gender	Age (years)	Response Rate / Follow-up Rate	Prevalence
Millar, A / 2004 High (6/9)	Cross sectional case-control	Not applicable	Self-reported Qu (validated), sleep laboratory investigations	**Cases:** remitted Bipolar I disorder subjects **Controls:** healthy subjects	**Cases:** DSM-IV criteria for Bipolar I disorder. **Controls:** No psychiatric disorders.	Cases: **Male**: 8 **Female**: 11 Controls: **Male**: 8 **Female**: 11	**Cases:** range: 26-68 **Controls:** range: 27-67	**Cases:** 59.3% (follow-up) **Controls:** Not specified	Percentage of reported longstanding sleep disturbances (Sleep History Questionnaire): **Cases:** 100%. **Controls:** 21% (95%CI: 2.7-39.3).
Robbins, L / 1995 Moderate (4/8)	Retrospective cross-sectional	Long-term patients of headache clinic/ random	Face-to-face interview	Patients with migraines	Chronic insomnia assessed by qualitative judgement of the neurologist and patient.	**Male:** 20.4% **Female:** 79.6%	Range: 18-60	100%	**Point:** Sleep onset insomnia: 27% (95% CI 23.1, 30.9). Sleep maintenance insomnia: 26% (95% CI 22.1, 29.9)
Sabbatini, M / 2002 Moderate (3/8)	Cross-sectional	Not specified	Face-to-face interview (non-validated)	Haemodialysis patients	Sleep complaints for at least one month.	**Male:** 55.5% **Female:** 44.5%	Mean±SD: 61.0±14.4	Not specified	**Point:** 45% (95%CI: 41.3-48.7).
Savard, J / 2001 Moderate (4/8)	Cross-sectional	Not specified/ non-random (consecutive)	Self-reported Qu (non-validated) and phone interview (validated)	Women with metastatic breast cancer	Insomnia symptoms, insomnia syndrome and chronic insomnia syndrome defined by sleep complaints for at least six months (DSM-IV criteria).	All female	Range: 28-90	88%	**Point:** (Insomnia symptoms): 51.3% (95% CI: 45.7-56.9); (Insomnia syndrome): 19% (95%CI: 14.6-23.4); (Chronic Insomnia syndrome): 17.6% (95%CI: 13.3-21.9).

Abbreviations: **CI** = confidence interval; **DSM-III-R** = Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised; **DSM-IV** = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; **ICSD** = International Classification of Sleep Disorders; **MSK** = musculoskeletal injury; **Qu =** questionnaire; **rehab** = rehabilitation; **SCI** = spinal cord injury; **TBI** = traumatic brain injury

Table 4. Natural history of chronic insomnia in adults

Author/Year Quality (Score)	Study Design	Time Frame	Response Rate / Follow-up Rate	Participants	Duration Of Sleep Complaints	Gender	Age (years)	Natural History
Hohagen, F / 1994 Moderate (4/8)	Cross-sectional and pro-spective cohort	Four months	Response rate (cross-sectional): 97.9% Follow-up rate (cohort): 42.2%	Outpatients from general practices	Sleep complaints for at least one month	**Cross-sectional:** Male: 44.7% Female: 55.3% **Cohort:** Male: 60.4% Female: 39.6%.	Range:18-65	**Cross-sectional**: One-month prevalence: 31% (95%CI: 29.2-32.8). **Cohort:** Once-month prevalence within insomniac group identified in cross-sectional study, after four months: 86.9% (95%CI: 83.2-90.5).

Abbreviations: **CI =** confidence interval

Table 5. Factors associated with chronic insomnia in adults

Author / Year Quality (Score)	Study Design	Participants	Duration of Sleep Complaints	Gender	Age (years)	Response / Follow-up Rate	Summary of Findings
Bastien, CH / 2003 Moderate (5/9)	Cross-sectional case-control (unmatched)	**Cases:** chronic insomniacs **Controls:** normal sleepers	**Cases:** insomnia complaint for at least six months (ICSD-10 and DSM-IV criteria combined) **Controls:** no sleep complaints	**Cases:** chronic insomniacs using benzodiazepines: Male: 10, Female: 10. Drug-free insomniacs: Male: 9, Female: 11 **Controls:** Male: 11, Female: 9.	**Cases and controls:** Over 55	Not specified	Insomnia associated with anxiety and depression.
Bixler, EO / 2002 Moderate (3/8)	Cross-sectional	General population	Insomnia complaint for at least one year	Male: 42.6% Female: 57.4%	Over 20	66.6%	Insomnia associated with female gender, non-Caucasian minority, depression and medical conditions. No association between age and insomnia was found.
Bixler, EO / 1979 Moderate (3/8)	Cross-sectional	General population	Current or past sleep disorders; results provided for chronic insomniacs	Male: 44% Female: 56%	Over 18	Not specified	Insomnia associated with general health problems, hospitalizations, tension, depression, and loneliness.
Bliwise, NG / 1992 Low (1/9)	Cross-sectional case-control (unmatched)	**Cases:** poor sleepers **Controls:** good sleepers	**Cases:** sleep complaint for at least five years **Controls:** no sleep complaints	All women	**Cases:** mean ± SD: 68.4 ± 8.7, range: 49-82 **Controls:** mean ± SD: 67.5 ± 9.9, range: 52-95	Not specified	Insomnia associated with psychological problems (anxiety, paranoid ideation, psychoticism, obsessive compulsiveness and depression).
Bonnet, MH / 1995 High (7/9)	Cross-sectional case-control (matched)	**Cases:** chronic insomniacs **Controls:** normal sleepers	**Cases:** sleep complaints for at least one year **Controls:** no sleep complaints	Not specified	**Cases:** range: 18-50 **Controls:** range: 18-50	**Cases:** 50% **Controls:** 50%	Insomnia associated with hyperarousal and degraded mood. No association between cognitive function (vigilance and proof-reading) and insomnia were found.
Braga-Neto, P / 2004 Low (2/8)	Cross-sectional	Parkinson's Disease patients	Sleep complaints over the last month	Male: 64% Female: 36%	Range: 34-86	Not specified	No associations between age or disease duration and insomnia were found.

Table 5. Factors associated with chronic insomnia in adults (continued)

Author / Year Quality (Score)	Study Design	Participants	Duration of Sleep Complaints	Gender	Age (years)	Response / Follow-up Rate	Summary of Findings
Broman, JE / 1996 High (6/8)	Cross-sectional	General population	Sleep complaints during the last three months	Male: 46.9% Female: 53.1%	Range: 20-64	68%	Insomnia associated with higher dysphoric mood, somatic symptoms, and cognitive/behavioral fatigue. No association between gender and insomnia was found.
Broman, JE / 1992 Moderate (5/9)	Cross-sectional case-control (matched)	**Cases:** persistent primary insomniacs **Controls:** normal sleepers	**Cases:** persistent sleep complaints **Controls:** no sleep complaints	**Cases:** Male: 5, Female: 15 **Controls:** Male: 5, Female: 15	**Cases:** mean ± SD: 45.8 ± 11.5 **Controls:** mean ± SD: 45.0 ± 10.2	Not specified	Insomnia associated with anxiety. No association between cognitive performance (reaction time, memory, motor performance), tension, excitement, stress, concentration, or a measure of behavior, and insomnia was found.
Chambers, MJ / 1993 Low (1/9)	Cross-sectional case-control (unmatched)	**Cases:** chronic insomniacs referred to a sleep clinic **Controls:** good sleepers	**Cases:** sleep complaints for at least six months (ASDA criteria) **Controls:** no sleep complaints	**Cases:** Male: 35.5%, Female: 64.5% **Controls:** Male: 40%, Female: 60%	**Cases:** mean ± SD: 47.5 ± 10.9 **Controls:** mean ± SD: 45.9 ± 16.0	Not specified	Insomnia associated with anxiety.
Coursey, RD / 1975 High (7/9)	Cross-sectional case-control (matched)	**Cases:** chronic insomniacs **Controls:** normal sleepers	**Cases:** sleep complaints for at least two years **Controls:** no sleep complaints	**Cases:** Male: 13, Female: 5 **Controls:** Male: 13, Female: 5	**Cases and controls:** mean ± SD: 44.7 ± 16.8	Not specified	Insomnia associated with depression, anxiety, lower cognitive function (sensory-reduced, lower perceptual-motor skills), obsessive worrying, and hypochondriacal concerns.
Crenshaw, MC / 1999 Moderate (3/9)	Cross-sectional case-control (age-matched)	**Cases:** insomniacs **Controls:** normal sleepers	**Cases:** history of insomnia complaints for ≥ 6 months **Controls**: no sleep complaints	**Cases:** Male: 50% Female: 50% **Controls:** Male: 50%, Female: 50%	**Cases:** mean ± SD: 67.7 ± 4.8 **Controls:** mean ± SD: 67.5 ± 5.7	Not specified	No association between cognitive function (reaction time) and insomnia was found.

Table 5. Factors associated with chronic insomnia in adults (continued)

Author / Year Quality (Score)	Study Design	Participants	Duration of Sleep Complaints	Gender	Age (years)	Response / Follow-up Rate	Summary of Findings
Dorsey, CM / 1997 Low (2/9)	Cross-sectional case-control (unmatched)	**Cases:** chronic insomniacs (subjective and objective) **Controls:** normal sleepers	**Cases:** sleep complaints > 6 months **Controls:** no sleep complaints	Male: 17 Female: 14	**Cases and controls:** range: 18-25	Not specified	Insomnia associated with neuroticism (subjective insomniacs) and introversion (objective insomniacs). No association between gender and insomnia was found.
Edinger, JD / 2000 High (8/9)	Cross-sectional case-control (matched)	**Cases:** persistent primary insomniacs **Controls:** normal sleepers	**Cases:** sleep complaints > 6 months (DSM-IV criteria) **Controls:** no sleep complaints	**Cases:** Male: 32, Female: 32 **Controls:** Male: 30, Female: 31	**Cases and controls:** range: 40-79	**Cases**: 100% (64/64); **Controls**: 95.3% (61/64)	No association between mood or anxiety and insomnia was found.
Edinger, JD / 2000 Moderate (4/9)	Cross-sectional case-control (age and gender-matched)	**Cases:** insomniacs **Controls:** normal sleepers	**Cases:** history of insomnia complaints for ≥ 6 months **Controls:** no sleep complaints	**Cases:** Male: 44.4%, Female: 55.6% **Controls**: Male: 48.4% Female: 51.6%	**Cases and controls:** range: 40-79	**Cases:** 84.4% **Controls:** 96.9%	No association for most measures of cognitive performance and insomnia.
Hajak, G / 2001 High (6/8) - cross-sectional High (7/9) - case control	Cross-sectional and case-control (matched)	Cross-sectional: General population Case-control: **Cases:** severe insomniacs **Controls:** normal sleepers	Cross-sectional: Insomnia disorders during the previous month (DSM-III-R and DSM-IV criteria). Severe insomnia: Sleep complaints during the previous month. Case-control: **Cases**: severe insomnia as defined above **Controls**: no sleep complaints	**Cross-sectional:** Male: 46.8% Female: 53.1%	Over 18	Not specified	Insomnia associated with impaired vitality/energy/activity level. Severe insomnia associated with higher healthcare utilization, female gender, and separation/divorce. Age not associated with severe insomnia.

Table 5. Factors associated with chronic insomnia in adults (continued)

Author / Year Quality (Score)	Study Design	Participants	Duration of Sleep Complaints	Gender	Age (years)	Response / Follow-up Rate	Summary of Findings
Han, SY / 2002 Low (2/8)	Cross-sectional	Diabetic haemo-dialysis patients	Sleep complaints for at least two months (DSM-IV criteria modified)	Male: 61% Female: 39%	Range: 27-78	Not specified	Insomnia associated with increased age and depression. No association was found between gender, education, or pain and insomnia.
Harvey, AG / 2003 Moderate (3/9)	Cross-sectional case-control (unmatched)	**Cases:** insomniacs **Controls:** normal sleepers	**Cases:** sleep complaints for at least one month (DSM-IV criteria) **Controls:** no sleep complaints	**Cases:** Male: 40% Female: 60% **Controls:** Male: 36.7% Female: 63.3%	**Cases:** mean ± SD: 20.4 ± 4.7 **Controls:** mean ± SD: 22.3 ± 8.9	Not specified	Insomnia associated with worry.
Hauri, PJ / 1997 High (7/9)	Cross-sectional case-control (matched)	**Cases:** chronic insomniacs **Controls:** normal sleepers	**Cases**: sleep complaints for at least six months **Controls:** no sleep complaints	**Cases:** Male: 7, Female: 19 **Controls:** Male: 7, Female: 19	**Cases and controls:** mean ± SD: 47.7 ± 11.8	Not specified	Insomnia associated with impaired cognitive function for some cognitive parameters (reaction time). No association between some cognitive parameters (divided attention, recent memory and auditory/verbal patterns) and insomnia was found.
Healey, ES / 1981 High (8/9)	Cross-sectional case-control (matched)	**Cases:** chronic insomniacs **Controls:** normal sleepers	**Cases:** sleep complaints within the previous eight years; defined as “chronic” insomniacs **Controls:** no sleep complaints	**Cases:** Male: 9, Female: 22 **Controls:** Male: 9, Female: 22	**Cases:** range: 19-63 **Controls:** range: 18-63	Not specified	Insomnia associated with more stressful life events preceding sleep problem, more health problems and tendency to somatize and internalize stress, lower self-concept, less satisfaction with life.
Hidalgo, MP / 2002 Moderate (5/8)	Cross-sectional	Medical students	Sleep complaints for at least one month during the past year	Male: 58.2% Female: 41.8%	Range: 18-35	Not specified	Insomnia associated with minor psychiatric disorders.

Table 5. Factors associated with chronic insomnia in adults (continued)

Author / Year Quality (Score)	Study Design	Participants	Duration of Sleep Complaints	Gender	Age (years)	Response / Follow-up Rate	Summary of Findings
Hohagen, F / 1994 Moderate (4/8)	Cross-sectional	Elderly outpatients from general practices	Sleep complaints for at least one month (DSM-III-R criteria)	Male: 28% Female: 72%	Over 65	97.5%	Insomnia associated with psychiatric disorders such as depression. No association between age and insomnia was found.
Hohagen, F / 1993 Moderate (4/8)	Cross-sectional	Outpatients from general practices	Sleep complaints during the past month (DSM-III-R criteria)	Male: 44.7% Female: 55.3%	Range: 18-65	97.9%.	Moderate and severe insomnia associated with psychiatric disorders. No association between mild insomnia and psychiatric problems was found.
Ishigooka, J / 1999 Moderate (5/8)	Cross-sectional	Outpatients from general hospitals	Sleep complaints for more than 1 month	Male: 41.9% Female: 58.1%	Range: 15-65	88.3%	Insomnia associated with old age, female gender and visits to neurology and psychiatric departments.
Kageyama, T / 2001 Moderate (5/8)	Cross-sectional	Hospital nurses	Sleep complaints for at least one month	Not specified	Range: 24-59	Not specified	Insomnia associated with being 24 or less years old, having three or less night shifts per month within last three months, receiving less support form colleagues, and taking care of severely ill patients. Insomnia not associated with marital status, having a young child, undergoing medical treatment, recent major life events or work stress.

Table 5. Factors associated with chronic insomnia in adults (continued)

Author / Year Quality (Score)	Study Design	Participants	Duration of Sleep Complaints	Gender	Age (years)	Response / Follow-up Rate	Summary of Findings
Kageyama, T / 1997 High (6/8)	Cross-sectional	Adult women living in urban areas	Sleep complaints for at least one month (ICD-10 and DSM-IV criteria)	All women	Range: 20-80	Varied between district 51-59%	Insomnia associated with being age 70 or older, living with young children, undergoing medical treatment, experiencing one or more major life events within the past six months, having an irregular bedtime, and having sleep apnea-like symptoms. No association between marital status, job status or medical disease and insomnia was found.
Kales, JD / 1984 Low (1/9)	Cross-sectional case-control (unmatched)	**Cases:** 100 patients with sleep com-plaints for at least one year, + 114 insomniacs (appropriate data was available) **Controls:** normal sleepers	**Cases:** sleep complaints for at least one year **Controls:** no sleep complaints	**Cases:** Male: 41.1% Female: 58.9% **Controls:** Male: 41% Female: 59%	**Cases:** mean: 43.1 **Controls:** mean ± SD: 48.2 ± 1.5 range: 24-80	**Cases:** not specified **Controls:** 94%	Insomnia associated with tension, anxiety, worry, depression and poor mental and physical health.
Kales, AK / 1983 Moderate (4/9)	Cross-sectional case-control	**Cases:** chronic insomniacs **Controls:** normal sleepers	**Cases:** defined as **"**chronic" insomniacs **Controls:** no sleep complaints	**Cases:** Male: 41% Female: 59% **Controls:** Male: 41%. Female: 59%	**Cases:** mean ± SD: 43.1 ± 0.9 range: 18-84 **Controls:** mean ± SD: 40.9 ± 1.5 range: 19-74	**Cases:** 93% **Controls:** 97%	Insomnia associated with depression, rumination and anxiety.

Table 5. Factors associated with chronic insomnia in adults (continued)

Author / Year Quality (Score)	Study Design	Participants	Duration of Sleep Complaints	Gender	Age (years)	Response / Follow-up Rate	Summary of Findings
Kales, A / 1982 Low (2/9)	Cross-sectional case-control (unmatched)	**Cases:** chronic insomniacs **Controls:** normal sleepers	**Cases:** sleep complaints > 6 months **Controls:** no sleep complaints	**Cases:** Male: 82, Female: 118 **Controls:** Male: 41, Female: 59	**Cases:** range: 18-78 **Controls:** range: 18-74	Not specified	Insomnia associated with psychopathology.
Kappler, C / 2003 Low (2/8)	Cross-sectional	Outpatients from general practices	Insomnia disorders diagnosed according to DSM-III-R criteria	Male: 49.9% Female: 50.1%	Range: 18-65	37.6%	Insomnia associated with increased age, conflicts with relatives, work and housekeeping stress, psychiatric disorders, medical illness or surgery in relatives and social status. No association between gender and insomnia was found.
Kawada, T / 2003 High (6/8)	Cross-sectional	Women from the general population	Sleep complaints for at least one month (ICD-10 and DSM-IV criteria)	All female	Range: 20-80	50.4%	Insomnia associated with major life events, poor health, and depression.
Leger, D / 2000 High (6/8)	Cross-sectional	General population	Sleep complaints for at least one month (DSM-IV criteria). Sleep complaints over a four-month period was considered "severe insomnia".	Male: 47% Female: 53%	Over 18	85.2%	Insomnia associated with female gender and with being 24-34 years old (but not older). Severe insomnia associated with older age. No association between employment or marital status and insomnia was found.

Table 5. Factors associated with chronic insomnia in adults (continued)

Author / Year Quality (Score)	Study Design	Participants	Duration of Sleep Complaints	Gender	Age (years)	Response / Follow-up Rate	Summary of Findings
Leppavuori, A / 2002 Moderate (4/8)	Cross-sectional	Stroke patients	Insomnia complaints for at least one month (DSM-IV criteria)	Male: 50.9% Female: 49.1%	Range: 55-85	Not specified	Insomnia associated with female gender, older age, psychological stress, anxiety, depression, health problems (including migraine), and impaired psychosocial function. No association between sleep apnea and insomnia was found.
Levitt, H / 2004 Low (2/9) - case control Low (0/9) - cross sectional	Cross-sectional and case-control (age-matched)	**Cases:** insomniacs **Controls:** normal sleepers	**Cases:** primary insomnia diagnosed according to DSM-IV criteria **Controls:** no sleep complaints	**Cases:** Male: 14.3% Female: 85.7% **Controls:** Male: 12.5% Female: 87.5%	**Cases:** mean ± SD: 24.1 ± 3.4 range: 20-30 **Controls:** mean ± SD: 23.3 ± 1.9 range: 20-30	100%	Insomnia associated with decreased cognitive function (concentration), fatigue, lower mood and lower ability to complete tasks.
Lichstein, KL / 2001 Moderate (5/9)	Cross-sectional case-control (unmatched)	**Cases:** primary or secondary insomniacs **Controls:** normal sleepers	**Cases:** sleep complaints of at least six months (ASDA criteria) **Controls:** no sleep complaints	**Cases:** Primary insomnia: Male: 24, Female: 58 Secondary insomnia: Male: 23, Female: 23 **Controls:** Male: 26, Female: 35	**Cases and controls:** Over 58	Not specified	Insomnia associated with anxiety and depression. No association between gender and insomnia was found.
Linzmayer, L / 2002 Low (1/9)	Cross-sectional case-control (unmatched)	**Cases:** non-organic insomniacs associated with different mental disorders **Controls:** normal sleepers	**Cases:** Group A: nonorganic insomnia: ICSD classification of psychophysiological insomnia, DSM-IV classification of primary insomnia. All other cases had insomnia plus a concomitant mental disorder. **Controls:** no sleep complaints	**Cases:** Female: 51.1% Male: 48.9%	Range: 22-63	Not specified	Insomnia not associated with lower intelligence. Insomnia associated with lower memory and wakefulness.

Table 5. Factors associated with chronic insomnia in adults (continued)

Author / Year Quality (Score)	Study Design	Participants	Duration of Sleep Complaints	Gender	Age (years)	Response / Follow-up Rate	Summary of Findings
Lundh, LG / 1997 Moderate (5/9)	Cross-sectional case-control (matched)	**Cases:** persistent insomnia **Controls:** normal sleepers	**Cases:** long-standing problems with insomnia **Controls:** no sleep complaints	**Cases:** Male: 4, Female: 16 **Controls:** Male: 4, Female: 16	**Cases and controls:** range: 20-65 **Cases** mean ± SD: 46.5 ± 11.3 **Controls** mean ± SD: 45.5 ± 11.1	Not specified	Insomnia associated with depression and lower verbal ability. No association between anxiety or memory and insomnia was found.
Martikainen, K / 2003 Moderate (5/8)	Cross-sectional	General population	Sleep complaints during the previous three months	Male: 42.2% Female: 57.8%	Range: 41-55	52.6%	Insomnia associated with poorer working conditions, worry, nervousness, and tension. No association between marital status or shift-work and insomnia was found.
Mendelson, WB / 1984 Moderate (4/9)	Cross-sectional case-control (matched)	**Cases:** insomniacs **Controls:** normal sleepers	**Cases:** sleep complaints for at least one year **Controls:** no sleep complaints	**Cases:** Male: 1, Female: 9 **Controls:** Male: 1, Female: 9	**Cases and controls:** range: 22-44	Not specified	Insomnia associated with decreased memory for some parameters, distress, depression and introversion. No association between psychomotor performance and insomnia was found.
Niemcewicz, S / 2001 Low (2/9)	Case-control (matched for gender, age, and education)	**Cases:** primary insomniacs recruited from sleep disorder clinic. **Controls:** normal sleepers	**Cases:** primary insomnia diagnosed according to DSM-IV criteria **Controls:** no sleep complaints	**Cases:** Male: 44%, Female: 56% **Controls:** Male: 44%, Female: 56%	Mean ± SD: 40.8 ± 11.3 Range: 21-55	100%	Insomnia associated with hypochondria, depression, hysteria, psychasthenia, hyperarousal, impaired memory, and impaired cognitive function (reaction time).
Ohayon, MM / 2003 High (7/8)	Cross-sectional	General population	Sleep complaints > 6 months	Male: 47.9% Female: 52.1%	Over 15	78.6%	Insomnia associated with past psychiatric illness such as anxiety and/or mood disorders.

Table 5. Factors associated with chronic insomnia in adults (continued)

Author / Year Quality (Score)	Study Design	Participants	Duration of Sleep Complaints	Gender	Age (years)	Response / Follow-up Rate	Summary of Findings
Ohayon, MM / 2002 High (8/8)	Cross-sectional	General population	Chronic insomnia diagnosed according to ICSD and DSM-IV criteria	Male: 49.5% Female: 50.5%	Range: 15-90	91.4%	Insomnia associated with being elderly. No association between gender and insomnia was found.
Ohayon, MM / 2002 High (8/8)	Cross-sectional	General population	Sleep complaints during the past year (DSM-IV criteria)	Male: 48.2% Female: 51.8%	Over 15	89.4%	Insomnia associated with female gender.
Ohayon, MM / 2001 High (8/8)	Cross-sectional	General population	Chronic Insomnia diagnosed according to DSM-IV criteria	Male: 47.9% Female: 52.1%	Over 15	78%	Insomnia associated with inactivity, dissatisfaction with social life, and the presence of organic diseases and mental disorders. No association between increased age and insomnia was found.
Pallesen, S / 2002 High (7/9)	Cross-sectional case-control (matched)	**Cases:** chronic primary insomniacs **Controls:** 1) normal sleepers, 2) community sample	**Cases:** chronic primary insomnia diagnosed according to DSM-IV criteria **Controls:** 1) no sleep complaints, 2) community sample	**Cases:** Male: 11, Female: 49. **Controls:** Good sleepers: Male: 9, Female: 32 Community: Male: 19, Female: 41	**Cases:** range: 60-84 **Controls:** Good sleepers: 63-83; Community: 60-86	**Cases:** not specified **Controls:** Good sleepers: not specified Community: 82.6%.	Insomnia associated with higher levels of psychological distress, depression, worry, somatization, and obsessive-compulsiveness. No association between number of life events or their subjective impact or recent life events and insomnia.
Pavlova, M / 2001 Moderate (4/9)	Cross-sectional case-control (unmatched)	**Cases:** primary insomniacs **Controls:** normal sleepers	**Cases:** primary Insomnia diagnosed according to DSM-IV criteria **Controls:** no sleep complaints	Not specified	**Cases:** mean ± SD: 45.9 ± 14 **Controls:** mean ± SD: 44.6 ± 15	Not specified	Insomnia associated with hyperarousal and introspectiveness.

Table 5. Factors associated with chronic insomnia in adults (continued)

Author / Year Quality (Score)	Study Design	Participants	Duration of Sleep Complaints	Gender	Age (years)	Response / Follow-up Rate	Summary of Findings
Perlis, ML / 2001 Moderate (5/9)	Cross-sectional case-control (matched for age, sex, and body mass)	**Cases:** insomniacs **Controls:** good sleepers	**Cases:** psychophysiologic insomnia for ≥ 6 months (ICSD criteria) **Controls:** no sleep complaints	**Cases**: Male: 50%, Female: 50% **Controls:** Male: 40%, Female: 60%	**Cases:** mean ± SD: 30.6 ± 8.9 **Controls:** mean ± SD: 32.3 ± 11.5	Not specified	Insomnia associated with better memory of presentations made at sleep onset. No association between some measures of cognitive function (reaction time, words heard and repeated during stimuli presentation, free recall) and insomnia was found.
Riedel, BW / 2004 High (6/8)	Cross-sectional	General population	Sleep complaints for at least six months (ICSD criteria)	Male: 49.3% Female: 50.7%	Range: 20-98	43.4%	Insomnia associated with being white, having a medical condition, depression and anxiety. Insomnia not significantly associated with age, gender, and neurological problems.
Rocha, FL / 2002 High (7/8)	Cross-sectional	Elderly from the general population	Sleep complaint during the last 30 days	Male: 38.9% Female: 61.1%	Over 60	87%	Insomnia associated with female gender and poor health. No association between lower education or age and insomnia was found.
Rocha, FL / 2002 High (7/8)	Cross-sectional	General population	Sleep complaints in the last month	Male: 44.3% Female: 55.7%	Over 18	87.3%	Insomnia associated with female gender, increased age and less education. No association between ethnicity, marital status and insomnia was found.

Table 5. Factors associated with chronic insomnia in adults (continued)

Author / Year Quality (Score)	Study Design	Participants	Duration of Sleep Complaints	Gender	Age (years)	Response / Follow-up Rate	Summary of Findings
Roth, T / 1999 Moderate (3/8)	Cross-sectional	General population	Sleep complaints on a frequent basis; defined as "chronic" insomniacs	Not specified	Range: 18-65	51.2%	Insomnia associated with lower quality of life: impaired concentration, decreased ability to accomplish tasks, decreased enjoyment of interpersonal relationships, and decrements in perceived mood and wellness.
Sabbatini, M / 2002 Moderate (3/8)	Cross-sectional	Haemo-dialysis patients	Sleep complaints for at least one month	Male: 55.5% Female: 44.5%	Mean ± SD: 61.0 ± 14.4	Not specified	Insomnia associated with anxiety, pruritis, more time spent on dialysis. No association between, pain, depression or tremors and insomnia was found.
Saletu-Zyhlarz, G / 1997 Low (1/9)	Cross-sectional case-control (unmatched)	**Cases:** non-organic insomniacs with concomitant generalized anxiety disorder (ICD-10) **Controls:** normal sleepers	**Cases:** sleep complaint for at least one month **Controls:** no sleep complaints	**Cases:** Male: 43.2%, Female: 56.8% **Controls:** Male: 45.5%, Female: 54.5%	**Cases:** mean ± SD: 43.2 ±11.7 range: 24-65 **Controls:** mean ± SD: 43.0 ±11.7 range: 24-65	**Cases:** 100% **Controls:** 77.3%	Insomnia associated with decreased psychomotor performance. No association between alertness, concentration or memory and insomnia was found.
Savard, J / 2001 Moderate (4/8)	Cross-sectional	Women with metastatic breast cancer	Insomnia symptoms, insomnia syndrome and chronic insomnia syndrome with sleep complaints for at least six months (DSM-IV criteria)	All female	Range: 28-90	88%	Insomnia associated with being unemployed, separated, widowed, as well as chemotherapy, lumpectomy and higher education. No association between psychological co-morbidity, or hormone therapy and insomnia was found.

Table 5. Factors associated with chronic insomnia in adults (continued)

Author / Year Quality (Score)	Study Design	Participants	Duration of Sleep Complaints	Gender	Age (years)	Response / Follow-up Rate	Summary of Findings
Schneider-Helmert, D / 1987 High (7/9)	Cross-sectional case-control (matched)	**Cases:** chronic insomniacs referred to a sleep clinic **Controls:** normal sleepers	**Cases:** persistent psychophysiological insomnia diagnosed by ASDC criteria **Controls:** no sleep complaints	**Cases:** Male: 7, Female: 9 **Controls:** Male: 7, Female: 9	**Cases:** range: 32-61 **Controls:** range: 28-61	Not specified	A difference in personality traits between insomniacs and controls was found.
Shochat, T / 1999 Low (1/8)	Cross-sectional	Patients consulting their primary care physician	**Occasional-insomniacs**: sleep complaints on an occasional basis **Chronic insomniacs**: sleep complaints on a frequent basis; defined as "chronic" insomniacs **Normal Sleepers**: no sleep complaints	Male: 42% Female: 58%	Range: 18-87	Not specified	Insomnia associated with poor daytime functioning on a variety of measures: impaired quality of life, mood, memory, concentration, quality of relationship with spouse and ability to accomplish tasks in the day.
Seidel, WF / 1984 High (6/9)	Cross-sectional case-control (matched)	**Cases:** chronic insomniacs **Controls:** normal sleepers	**Cases:** sleep complaints for at least three months (ASDC criteria) **Controls:** no sleep complaints	**Cases:** Male: 15, Female: 23 **Controls:** Male: 15, Female: 23	**Cases and controls:** mean ± SD: 29 ± 5	Not specified	No association between personality traits or mood and insomnia was found.
Sharpley, AL / 1997 Moderate (5/9)	Cross-sectional case-control (gender matched)	**Cases:** insomniacs **Controls:** normal sleepers	**Cases:** primary insomnia diagnosed according to DSM-II-R diagnosis **Controls:** no sleep complaint	**Cases:** Male: 50% Female: 50% **Controls:** Male: 50% Female: 50%	**Cases:** mean ± SD: 54.7 ± 40-69 **Controls:** mean ± SD: 53.9 ± 40-68	100% both groups	Insomnia associated with a past psychiatric illness.

Table 5. Factors associated with chronic insomnia in adults (continued)

Author / Year Quality (Score)	Study Design	Participants	Duration of Sleep Complaints	Gender	Age (years)	Response / Follow-up Rate	Summary of Findings
Shaver, JLF / 2002 High (6/9)	Cross-sectional case-control (unmatched)	**Cases:** Psycho physiologic-type insomniacs and subjective-only type insomniacs **Controls:** normal sleepers	**Cases:** sleep complaints for at least three months **Controls:** no sleep complaints	All women	**Cases:** PP-type insomnia: mean ± SD: 46.7 ± 3.3, SO-type insomnia: mean ± SD: 46.1 ± 4.4 **Controls:** mean ± SD: 44.4 ± 3.5	Not specified	Insomnia associated with higher psychological distress. No association between stress exposure over the past year and insomnia was found.
Sugerman, JL / 1985 High (6/9)	Cross-sectional case-control (matched)	**Cases:** insomniacs **Controls:** normal sleepers	**Cases:** sleep complaints for at least six months **Controls:** no sleep complaints	**Cases:** 1) Objective insomnia: Male: 2, Female: 6 2) Subjective insomnia: Male: 2, Female: 6 **Controls:** Male: 2, Female: 6	**Cases and controls:** range: 21-55	Not specified	Insomnia associated with impaired waking performance in subjective insomniacs, but not in objective insomniacs. No association between mood (depression, tension, fatigue, and confusion) and insomnia was found.
Taylor, DJ / 2003 High (6/8)	Cross-sectional	Community volunteers	Sleep complaints for at least six months	Male: 49.4% Female: 50.6%	Range: 20-98	49%	Insomnia associated with female gender, older age, medical conditions, anxiety and depression.
Terzano, MG / 2004 Moderate (4/8)	Cross-sectional	Patients presenting to their GP for medical problems other than sleep disorders	Sleep complaints for at least one month	Male: 39.1% Female: 60.9%	Over 18	Not specified	Insomnia associated with female gender, older age, lower education, depression, medical conditions (cardiovascular condition most common), absenteeism, increased healthcare utilization, and lower quality of life.

Table 5. Factors associated with chronic insomnia in adults (continued)

Author / Year Quality (Score)	Study Design	Participants	Duration of Sleep Complaints	Gender	Age (years)	Response / Follow-up Rate	Summary of Findings
Vgontzas, AN / 1995 Low (2/9)	Cross-sectional case-control (unmatched)	**Cases**: insomniacs from the community and a sleep clinic **Controls:** normal sleepers from the community	**Cases:** sleep complaints for more than six months **Controls:** no sleep complaints	**Cases:** Male: 49.9% Female: 50.1% **Controls:** Male: 41.3% Female: 58.7%	**Cases:** range: 18-86 **Controls:** range: 16-80	Not specified	No association between sleep apnea or nocturnal myoclonus and insomnia was found.
Vignola, A / 2000 Moderate (5/9)	Cross-sectional case-control (unmatched)	**Cases:** chronic insomniacs (using or not benzo-diazepines) **Controls:** normal sleepers	**Cases:** sleep complaints > 6 months **Controls:** no sleep complaints	**Cases:** Chronic insomnia using benzodiazepines: Male: 10, Female: 10. Drug-free insomnia: Male: 9, Female: 11 **Controls:** Male: 11, Female: 9	**Cases and Controls:** Over 55	Not specified	Insomnia associated with decreased attention, concentration, fatigue, tension, alertness and energy. No association between some cognitive function parameters (visual and verbal memory, psychomotor speed, executive functions) and insomnia was found.
Vincent, NK / 2000 Moderate (4/9)	Cross-sectional case-control (unmatched)	**Cases:** chronic insomniacs from the community **Controls:** normal sleepers	**Cases:** sleep complaints for at least the previous six months (DSM-IV criteria) **Controls:** no sleep complaints	**Cases:** Male: 28%, Female: 72% **Controls:** Not specified	**Cases:** mean ± SD: 46.91±10.04 **Controls:** mean ± SD: 39.64±11.49	Not specified	Insomnia associated with a tendency for maladaptive perfectionism and worry.
Wang, W / 2001 Moderate (4/9)	Cross-sectional case-control (unmatched)	**Cases:** chronic primary insomniacs. **Controls:** Normal sleepers	**Cases:** diagnosis of chronic primary insomnia according to DSM-IV criteria **Controls:** no sleep complaints	**Cases:** Male: 11, Female: 12 **Controls:** Male: 9, Female: 19	**Cases:** mean ± SD: 30.2 ± 7.0 **Controls:** mean ± SD: 27.2 ± 5.0	**Cases:** 100% **Controls:** 89.2%	Insomnia associated with depression, anxiety, neuroticism, impulsivity and lower thrill and adventure-seeking behavior.

Table 5. Factors associated with chronic insomnia in adults (continued)

Author / Year Quality (Score)	Study Design	Participants	Duration of Sleep Complaints	Gender	Age (years)	Response / Follow-up Rate	Summary of Findings
Yeo, BKL / 1996 Moderate (3/8)	Cross-sectional	General population	Sleep complaints for the past year	Male: 50% Female: 50%	Range: 15-55	Not specified	Insomnia associated with female gender, increased stress level, phobia, depression and anxiety. No association found between education level and insomnia.
Zammit, GK / 1999 Moderate (4/9)	Cross-sectional case-control (unmatched)	**Cases**: primary insomniacs **Controls**: normal sleepers	**Cases:** sleep complaints for at least one month **Controls:** no sleep complaints	**Cases:** Male: 104, Female: 157 **Controls:** Male: 38, Female: 63	**Cases:** mean ± SD: 44.1 ± 14.04 **Controls:** mean ± SD: 37.1 ± 12.7	Not specified	Insomnia associated with more health concerns and poorer general health, bodily pain, less vitality, more emotional problems, depression, anxiety, decreased cognitive function (attention, concentration, mental acuity, reasoning and problem-solving ability, mental reactivity), impaired occupational functioning, increased absenteeism from work.

Abbreviations: **ASDA** = American Sleep Disorders Association; **ASDC** = Association of Sleep Disorders Centers; **DSM-III-R** = Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised; **DSM-IV** = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; **GP** = general practitioner; **ICD-10** = International Classification for Disease Version 10; **PP** = psychophysiologic; **SD** = standard deviation; **SO** = subjective only

Table 6. Sleep onset latency: benzodiazepines versus placebo

Categorization	Sub-group	No. of studies	No. of Participants		Point Estimate (min.)	95% Confidence Interval (min.)	Heterogeneity	Deeks' Chi-Square *P*-value
			Tr.	Pl.				
	All Studies	32	1345	961	-16.5	(-20.5, -12.5)	Substantial (I^2: 72.4%)	NA
Drug Type (*)	Brotizolam	5	101	92	-10.5	(-16.2, -4.8)	Negligible (I^2: 0%)	**< 0.001**
	Estazolam	3	235	125	-10.2	(-14.5, -5.9)	Negligible (I^2: 0%)	
	Flunitrazepam	2	49	30	-23.6	(-62.8, 15.6)	Substantial (I^2: 74.4%)	
	Flurazepam	10	317	215	-23.2	(-34.3, -12.2)	Substantial (I^2: 51.8%)	
	Lormetazepam	4	137	112	-14.8	(-21.8, -7.7)	Minimal (I^2: 7.7%)	
	Nitrazepam	1	37	19	-47.4	(-76.6, -18.2)	NA	
	Quazepam	3	51	41	-14.2	(-23.7, -4.6)	Negligible (I^2: 0%)	
	Temazepam	4	128	78	-11.6	(-23.6, 0.4)	Substantial (I^2: 84.0%)	
	Triazolam	8	290	249	-19.7	(-28.4, -11.0)	Substantial (I^2: 69.2%)	
Psychiatric Illness	Absent	28	1147	803	-15.4	(-19.5, -11.2)	Substantial (I^2: 70.7%)	**0.001**
	Present	4	198	158	-25.8	(-41.7, -9.8)	Substantial (I^2: 72.3%)	
Length of Treatment	Short Term	30	1275	898	-16.5	(-20.5, -12.4)	Substantial (I^2: 74.1%)	0.53
	Long Term	2	70	63	-18.5	(-51.3, 14.4)	Negligible (I^2: 0%)	
Age	Adult	26	999	775	-15.4	(-19.9, -10.9)	Substantial (I^2: 75.2%)	**0.001**
	Elderly	6	346	186	-19.2	(-26.6, -11.7)	Moderate (I^2: 32.4%)	
Gender	Male	3	43	43	-17.0	(-29.5, -4.5)	Negligible (I^2: 0%)	0.14
	Female	1	6	6	-10.0	(-19.4, -0.6)	NA	
	Mixed	28	1296	912	-16.9	(-21.2, -12.6)	Substantial (I^2: 74.5%)	
Method of Measurement (*)	PSG	9	181	170	-7.1	(-12.5, -1.7)	Substantial (I^2: 57.8%)	**< 0.001**
	Sleep Diary	25	1216	842	-18.3	(-22.0, -12.4)	Moderate (I^2: 41.2%)	

Table 6. Sleep onset latency: benzodiazepines versus placebo (continued)

Categorization	Sub-group	No. of studies	No. of Participants		Point Estimate (min.)	95% Confidence Interval (min.)	Heterogeneity	Deeks' Chi-Square *P*-value
Study Quality	Moderate	18	648	400	-13.5	(-18.7, -8.3)	Substantial (I^2: 62.8%)	**< 0.001**
	High	14	697	561	-19.2	(-24.7, -13.7)	Substantial (I^2: 68.1%)	

Abbreviations: min. = minutes; **NA** = not applicable; **No.** = number; **Pl.** = placebo group; **PSG =** polysomnography; **Tr.** = treatment group
*****Sum of studies in each group is greater than total studies because some studies are included in multiple groups.

Table 7. Other outcomes: benzodiazepines versus placebo

Outcome (units)	Comparison	No. of studies	No. of Participants		Point Estimate (min.)	95% Confidence Interval	Heterogeneity
			Tr.	Pl.			
Efficacy Outcomes							
Wakefulness After Sleep Onset (min.)	Mean Difference	8	153	137	-23.1	(-35.7, -10.5)	Substantial (I^2: 51.4%)
Sleep Efficiency (%)	Mean Difference	10	187	168	6.3	(4.7, 8.0)	Negligible (I^2: 0%)
Total Sleep Time (min.)	Mean Difference	17	416	404	39.1	(27.2, 51.0)	Substantial (I^2: 66.9%)
Sleep Quality (SD)	Standardized Mean Difference	24	1243	857	0.80	(0.66, 0.94)	Moderate (I^2: 47.6%)
Safety Outcomes							
Adverse Events	Risk Difference	34	2566	1595	0.15	(0.10, 0.20)	Substantial (I^2: 69.6%)

Abbreviations: min. = minutes; **No.** = number; **Pl.** = placebo group; **SD** = standard deviation; **Tr.** = treatment group

Table 8. Sleep onset latency: non-benzodiazepines versus placebo

Categorization	Sub-group	No. of studies	No. of Participants		Point Estimate (min.)	95% Confidence Interval (min.)	Heterogeneity	Deeks' Chi-Square *P*-value
			Tr.	Pl.				
	All Studies	29	2913	1614	-18.1	(-22.5, -13.7)	Substantial (I^2: 67.2%)	NA
Drug Type (*)	Eszopiclone	1	593	195	-16.7	(-29.4, -4.0)	NA	**0.02**
	Zaleplon	8	1145	433	-20.1	(-29.8, -10.5)	Substantial (I^2: 85.7%)	
	Zolpidem	17	997	808	-12.8	(-16.4, -9.1)	Minimal (I^2: 4.5%)	
	Zopiclone	5	178	178	-30.9	(-49.4, -12.4)	Substantial (I^2: 73.9%)	
Psychiatric Illness	Absent	28	2837	1534	-18.7	(-23.2, -14.2)	Substantial (I^2: 67.0%)	0.06
	Present	1	76	80	-3.7	(-16.1, 8.7)	NA	
Length of Treatment (*)	Short Term	24	2591	1338	-18.4	(-23.4, -13.4)	Substantial (I^2: 71.0%)	0.79
	Long Term	6	915	471	-16.8	(-25.1, -8.6)	Moderate (I^2: 37.2%)	
Age	Adult	26	2520	1355	-18.7	(-23.9, -13.5)	Substantial (I^2: 70.2%)	0.75
	Elderly	3	393	259	-16.1	(-21.2, -10.9)	Negligible (I^2: 0%)	
Gender	Male	1	12	12	-10.3	(-36.6, 16.0)	NA	0.69
	Female	1	6	6	-34.8	(-84.6, 15.0)	NA	
	Mixed	27	2895	1596	-18.2	(-22.7, -13.6)	Substantial (I^2: 69.1%)	
Method of Measurement (*)	PSG	9	278	185	-16.7	(-24.3, -9.0)	Moderate (I^2: 40.7%)	0.21
	Sleep Diary	24	2809	1543	-18.5	(-23.4, -13.6)	Substantial (I^2: 68.6%)	
Study Quality	Moderate	20	2462	1219	-14.1	(-16.9, -11.3)	Negligible (I^2: 0%)	0.29
	High	9	451	395	-29.7	(-43.7, -15.6)	Substantial (I^2: 88.8%)	

Abbreviations: min. = minutes; **NA** = not applicable; **No.** = number; **Pl.** = placebo group; PSG = polysomnography; **Tr.** = treatment group
***Sum of studies in each group is greater than total studies because some studies are included in multiple groups.

Table 9. Other outcomes: non-benzodiazepines versus placebo

Outcome (units)	Comparison	No. of studies	No. of Participants		Point Estimate	95% Confidence Interval	Heterogeneity
			Tr.	Pl.			
Efficacy Outcomes							
Wakefulness After Sleep Onset (min.)	Mean Difference	9	950	552	-12.6	(-23.0, -2.3)	Substantial (I^2: 64.6%)
Sleep Efficiency (%)	Mean Difference	7	172	115	5.9	(3.7, 8.0)	Negligible (I^2: 0%)
Total Sleep Time (min.)	Mean Difference	23	2505	1247	28.0	(21.3, 34.6)	Moderate (I^2: 44.3%)
Sleep Quality (SD)	Standardized Mean Difference	20	2818	1554	0.48	(0.37, 0.59)	Substantial (I^2: 56.1%)
Quality of Life (SD)	Standardized Mean Difference	1	231	227	0.45	(0.27, 0.64)	NA
Safety Outcomes							
Adverse Events	Risk Difference	21	3718	1951	0.05	(0.01, 0.09)	Substantial (I^2: 57.6%)

Abbreviations: min. = minutes; **NA** = not applicable; **No.** = number; **Pl.** = placebo group; **SD** = standard deviation; **Tr.** = treatment group

Table 10. Sleep onset latency: antidepressants versus placebo

Categorization	Sub-group	No. of studies	No. of Participants		Point Estimate (min.)	95% Confidence Interval (min.)	Heterogeneity	Deeks' Chi-Square *P*-value
			Tr.	Pl.				
	All Studies	6	159	166	-7.4	(-10.5, -4.4)	Minimal (I^2: 4.5%)	NA
Drug Type	Doxepin	3	40	40	-6.7	(-10.7, -2.6)	Moderate (I^2: 49.3%)	0.45
	Trazodone	2	100	108	-12.2	(-22.3, -2.2)	Negligible (I^2: 0%)	
	Trimipramine	1	19	18	-15.4	(-36.8, 6.0)	NA	
Psychiatric Illness	Absent	5	152	159	-7.2	(-10.3, -4.1)	Minimal (I^2: 17.6%)	0.30
	Present	1	7	7	-17.4	(-36.8, 2.0)	NA	
Length of Treatment (*)	Short Term	6	159	166	-7.8	(-10.2, -5.4)	Negligible (I^2: 0%)	0.11
	Long Term	1	10	10	-4.4	(-7.7, -1.1)	NA	
Method of Measurement	PSG	4	59	59	-7.0	(-10.7, -3.3)	Moderate (I^2: 34.1%)	0.32
	Sleep Diary	2	100	108	-12.2	(-22.3, -2.2)	Negligible (I^2: 0%)	
Study Quality	Moderate	5	152	159	-7.2	(-10.3, -4.1)	Minimal (I^2: 17.6%)	0.30
	High	1	7	7	-17.4	(-36.8, 2.0)	NA	

Abbreviations: min. = minutes; **NA** = not applicable; **No.** = number; **Pl.** = placebo group; **PSG** = polysomnography; **Tr.** = treatment group
*****Sum of studies in each group is greater than total studies because some studies are included in multiple groups.

Table 11. Other outcomes: antidepressants versus placebo

Outcome (units)	Comparison	No. of studies	No. of Participants		Point Estimate	95% Confidence Interval	Heterogeneity
			Tr.	Pl.			
Efficacy Outcomes							
Wakefulness After Sleep Onset (min.)	Mean Difference	3	123	131	-11.4	(-16.2, -6.6)	Negligible (I^2: 0%)
Sleep Efficiency (%)	Mean Difference	4	59	58	13.8	(9.6, 18.0)	Negligible (I^2: 0%)
Total Sleep Time (min.)	Mean Difference	5	66	65	53.1	(2.8, 103.5)	Substantial (I^2: 85.4%)
Sleep Quality (SD)	Standardized Mean Difference	3	162	169	0.63	(0.27, 0.99)	Substantial (I^2: 52.6%)
Safety Outcomes							
Adverse Events	Risk Difference	3	143	145	0.09	(0.01, 0.18)	Negligible (I^2: 0%)

Abbreviations: min. = minutes; **No.** = number; **Pl.** = placebo group; **SD** = standard deviations; **Tr.** = treatment group

Table 12. All outcomes: L-trytophan versus placebo

Outcome (units)	Comparison	No. of studies	No. of Participants		Point Estimate	95% Confidence Interval	Heterogeneity
			Tr.	Pl.			
Efficacy Outcomes							
Sleep Onset Latency (min.)	Mean Difference	2	47	41	-11.0	(-33.0, 11.1)	Substantial (I^2: 61.5%)

Abbreviations: min. = minutes; **No.** = number; **Pl.** = placebo group; **Tr.** = treatment group

Table 13. All outcomes: melatonin versus placebo

Outcome (units)	Comparison	No. of studies	No. of Participants		Point Estimate	95% Confidence Interval	Heterogeneity
			Tr.	Pl.			
Efficacy Outcomes							
Sleep Onset Latency (min.)	Mean Difference	8	103	103	-8.3	(-14.5, -2.0)	Moderate (I^2: 44.2%)
Wakefulness After Sleep Onset (min.)	Mean Difference	5	68	68	-9.7	(-33.6, 14.3)	Substantial (I^2: 89.8%)
Sleep Efficiency (%)	Mean Difference	8	121	121	3.3	(-0.4, 6.9)	Substantial (I^2: 81.2%)
Total Sleep Time (min.)	Mean Difference	7	95	95	5.8	(-13.2, 24.8)	Substantial (I^2: 72.3%)
Sleep Quality (SD)	Standardized Mean Difference	3	35	35	0.25	(-0.22, 0.73)	Negligible (I^2: 0%)
Safety Outcomes							
Adverse Events	Risk Difference	2	27	27	0.09	(-0.11, 0.29)	Moderate (I^2: 30.0%)

Abbreviations: min. = minutes; **No.** = number; **Pl.** = placebo group; **SD** = standard deviation; **Tr.** = treatment group

Table 14. All outcomes: valerian versus placebo

Outcome (units)	Comparison	No. of studies	No. of Participants		Point Estimate	95% Confidence Interval	Heterogeneity
			Tr.	Pl.			
Efficacy Outcomes							
Sleep Onset Latency (min.)	Mean Difference	3	51	50	-1.3	(-21.4, 18.9)	Substantial (I^2: 77.6%)
Wakefulness After Sleep Onset (min.)	Mean Difference	1	10	9	-8.4	(-15.9, -1.0)	NA
Sleep Efficiency (%)	Mean Difference	2	26	25	-0.1	(-3.4, 3.2)	Negligible (I^2: 0%)
Total Sleep Time (min.)	Mean Difference	1	10	9	0.8	(-50.6, 52.2)	NA
Sleep Quality (SD)	Standardized Mean Difference	3	50	49	1.38	(-0.49, 3.25)	Substantial (I^2: 93.1%)
Safety Outcomes							
Adverse Events	Risk Difference	3	51	50	-0.06	(-0.48, 0.35)	Substantial (I^2: 90.3%)

Abbreviations: min. = minutes; **NA** = not applicable; **No.** = number; **Pl.** = placebo group; **SD** = standard deviation; **Tr.** = treatment group

Table 15. Sleep onset latency: relaxation therapy versus placebo

Categorization	Sub-group	No. of studies	No. of Participants		Point Estimate (min.)	95% Confidence Interval (min.)	Heterogeneity	Deeks' Chi-Square *P*-value
			Tr.	Pl.				
	All Studies	13	199	185	-14.6	(-29.3, 0.2)	Substantial (I^2: 96.1%)	NA
Relaxation Description(*)	Autogenic Training	1	8	4	-27.0	(-126.2, 72.2)	NA	**< 0.001**
	Breathing Training	1	23	23	-60.0	(-64.5, -55.5)	NA	
	EMG Feedback Training	3	27	27	-5.3	(-28.4, 17.8)	Substantial (I^2: 62.3%)	
	Group	1	14	14	-5.5	(-10.8, -0.2)	NA	
	Hypnotic	1	15	15	-16.3	(-24.3, -8.3)	NA	
	Progressive	5	61	55	-15.7	(-39.2, 7.8)	Moderate (I^2: 49.0%)	
	Relaxation	4	51	47	-5.3	(-17.3, 6.8)	Substantial (I^2: 67.7%)	
Length of Treatment	Short Term	9	124	114	-22.0	(-41.0, -2.9)	Substantial (I^2: 97.3%)	**< 0.001**
	Long Term	4	75	71	1.9	(-6.7, 10.6)	Minimal (I^2: 11.7%)	
Age	Adult	12	172	162	-15.9	(-31.5, -0.3)	Substantial (I^2: 96.2%)	**< 0.001**
	Elderly	1	27	23	-0.2	(-10.4, 10.0)	NA	
Gender	Female	1	14	14	-5.5	(-10.8, -0.2)	NA	**< 0.001**
	Mixed	12	185	171	-15.5	(-32.0, 0.9)	Substantial (I^2: 95.9%)	
Study Quality	Low	8	101	94	-9.1	(-16.0, -2.2)	Substantial (I^2: 58.4%)	**< 0.001**
	Moderate	5	98	91	-17.6	(-54.2, 19.0)	Substantial (I^2: 97.2%)	

Abbreviations: EMG = electromyographic; **min.** = minutes; **NA** = not applicable; **No.** = number; **Pl.** = placebo group; **Tr.** = treatment group;
***Sum of studies in each group is greater than total studies because some studies are included in multiple groups.

Table 16. Other outcomes: relaxation therapy versus placebo

Outcome (units)	Comparison	No. of studies	No. of Participants		Point Estimate	95% Confidence Interval	Heterogeneity
			Tr.	Pl.			
Efficacy Outcomes							
Wakefulness After Sleep Onset (min.)	Mean Difference	3	60	57	-1.6	(-14.1, 10.8)	Minimal (I^2: 0.2%)
Sleep Efficiency (%)	Mean Difference	2	50	47	0.4	(-3.7, 4.6)	Negligible (I^2: 0%)
Total Sleep Time (min.)	Mean Difference	3	60	57	23.0	(2.7, 43.4)	Negligible (I^2: 0%)
Sleep Quality (SD)	Standardized Mean Difference	3	50	47	0.37	(-0.49, 1.24)	Substantial (I^2: 79.2%)

Abbreviations: min. = minutes; **No.** = number; **Pl.** = placebo group; **SD** = standard deviation; **Tr.** = treatment group

Table 17. Sleep onset latency: cognitive/behavioral therapy versus placebo

Categorization	Sub-group	No. of studies	No. of Participants		Point Estimate (min.)	95% Confidence Interval (min.)	Heterogeneity	Deeks' Chi-Square *P*-value
			Tr.	Pl.				
	All Studies	9	152	124	-4.6	(-9.8, 0.6)	Minimal (I^2: 12.5%)	NA
Cognitive Behavioral Therapy Type (*)	Multi-component CBT	2	20	19	-2.6	(-15.4, 10.2)	Moderate (I^2: 49.0%)	0.65
	Paradoxical Intention	3	37	23	-3.7	(-28.7, 21.3)	Moderate (I^2: 38.0%)	
	Sleep Compression	1	24	23	-0.8	(-13.7, 12.1)	NA	
	Stimulus Control	4	58	46	-7.3	(-18.3, 3.7)	Moderate (I^2: 31.6%)	
	Non-Suppression	1	13	13	-9.7	(-24.2, 4.8)	NA	
Length of Treatment	Short Term	7	99	87	-4.3	(-10.4, 1.8)	Minimal (I^2: 19.9%)	0.84
	Long Term	2	53	37	-8.5	(-24.7, 7.8)	Moderate (I^2: 24.2%)	
Age	Adult	8	128	101	-5.3	(-11.4, 0.7)	Minimal (I^2: 19.0%)	0.58
	Elderly	1	24	23	-0.8	(-13.7, 12.1)	NA	
Study Quality	Low	5	60	62	-8.1	(-14.6, -1.6)	Negligible (I^2: 0%)	0.12
	Moderate	4	92	62	-1.2	(-7.8, 5.5)	Minimal (I^2: 4.4%)	

Abbreviations: min. = minutes; **NA** = not applicable; **No.** = number; **Pl.** = placebo group; **Tr.** = treatment group
***Sum of studies in each group is greater than total studies because some studies are included in multiple groups.

Table 18. Other outcomes: cognitive/behavioral therapy versus placebo

Outcome (units)	Comparison	No. of studies	No. of Participants		Point Estimate	95% Confidence Interval	Heterogeneity
			Tr.	Pl.			
Efficacy Outcomes							
Wakefulness After Sleep Onset (min.)	Mean Difference	8	128	120	-18.2	(-30.4, -6.0)	Substantial (I^2: 52.9%)
Sleep Efficiency (%)	Mean Difference	4	75	74	5.5	(1.2, 9.9)	Substantial (I^2: 57.9%)
Total Sleep Time (min.)	Mean Difference	5	85	84	0.7	(-28.1, 29.5)	Substantial (I^2: 65.6%)
Sleep Quality (SD)	Standardized Mean Difference	6	94	95	0.38	(0.09, 0.67)	Negligible (I^2: 0%)

Abbreviations: min. = minutes; **No.** = number; **Pl.** = placebo group; **SD** = standard deviation; **Tr.** = treatment group

Table 19. Sleep onset latency: indirect comparisons of main pharmacological treatment categories

Comparison	Difference in SOL (min.)	95% Confidence Interval (min.)	Difference Favours:	Significant Difference (Yes or No)
BNZ versus NBNZ	1.6	(-4.3, 7.5)	NBNZ	No
BNZ versus ADP	-9.1	(-14.1, -4.1)	BNZ	Yes
BNZ versus LT	-5.5	(-28.0, 17.0)	BNZ	No
BNZ versus MLT	-8.2	(-15.7, -0.7)	BNZ	Yes
BNZ versus VAL	-15.2	(-35.8, 5.4)	BNZ	No
NBNZ versus ADP	-10.7	(-16.0, -5.4)	NBNZ	Yes
NBNZ versus LT	-7.1	(-29.6, 15.4)	NBNZ	No
NBNZ versus MLT	-9.8	(-17.5, -2.1)	NBNZ	Yes
NBNZ versus VAL	-16.8	(-37.5, 3.9)	NBNZ	No
ADP versus LT	3.6	(-18.7, 25.9)	LT	No
ADP versus MLT	0.9	(-6.1, 7.9)	MLT	No
ADP versus VAL	-6.1	(-26.5, 14.3)	ADP	No
LT versus MLT	-2.7	(-25.7, 20.3)	LT	No
LT versus VAL	-9.7	(-39.6, 20.2)	LT	No
MLT versus VAL	-7.0	(-28.2, 14.2)	MLT	No

Abbreviations: ADP = antidepressants; **BNZ** = benzodiazepines; **LT** = L-tryptophan; **min.** = minutes; **MLT** = melatonin; **NBNZ** = non-benzodiazepines; **SOL** = sleep onset latency; **VAL** = valerian

Table 20. Adverse events: indirect comparisons of main pharmacological treatment categories

Comparison	Difference in risk difference	95% Confidence Interval	Difference Favors:	Significant Difference (Yes or No)
BNZ versus NBNZ	0.10	(0.04, 0.16)	NBNZ	Yes
BNZ versus ADP	0.06	(-0.04, 0.16)	ADP	No
BNZ versus MLT	0.06	(-0.15, 0.27)	MLT	No
BNZ versus VAL	0.21	(-0.20, 0.62)	VAL	No
NBNZ versus ADP	-0.04	(-0.14, 0.06)	NBNZ	No
NBNZ versus MLT	-0.04	(-0.24, 0.16)	NBNZ	No
NBNZ versus VAL	0.11	(-0.30, 0.52)	VAL	No
ADP versus MLT	0.00	(-0.22, 0.22)	neither	No
ADP versus VAL	0.15	(-0.27, 0.57)	VAL	No
MLT versus VAL	0.15	(-0.31, 0.61)	VAL	No

Abbreviations: **ADP** = antidepressants; **BNZ** = benzodiazepines; **MLT** = melatonin; **NBNZ** = non-benzodiazepines; **VAL** = valerian

Table 21. All outcomes: barbiturates versus placebo

Outcome (units)	Comparison	No. of studies	No. of Participants		Point Estimate	95% Confidence Interval	Heterogeneity
			Tr.	Pl.			
Efficacy Outcomes							
Sleep Onset Latency (min.)	Mean Difference	2	166	71	-4.5	(-14.2, 5.2)	Negligible (I^2: 0%)
Safety Outcomes							
Adverse Events	Risk Difference	1	144	48	0.02	(-0.10, 0.15)	NA

Abbreviations: min. = minutes; **NA** = not applicable; **No.** = number; **Pl.** = placebo group; **Tr.** = treatment group

Table 22. All outcomes: hormones versus placebo

Outcome (units)	Comparison	No. of studies	No. of Participants		Point Estimate	95% Confidence Interval	Heterogeneity
			Tr.	Pl.			
Efficacy Outcomes							
Sleep Onset Latency (min.)	Mean Difference	1	33	16	-6.9	(-17.3, 3.6)	NA
Sleep Efficiency (%)	Mean Difference	1	33	16	5.0	(0.3, 9.7)	NA
Total Sleep Time (min.)	Mean Difference	1	33	16	21.9	(-0.2, 44.1)	NA
Sleep Quality (SD)	Standardized Mean Difference	1	33	16	0.83	(0.21, 1.45)	NA

Abbreviations: min. = minutes; **NA** = not applicable; **No.** = number; **Pl.** = placebo group; **SD** = standard deviations; **Tr.** = treatment group

Table 23. All outcomes: alcohol versus placebo

Outcome (units)	Comparison	No. of studies	No. of Participants		Point Estimate	95% Confidence Interval	Heterogeneity
			Tr.	Pl.			
Efficacy Outcomes							
Sleep Onset Latency (min.)	Mean Difference	1	11	11	4.7	(-7.5, 16.9)	NA
Wakefulness After Sleep Onset (min.)	Mean Difference	1	11	11	11.3	(-9.1, 31.7)	NA
Sleep Efficiency (%)	Standardized Mean Difference	1	11	11	-3.4	(-8.7, 1.9)	NA

Abbreviations: min. = minutes; **NA** = not applicable; **No.** = number; **Pl.** = placebo group; **Tr.** = treatment group

Table 24. All outcomes: low energy emission therapy versus placebo

Outcome (units)	Comparison	No. of studies	No. of Participants		Point Estimate	95% Confidence Interval	Heterogeneity
			Tr.	Pl.			
Efficacy Outcomes							
Sleep Onset Latency (min.)	Mean Difference	1	49	48	-15.6	(-32.1, 0.9)	NA
Wakefulness After Sleep Onset (min.)	Mean Difference	1	49	48	-23.5	(-50.0, 3.0)	NA
Sleep Efficiency (%)	Mean Difference	1	49	48	10.5	(4.2, 16.8)	NA
Total Sleep Time (min.)	Mean Difference	1	49	48	56.0	(21.7, 90.3)	NA
Safety Outcomes							
Adverse Events	Risk Difference	1	49	48	0.04	(-0.11, 0.18)	NA

Abbreviations: min. = minutes; **NA** = not applicable; **No.** = number; **Pl.** = placebo group; **SD** = standard deviation; **Tr.** = treatment group

Table 25. All outcomes: relaxation therapy and cognitive/behavioral therapy versus placebo

Outcome (units)	Comparison	No. of studies	No. of Participants		Point Estimate	95% Confidence Interval	Heterogeneity
			Com.	Pl.			
Sleep Onset Latency (min.)	Mean Difference	4	45	46	-21.5	(-42.2, -0.8)	Substantial (I^2: 74.4%)
Wakefulness After Sleep Onset (min.)	Mean Difference	2	23	26	-7.6	(-26.3, 11.1)	Negligible (I^2: 0%)
Total Sleep Time (min.)	Mean Difference	1	10	10	24.0	(-15.8, 63.8)	NA
Sleep Quality (SD)	Standardized Mean Difference	2	23	26	0.69	(-0.34, 1.73)	Substantial (I^2: 65.4%)

Abbreviations: Com. = combined treatment group; **min.** = minutes; **NA** = not applicable; **No.** = number; **Pl.** = placebo group; **SD** = standard deviation

Table 26. All outcomes: relaxation therapy and cognitive/behavioral therapy versus relaxation therapy

Outcome (units)	Comparison	No. of studies	No. of Participants		Point Estimate	95% Confidence Interval	Heterogeneity
			Com.	Rel.			
Sleep Onset Latency (min.)	Mean Difference	2	18	16	-9.2	(-37.9, 19.5)	Moderate (I^2: 37.1%)
Wakefulness After Sleep Onset (min.)	Mean Difference	1	10	10	8.3	(-24.8, 41.4)	NA
Total Sleep Time (min.)	Mean Difference	1	10	10	-12.0	(-44.9, 20.9)	NA
Sleep Quality (SD)	Standardized Mean Difference	1	10	10	-0.08	(-0.95, 0.80)	NA

Abbreviations: Com. = combined treatment group; **min.** = minutes; **NA** = not applicable; **No.** = number; **Rel.** = relaxation group; **SD** = standard deviation

Table 27. All outcomes: relaxation therapy and cognitive/behavioral therapy versus cognitive/behavioral therapy

Outcome (units)	Comparison	No. of studies	No. of Participants		Point Estimate	95% Confidence Interval	Heterogeneity
			Com.	CBT			
Sleep Onset Latency (min.)	Mean Difference	2	23	24	-4.6	(-20.7, 11.5)	Negligible (I^2: 0%)
Wakefulness After Sleep Onset (min.)	Mean Difference	2	23	24	5.1	(-12.0, 22.2)	Negligible (I^2: 0%)
Total Sleep Time (min.)	Mean Difference	1	10	10	-24	(-84.8, 36.8)	NA
Sleep Quality (SD)	Standardized Mean Difference	2	23	24	0.20	(-0.38, 0.77)	Negligible (I^2: 0%)

Abbreviations: CBT = cognitive behavioral therapy group; **Com.** = combined treatment group; **min.** = minutes; **NA** = not applicable; **No.** = number; **SD** = standard deviation

Table 28. All outcomes: relaxation therapy and cognitive/behavioral therapy versus benzodiazepines

Outcome (units)	Comparison	No. of studies	No. of Participants		Point Estimate	95% Confidence Interval	Heterogeneity
			Com.	Ben.			
Sleep Onset Latency (min.)	Mean Difference	1	13	10	8.3	(-16.4, 33.0)	NA
Wakefulness After Sleep Onset (min.)	Mean Difference	1	13	10	7.3	(-12.5, 27.1)	NA
Sleep Quality (SD)	Standardized Mean Difference	1	13	10	-1.51	(-2.46, -0.55)	NA

Abbreviations: Ben. = benzodiazepine group; **Com.** = combined treatment group; **min.** = minutes; **NA** = not applicable; **No.** = number; **SD** = standard deviation

Table 29. All outcomes: benzodiazepine and cognitive/behavioral therapy versus placebo

Outcome (units)	Comparison	No. of studies	No. of Participants		Point Estimate	95% Confidence Interval	Heterogeneity
			Com.	Pl.			
Sleep Onset Latency (min.)	Mean Difference	1	8	7	-5.5	(-18.0, 7.0)	NA
Wakefulness After Sleep Onset (min.)	Mean Difference	1	19	18	-32.1	(-54.1, -10.2)	NA
Sleep Efficiency (%)	Mean Difference	1	19	18	12.8	(6.3, 19.3)	NA
Total Sleep Time (min.)	Mean Difference	2	27	25	23.2	(-2.3, 48.8)	Negligible (I^2: 0%)

Abbreviations: **Com.** = combined treatment group; **min.** = minutes; **NA** = not applicable**; No.** = number; **Pl.** = placebo group

Table 30. All outcomes: benzodiazepine and cognitive/behavioral therapy versus benzodiazepine

Outcome (units)	Comparison	No. of studies	No. of Participants		Point Estimate	95% Confidence Interval	Heterogeneity
			Com.	CBT			
Wakefulness After Sleep Onset (min.)	Mean Difference	1	19	17	-15.5	(-37.1, 6.1)	NA
Sleep Efficiency (%)	Mean Difference	1	19	17	6.8	(0.3, 13.3)	NA
Total Sleep Time (min.)	Mean Difference	1	19	17	-13.3	(-45.3, 18.7)	NA

Abbreviations: CBT = cognitive behavioral therapy group; **Com.** = combined treatment group; **min.** = minutes; **NA** = not applicable; **No.** = number

Table 31. All outcomes: benzodiazepine and cognitive/behavioral therapy versus cognitive/behavioral therapy

Outcome (units)	Comparison	No. of studies	No. of Participants		Point Estimate	95% Confidence Interval	Heterogeneity
			Com.	Ben.			
Wakefulness After Sleep Onset (min.)	Mean Difference	1	19	18	-10.1	(-34.6, 14.4)	NA
Sleep Efficiency (%)	Mean Difference	1	19	18	3.1	(-3.4, 9.6)	NA
Total Sleep Time (min.)	Mean Difference	1	19	18	7.0	(-23.8, 37.8)	NA

Abbreviations: Ben. = benzodiazepine group; **Com.** = combined treatment group; **min.** = minutes; **NA** = not applicable; **No.** = number

Table 32. All outcomes: non-benzodiazepine and cognitive/behavioral therapy (in combination) versus non-benzodiazepine and cognitive/behavioral therapy (sequential)

Outcome (units)	Comparison	No. of studies	No. of Participants		Point Estimate	95% Confidence Interval	Heterogeneity
			Com.	Seq.			
Sleep Efficiency (%)	Mean Difference	1	2	2	4.0	(-23.4, 31.4)	NA
Total Sleep Time (min.)	Mean Difference	1	2	2	-25.8	(-169.9, 118.3)	NA

Abbreviations: Com. = combined treatment group; **min.** = minutes; **NA** = not applicable; **No.** = number; **Seq.** = sequential treatment group

Table 33. All outcomes: cognitive/behavioral therapy and modafinil versus cognitive/behavioral therapy

Outcome (units)	Comparison	No. of studies	No. of Participants		Point Estimate	95% Confidence Interval	Heterogeneity
			Com.	CBT			
Sleep Onset Latency (min.)	Mean Difference	1	10	9	3.6	(-13.5, 20.7)	NA
Wakefulness After Sleep Onset (min.)	Mean Difference	1	10	9	2.0	(-28.4, 32.4)	NA
Total Sleep Time (min.)	Mean Difference	1	10	9	-7.0	(-69.3, 55.3)	NA

Abbreviations: CBT = cognitive behavioral therapy group; **Com.** = combined treatment group; **min.** = minutes; **NA** = not applicable; **No.** = number

Table 34. All outcomes: cognitive/behavioral therapy and modafinil versus modafinil

Outcome (units)	Comparison	No. of studies	No. of Participants		Point Estimate	95% Confidence Interval	Heterogeneity
			Com.	Mod.			
Sleep Onset Latency (min.)	Mean Difference	1	10	8	-2.0	(-29.2, 25.2)	NA
Wakefulness After Sleep Onset (min.)	Mean Difference	1	10	8	-25.4	(-61.1, 10.3)	NA
Total Sleep Time (min.)	Mean Difference	1	10	8	15.8	(-29.5, 61.1)	NA

Abbreviations: Com. = combined treatment group; **min.** = minutes; **Mod.** = modafinil group; **NA** = not applicable; **No.** = number

Figure 1. Meta graph: Sleep onset latency: benzodiazepines versus placebo

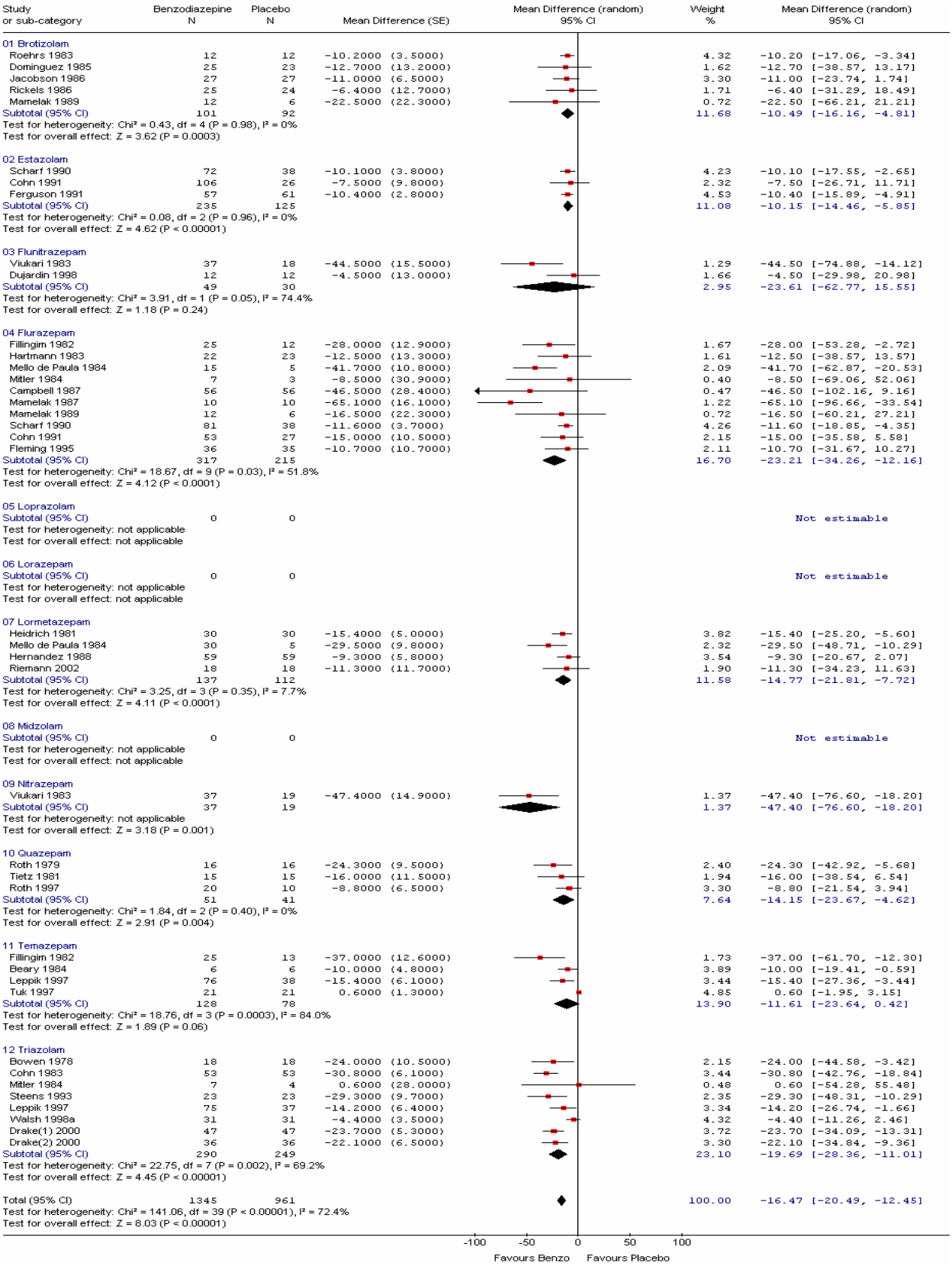


Figure 2. Funnel Plot: Sleep onset latency: benzodiazepines versus placebo

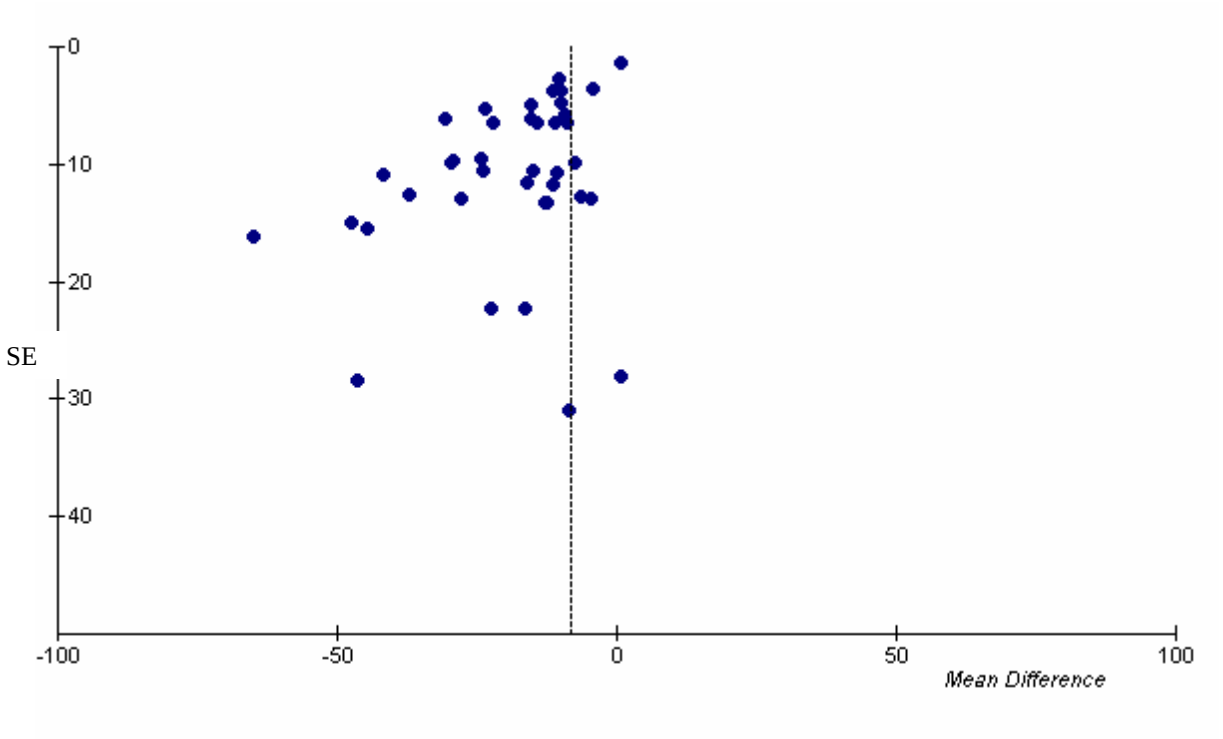


Figure 3. Meta graph: Wakefulness After Sleep Onset: benzodiazepines versus placebo

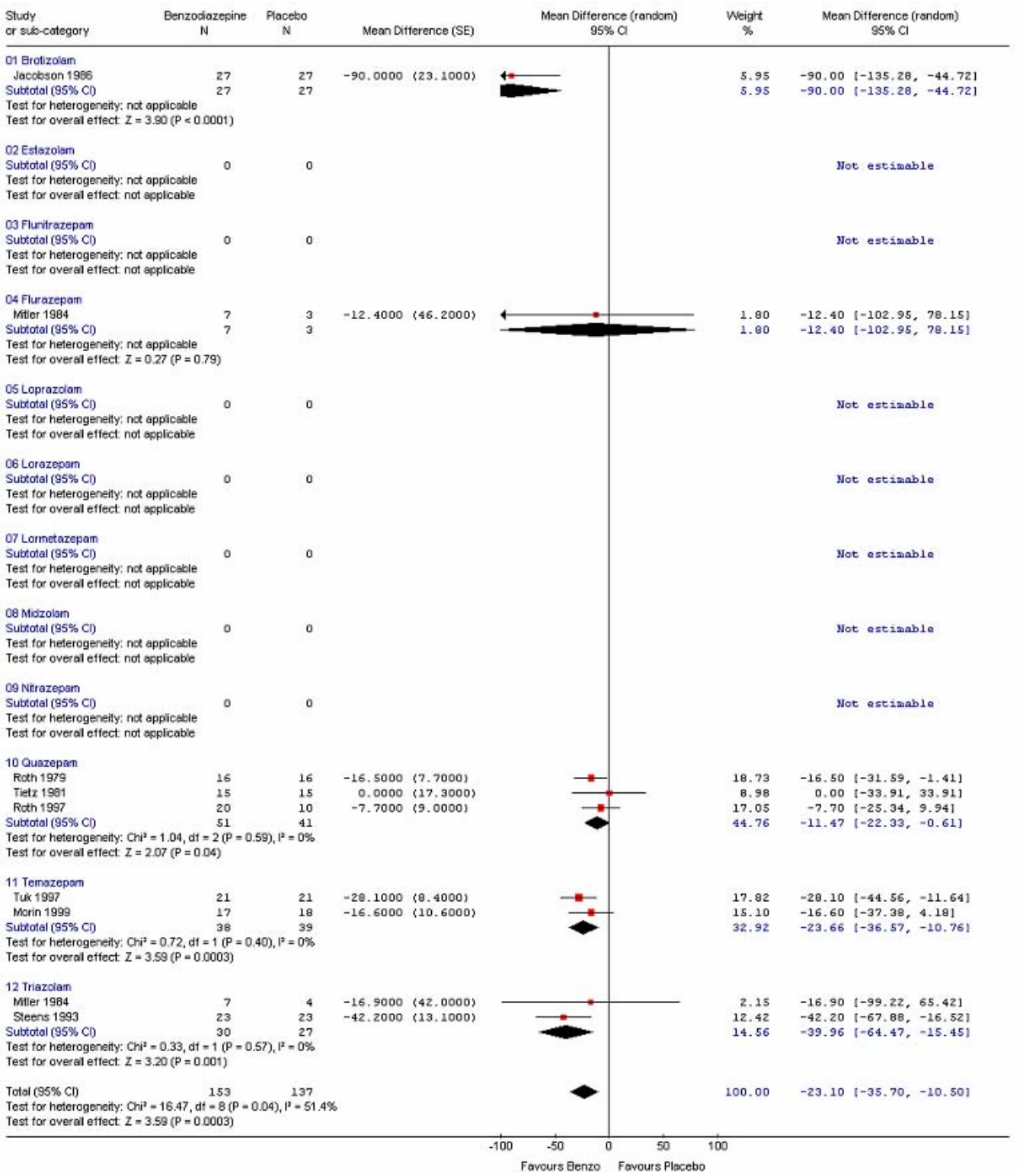


Figure 4. Meta graph: Sleep Onset Latency: non-benzodiazepines versus placebo

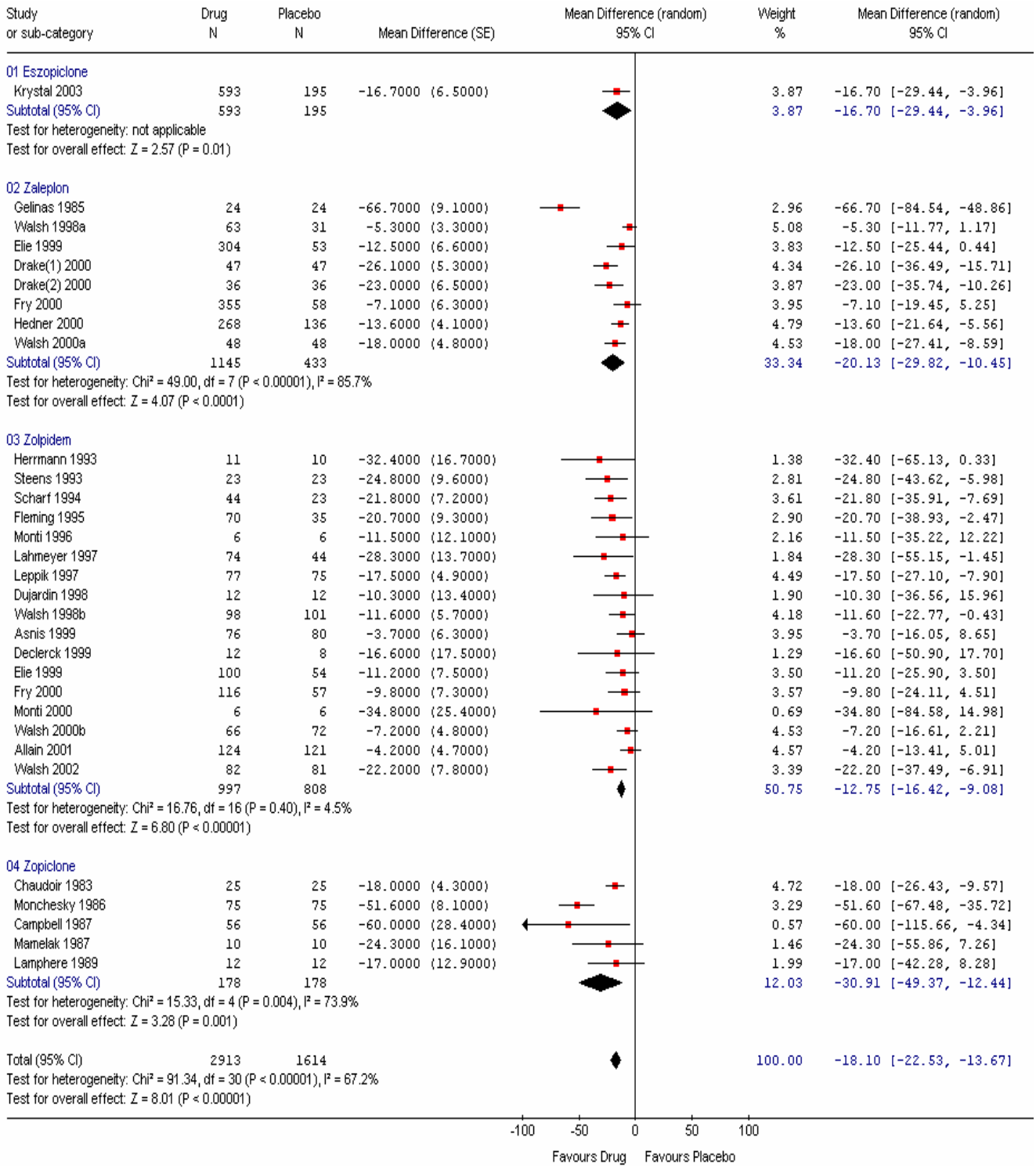


Figure 5. Funnel Plot: Sleep Onset Latency: non-benzodiazepines versus placebo

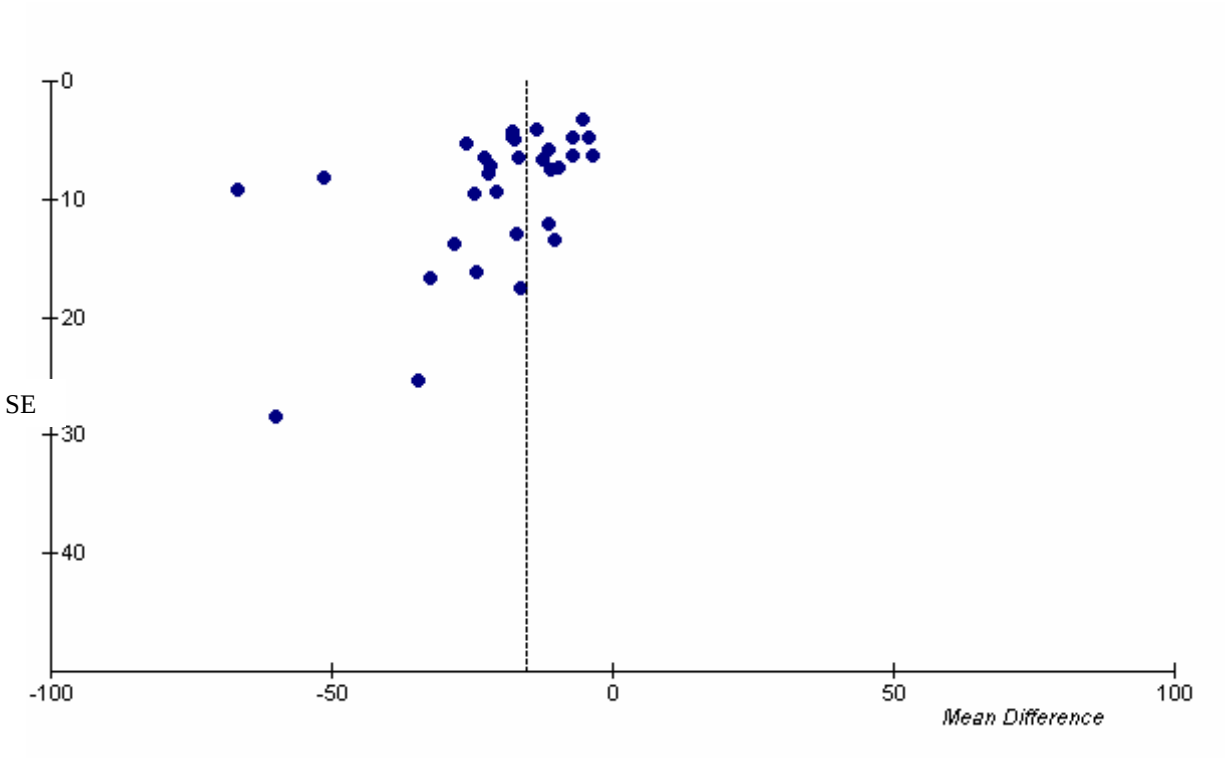


Figure 6. Meta graph: Wakefulness After Sleep Onset: non-benzodiazepines versus placebo

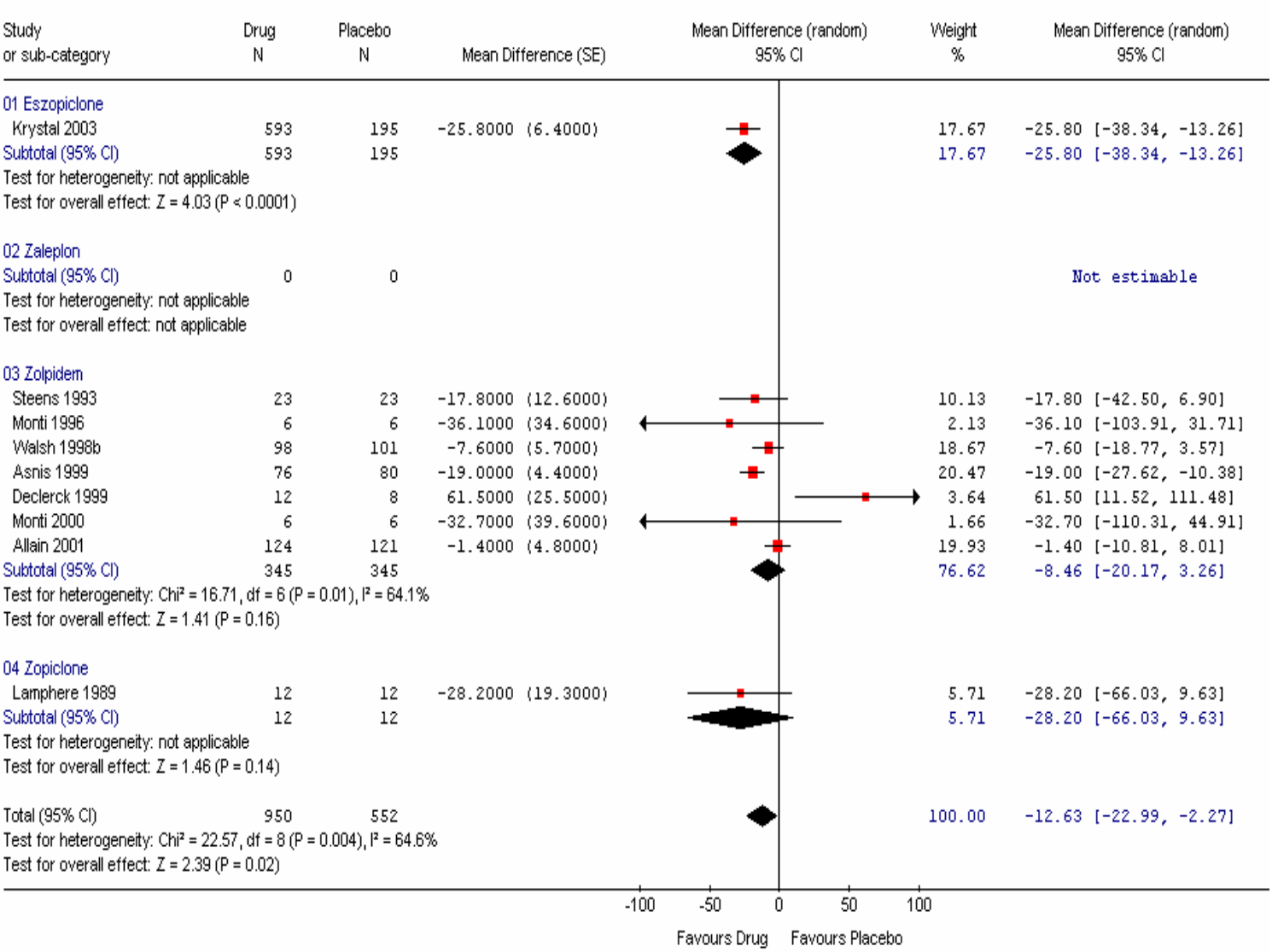


Figure 7. Meta graph: Sleep Onset Latency: antidepressants versus placebo

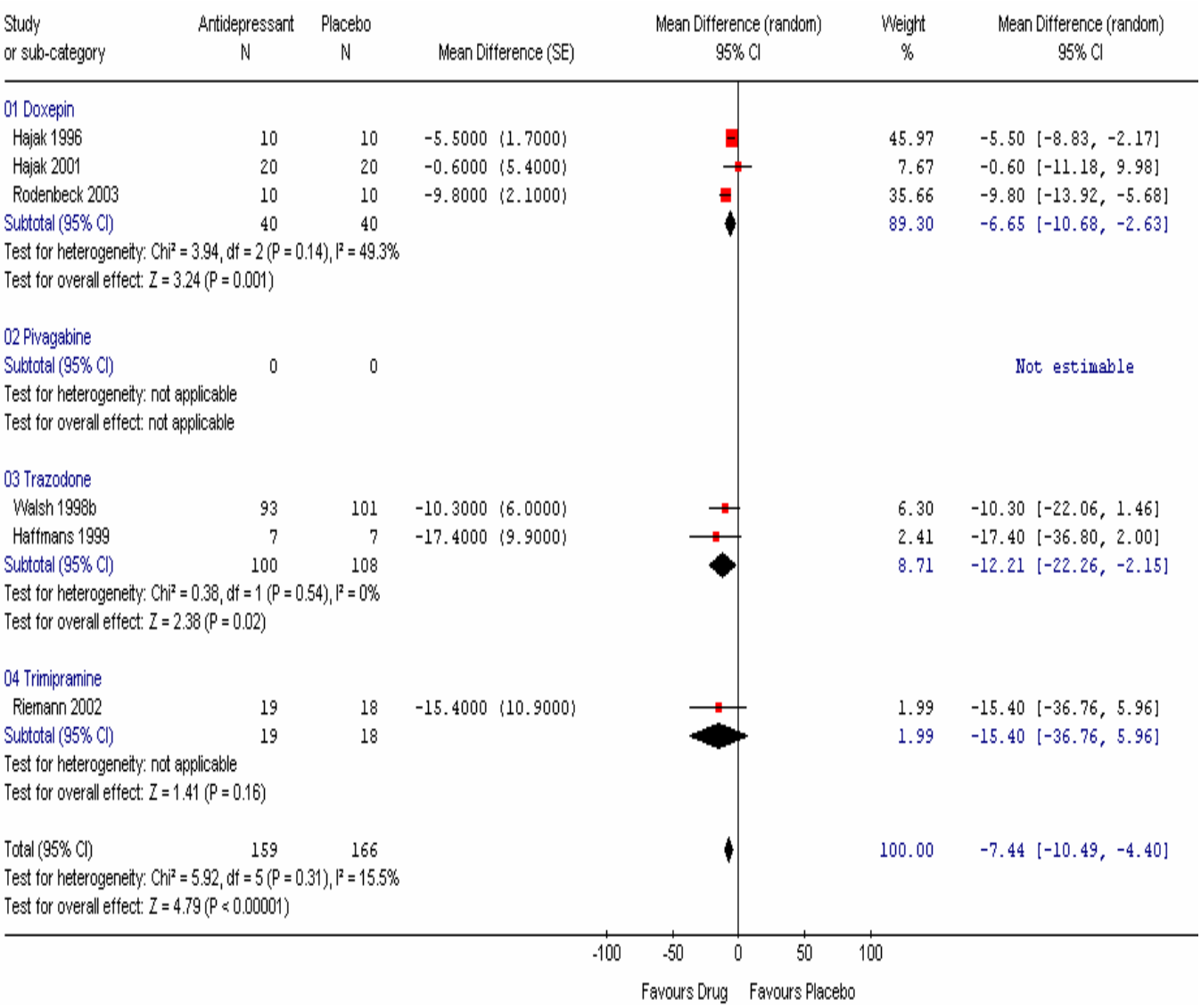


Figure 8. Meta graph: Wakefulness After Sleep Onset: antidepressants versus placebo

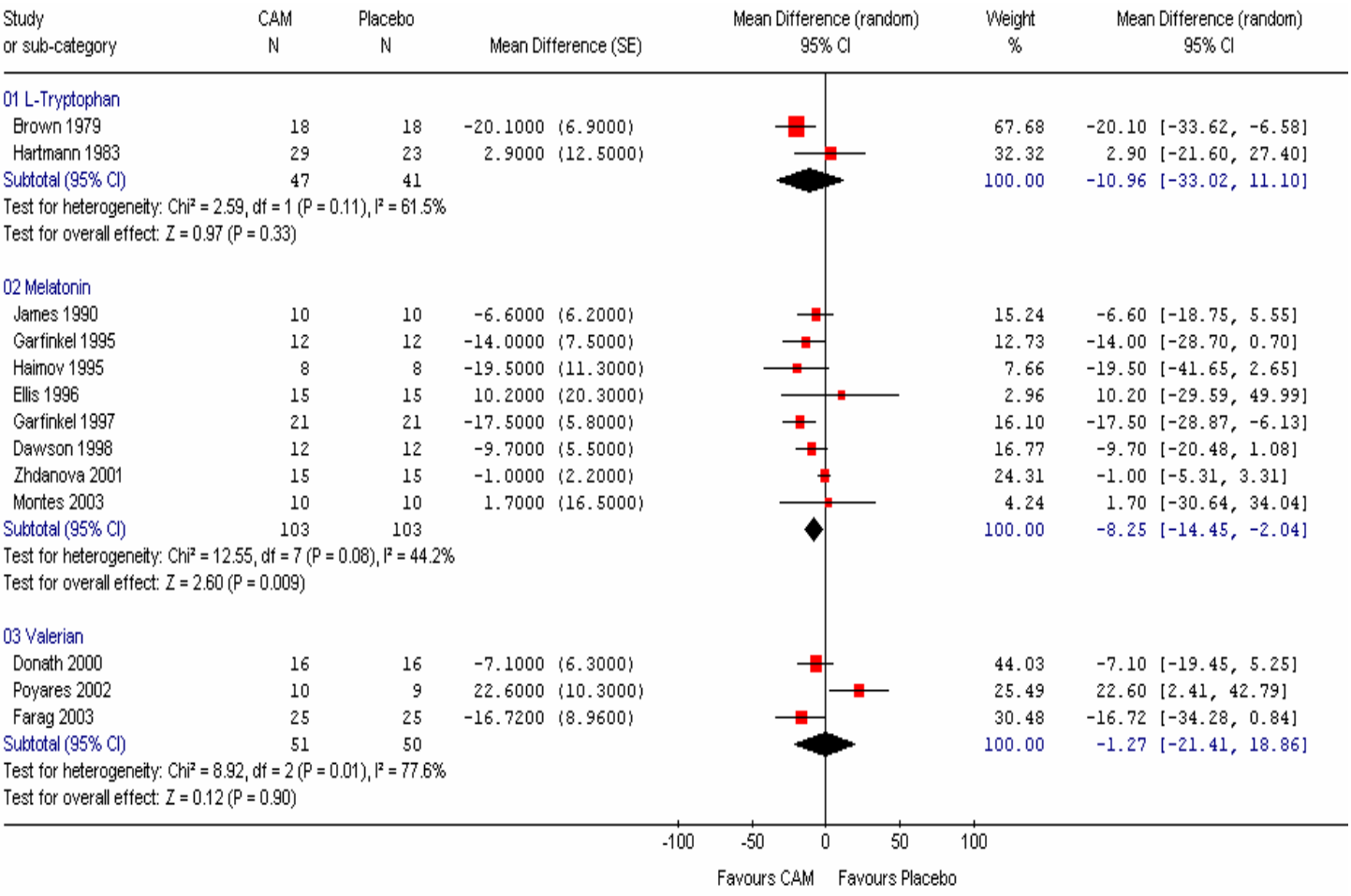


Figure 9. Meta graph: Sleep Onset Latency: complementary and alternative care versus placebo

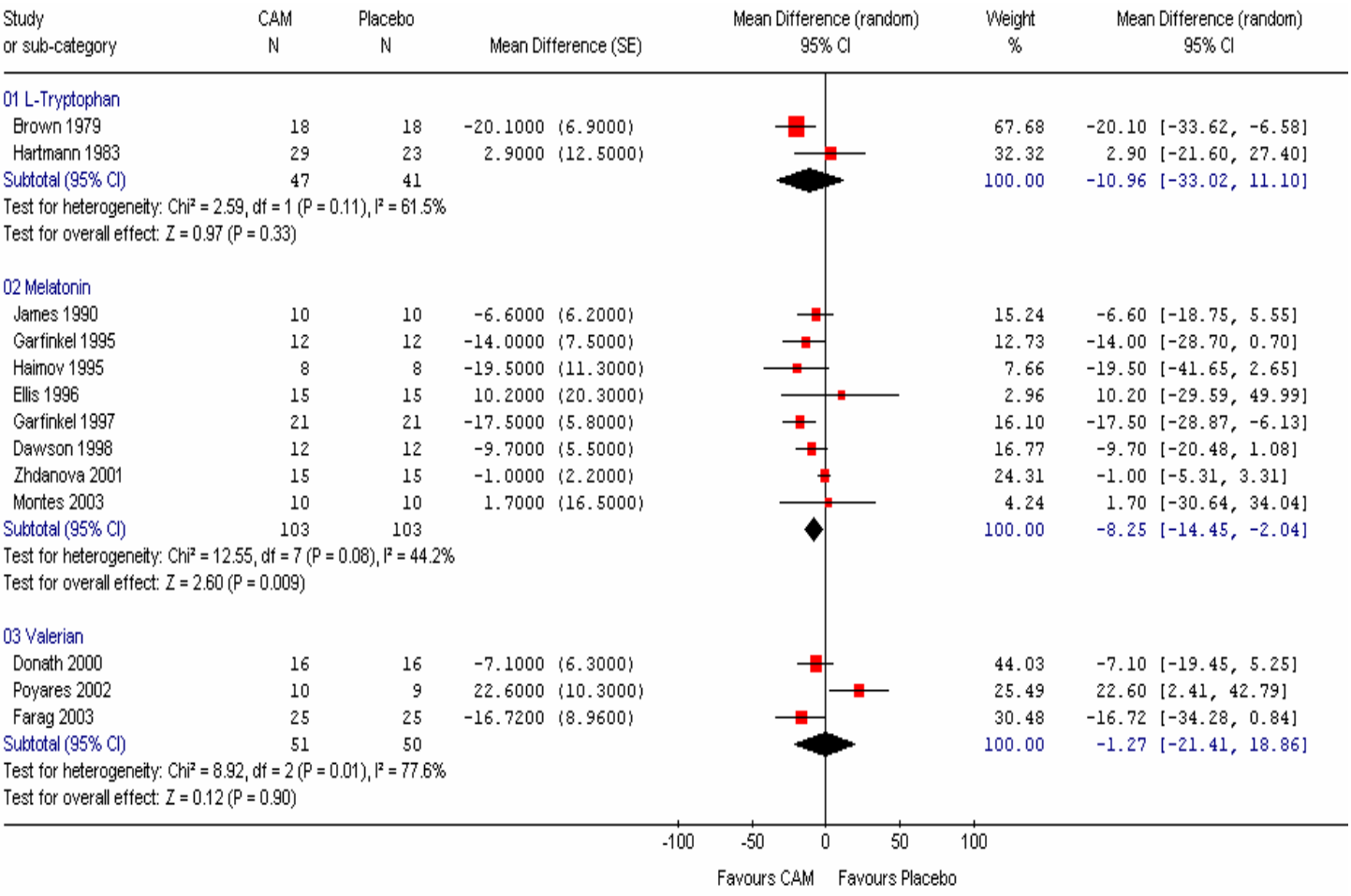


Figure 10. Funnel Plot: Sleep Onset Latency: melatonin versus placebo

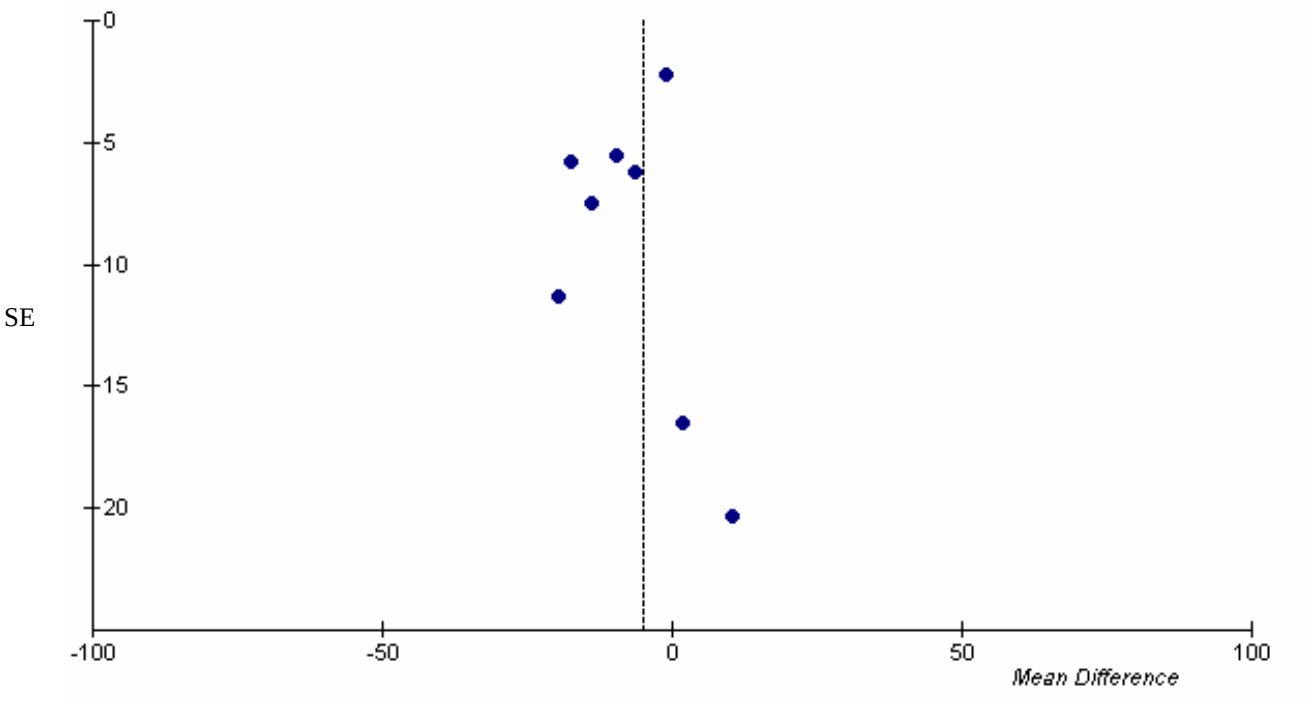


Figure 11. Meta graph: Wakefulness After Sleep Onset: complementary and alternative care versus placebo

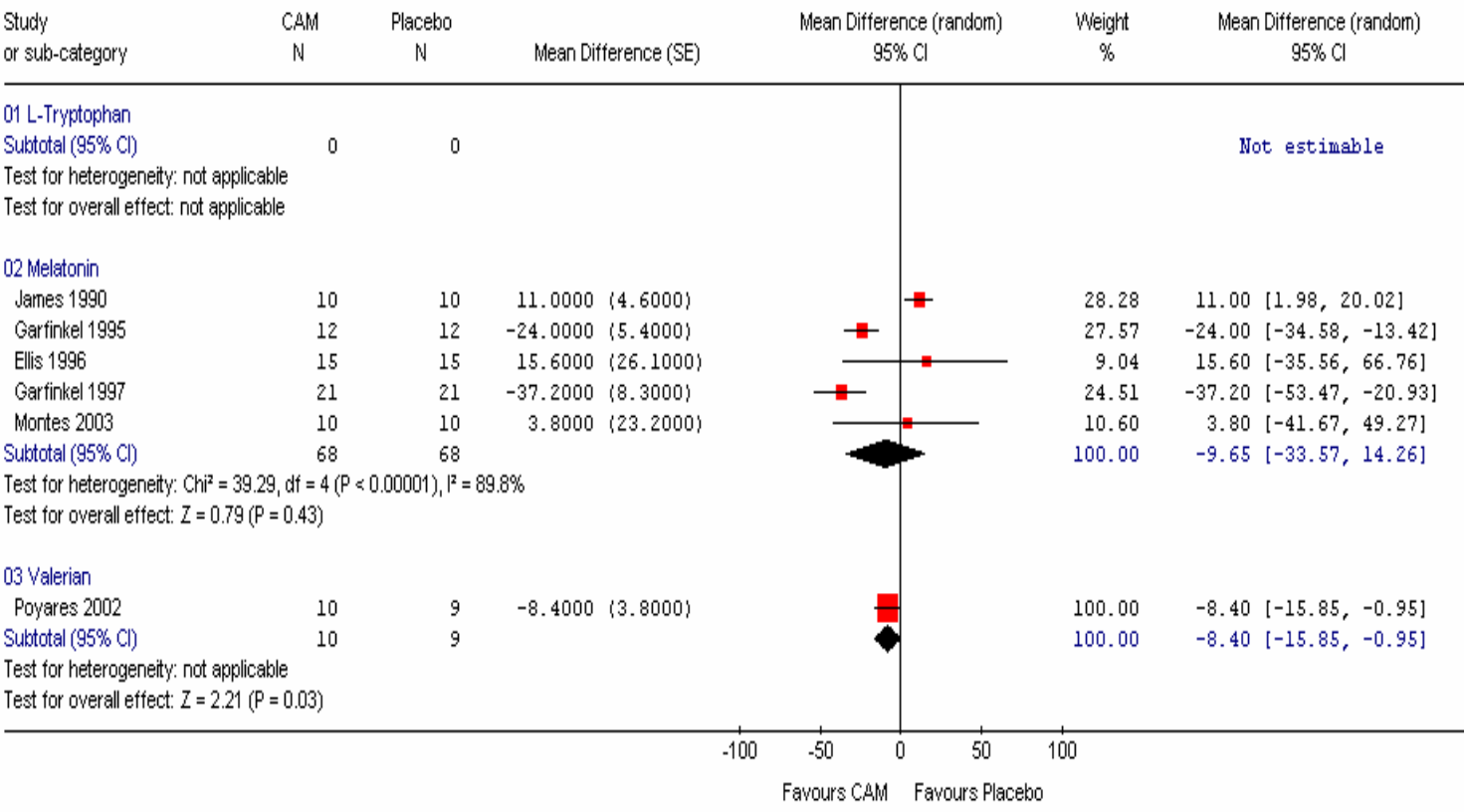


Figure 12. Meta graph: Sleep Onset Latency: relaxation therapy versus placebo

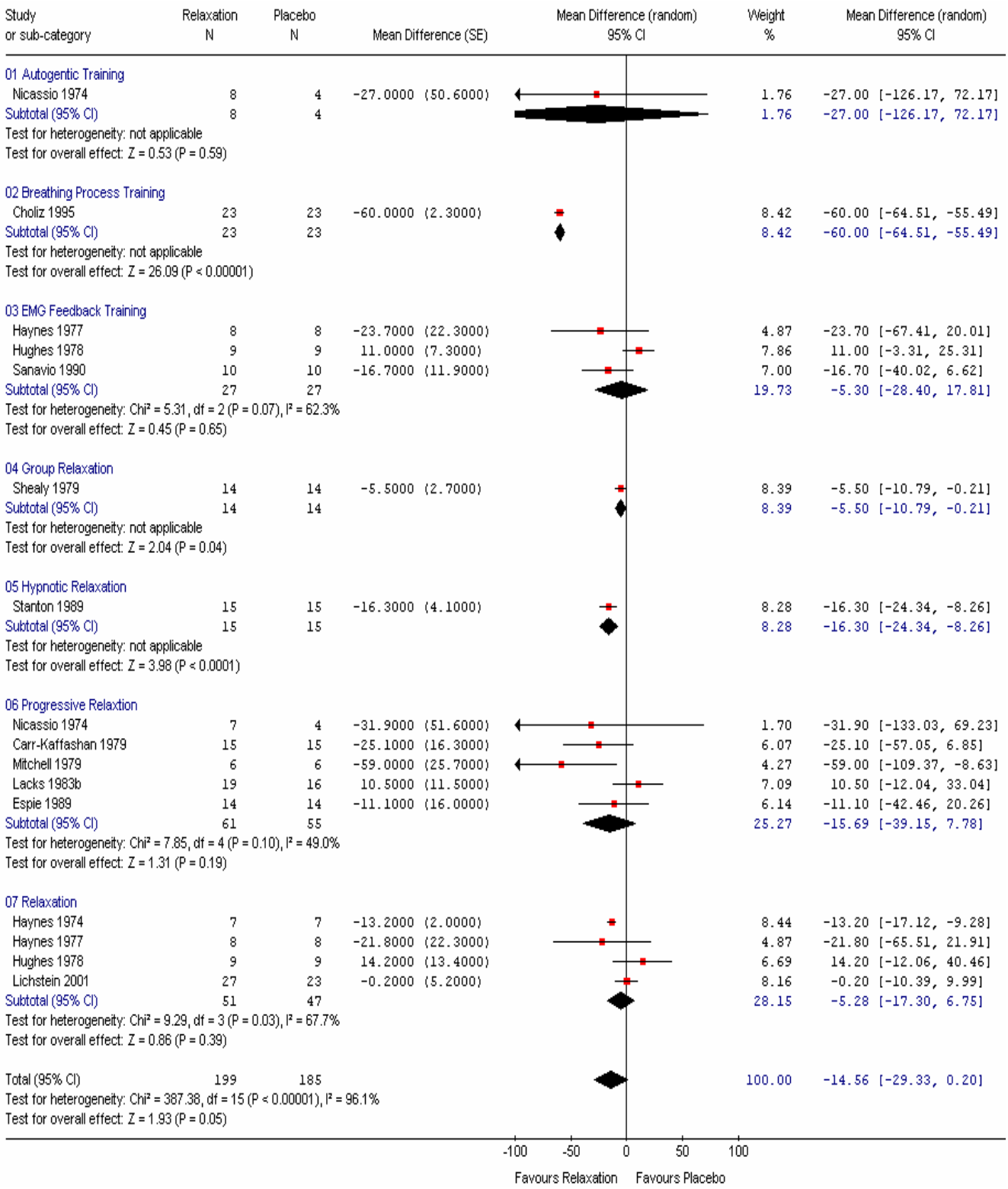


Figure 13. Funnel Plot: Sleep Onset Latency: relaxation therapy versus placebo

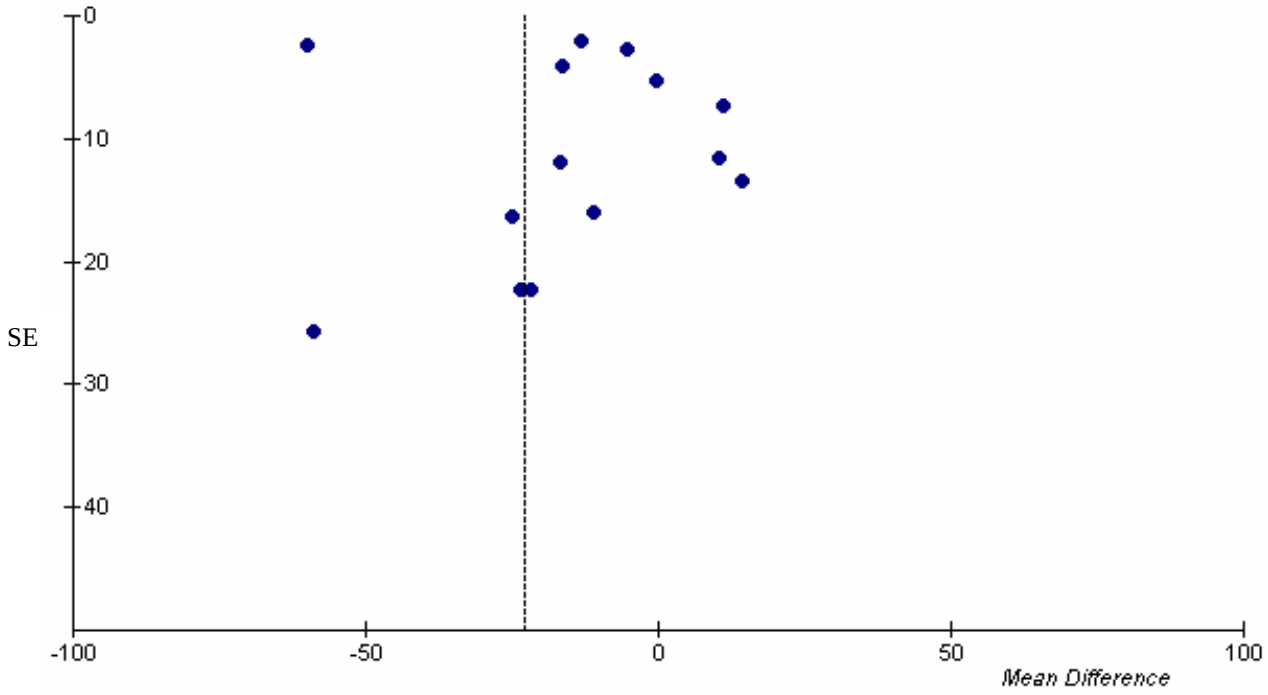


Figure 14. Meta graph: Wakefulness After Sleep Onset: relaxation therapy versus placebo

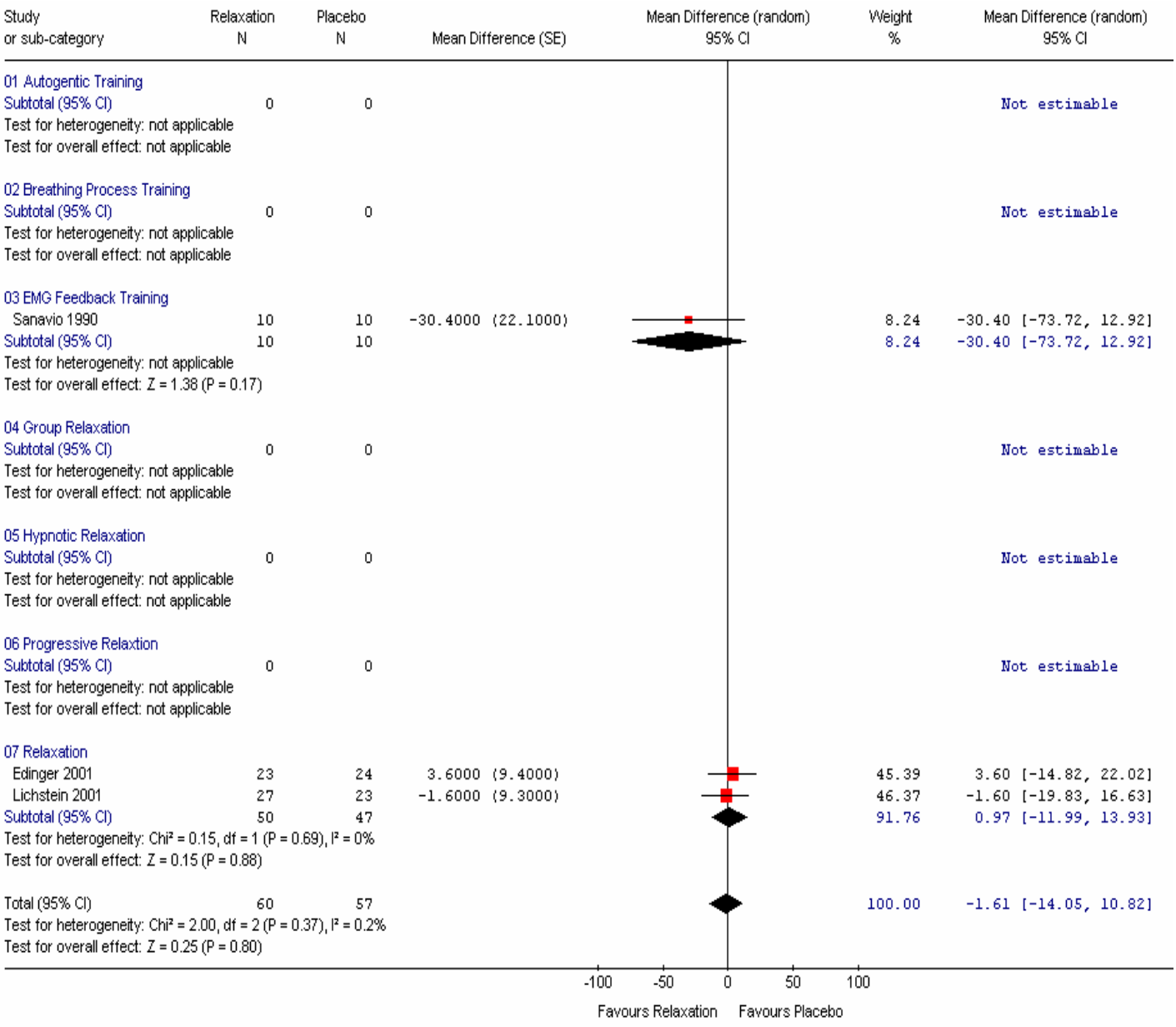


Figure 15. Meta graph: Sleep Onset Latency: cognitive/behavioral therapy versus placebo

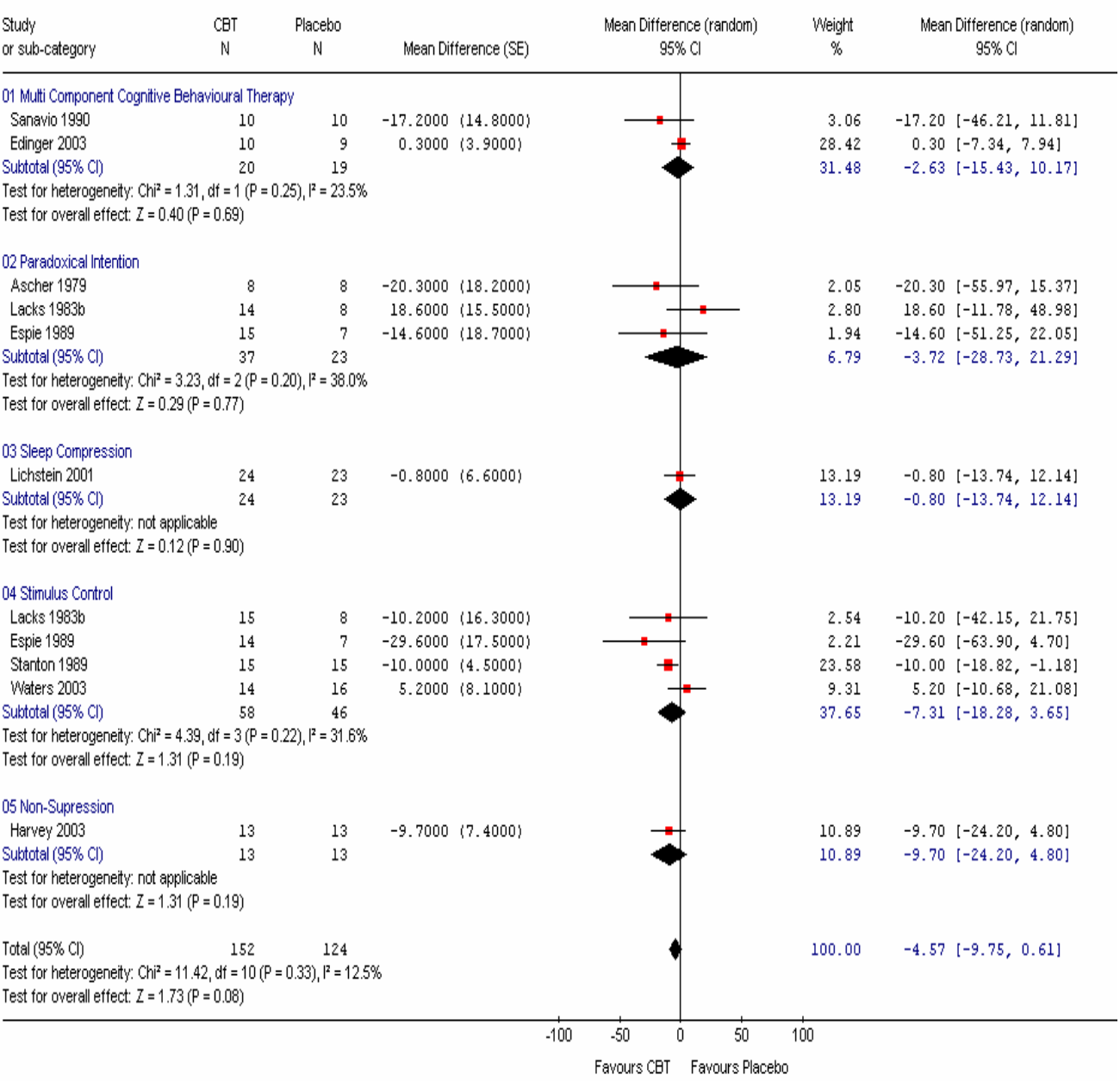


Figure 16. Funnel Plot: Sleep Onset Latency: cognitive/behavioral therapy versus placebo

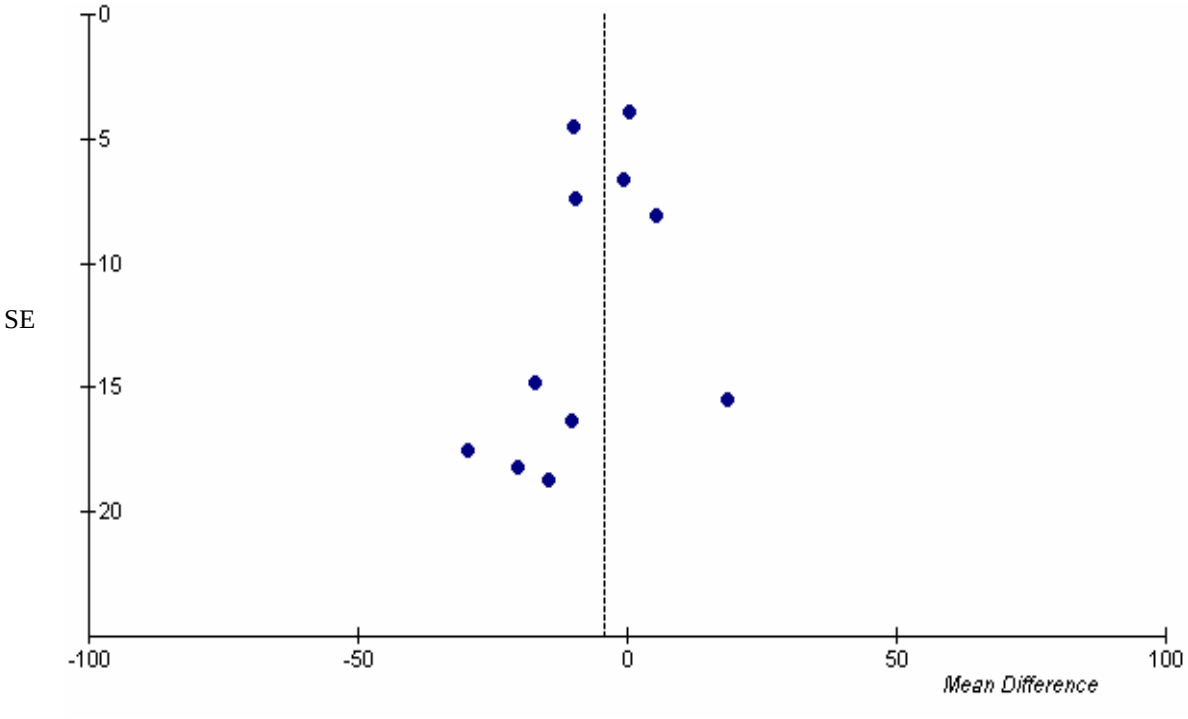
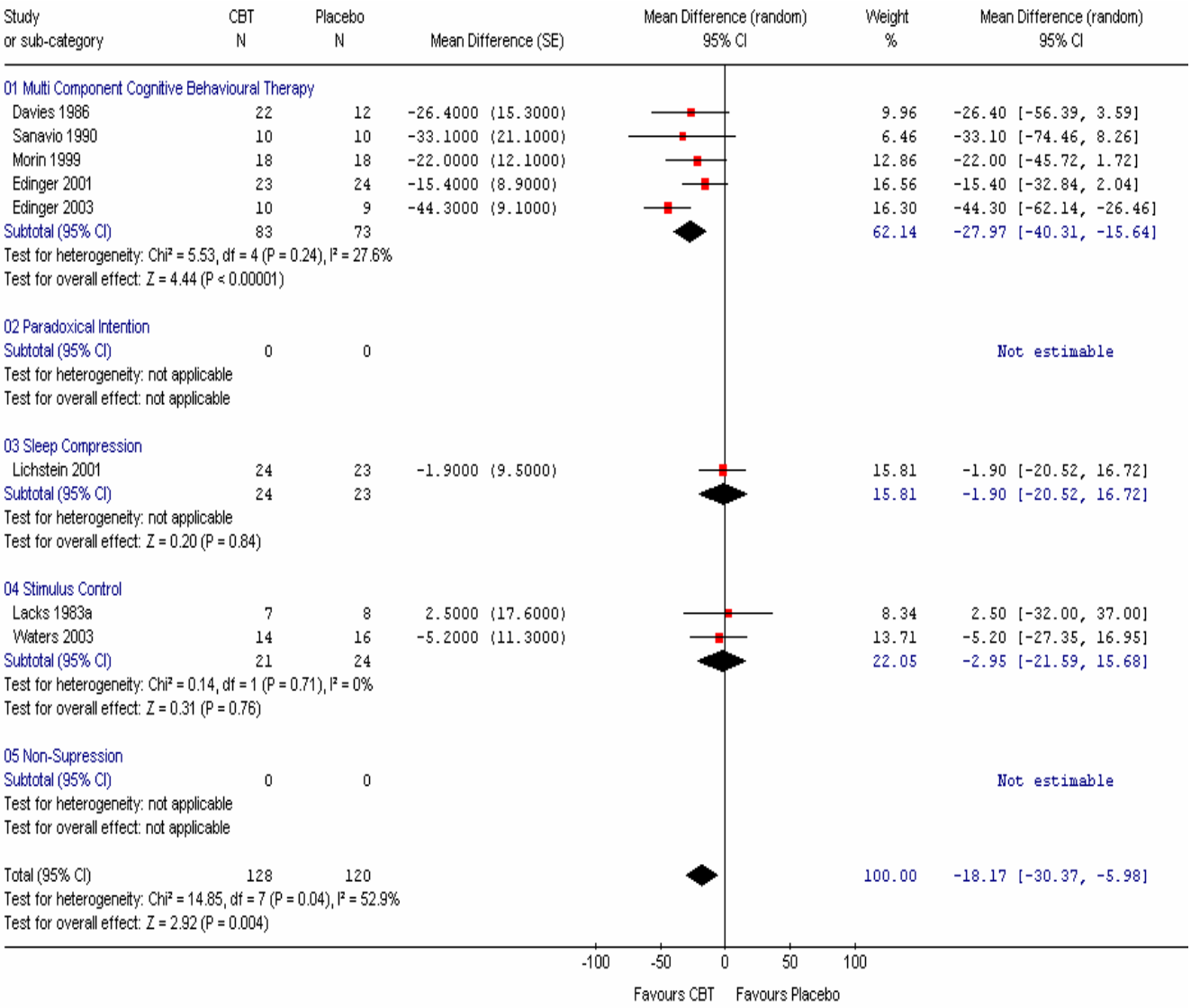


Figure 17. Meta graph: Wakefulness After Sleep Onset: cognitive/behavioral therapy versus placebo



Chapter 4. Discussion

Our inclusion criteria for age allowed for the inclusion of studies in the review for which participants between the ages of 15 and 18 years were eligible. This decision was in agreement with our aim to conduct a comprehensive review of the literature, since we would have otherwise excluded predominantly adult studies based on the possibility that their populations included a sub-population of adolescents. Only 10 out of 79 studies relevant to the manifestations of chronic insomnia explicitly stated that individuals under the age of 18 years were eligible for the study, and only two out of 116 studies relevant to the management of chronic insomnia explicitly stated that individuals under the age of 18 years were eligible for the study. Given the low number of included studies for which adolescents were eligible for inclusion, it is reasonable to assume that the findings of the review apply to adults.

We reviewed only English-language reports. The inclusion of non-English language reports in systematic reviews has been shown to increase treatment estimates in reviews of complementary and alternative medicine (CAM).[66] This effect is thought to occur due to the presence of publication bias in CAM literature, such that studies with negative CAM findings are more likely to be published in English-language journals, and studies with positive CAM findings are more likely to be published in non-English language journals.[66] However, we found no evidence of publication bias by three out of four tests conducted for studies on melatonin. There were not enough studies on L-tryptophan and valerian to conduct meaningful tests of publication bias for these interventions. Only seven non-English language reports were identified that were potentially relevant to this category of intervention, and given that the inclusion rate for the question on management of chronic insomnia was approximately 15 percent, only one study would likely have been relevant to the review. Given the relatively small sample sizes of the studies identified for this category of intervention, it is unlikely that the addition of one study to this category would have considerably affected treatment estimates.

Prevalence, Natural History, Incidence and Factors Associated with Chronic Insomnia

The range of prevalence of chronic insomnia in the three categories of populations analyzed was wide. This variability may be due to the cumulative effect of variation in a number of factors across studies such as the sampling frame and method of sampling, the response rate, whether the method of data collection was validated, the criteria for chronic insomnia, the age distribution of the population, and the presence of psychological or psychiatric problems in the population. Indeed, the criteria for the duration of insomnia varied across studies from one month to one year and the severity of chronic insomnia varied across these populations as well. The interquartile range of prevalence varied from 8.5-24.3 percent across high quality studies of general populations, to 19.8-53.7 percent across moderate quality studies of outpatient populations, to 27.8-43.0 percent across moderate quality studies of clinical populations. Therefore, the prevalence estimates for chronic insomnia in outpatient and clinical populations appear to be significantly higher than for the general population, a finding that is consistent with evidence of an association between chronic insomnia and medical conditions, poor general health and increased healthcare utilization. Although we identified a number of high quality studies examining a general population, we did not identify any high quality studies examining

outpatients of general practice and only one examining clinical populations, suggesting that high quality studies investigating the prevalence of chronic insomnia in outpatients of general practice and clinical populations are needed.

Only one study provided data on the natural history of chronic insomnia; the remission rate was 13.1 percent after a four-month follow-up. More research is necessary to determine the course of chronic insomnia in various populations. We did not identify any studies that provided evidence regarding the incidence of chronic insomnia; more research is needed in this area as well.

The majority of studies identified did not have designs that would support the categorization of associated factors of chronic insomnia as risk factors or consequences of the disorder. That is, most identified studies had designs in which both chronic insomnia and a factor of interest were assessed in a population at the same point in time. It is necessary that longitudinal cohort studies be conducted to elucidate the relationship between chronic insomnia and its associated factors. We found evidence to suggest that chronic insomnia is associated with older age, female gender, present or past psychiatric illness and psychological problems, medical conditions and poor general health, increased healthcare utilization, lower quality of life and social relationships, socioeconomic status (marital separation, unemployment, poorer working conditions and lower social status), and decrements in memory, mood and cognitive function. Some of the factors that are thought to contribute to insomnia in the elderly include multiple medical problems, polypharmacy and environmental factors, such as absence of zeitgebers (time/schedule cues).[50;67] Similarly, factors such as stress, pregnancy, menopause, medical conditions and complex home life may explain the higher prevalence of insomnia in females.[68] It is noteworthy that there were studies that did not find evidence of an association between these factors and chronic insomnia. One of the reasons for this finding may be the different methods of data analysis employed in these studies; some studies performed multivariate analyses, while others performed univariate analyses. Other factors that may explain this finding are the age and gender distribution of the population, the response rate, and the duration of insomnia. Similarly, studies showing a lack of association between variables may have been underpowered. The relationship between chronic insomnia and race/ethnicity, shift-work, and absenteeism and work performance is not clear; there were too few studies examining these relationships to arrive at any conclusions. We did not identify any studies that examined the relationship between chronic insomnia and accidents or falls in the elderly. There was also no evidence regarding the direct and indirect costs of the disorder. Research in these areas is required.

Efficacy and Safety of Treatments for Chronic Insomnia

The interventions for chronic insomnia that were investigated in included studies may be categorized as either benzodiazepines, non-benzodiazepines, antidepressants, complementary and alternative care (L-tryptophan, melatonin and valerian), relaxation therapy, cognitive/behavioral therapy, barbiturates, hormone therapy, alcohol, low energy emission therapy and combination therapy. The majority of studies were classified under the first six categories of the preceding list. The discussion of results relevant to the management of chronic insomnia is focused on the results as they pertain to the primary and secondary outcomes of this review, sleep onset latency (SOL) and wakefulness after sleep onset (WASO); however, any major discrepancies between the estimates for these outcomes and other outcomes will be discussed.

The benzodiazepines, non-benzodiazepines, antidepressants and melatonin significantly decreased SOL. L-tryptophan, valerian, relaxation therapy and cognitive/behavioral therapy reduced SOL, but the results were not statistically significant. Although the overall SOL estimate for relaxation therapy was not significantly different from placebo, when only short-term studies were analyzed, the effect became statistically significant in favour of relaxation therapy. The benzodiazepines, non-benzodiazepines and antidepressants significantly reduced WASO. Melatonin decreased WASO, but the result was not statistically significant. Melatonin had a non-significant effect on sleep efficiency, total sleep time and sleep quality. The studies on L-tryptophan did not report on any other outcomes besides SOL, and only one study on valerian provided data on WASO; valerian significantly reduced WASO in this study. Valerian did not have a significant effect on sleep efficiency, total sleep time or sleep quality. Relaxation therapy reduced WASO, but the result was not significant; however, this intervention significantly increased total sleep time (no significant effect on sleep efficiency or sleep quality). Cognitive/behavioral therapy significantly reduced WASO, and significantly increased sleep efficiency and sleep quality (no significant effect on total sleep time). The review provides evidence that benzodiazepines and non-benzodiazepines are effective treatments for chronic insomnia. The review provides some evidence that antidepressants are effective treatments for chronic insomnia, although more research is required in this area. There is some evidence that melatonin is an effective treatment for subsets of the chronic insomnia population, although more research is required in this area as well. The review provides evidence that relaxation therapy and cognitive/behavioral therapy are effective treatments in subsets of the chronic insomnia population. There were too few studies of L-tryptophan and valerian to draw conclusions regarding the efficacy of these treatments in the management of chronic insomnia: additional large-scale, randomized trials are needed. Additional large-scale, randomized trials are also needed in the area of relaxation therapy and cognitive/behavioral therapy in the management of chronic insomnia, in order to determine the efficacy of these interventions across subsets of the chronic insomnia population. The reduction in sleep onset latency by benzodiazepines and non-benzodiazepines was significantly greater than for antidepressants and melatonin, based on indirect comparisons. However, it should be noted that there were significantly fewer studies of antidepressants and melatonin compared to benzodiazepines and non-benzodiazepines, and additional large-scale, randomized trials of the former interventions are needed before firm conclusions can be drawn regarding the relative efficacy of these interventions.

The benzodiazepines, non-benzodiazepines and antidepressants had a significantly greater risk of harm than placebo, while melatonin did not. There were too few studies of L-tryptophan to draw conclusions regarding the safety of this intervention. Although there was no evidence that valerian poses a risk of harm, this result was based on only three studies of relatively small sample size. Therefore, more studies are needed before firm conclusions can be drawn regarding the safety of valerian. The risk for benzodiazepines was significantly greater than for non-benzodiazepines, based on indirect comparisons. Indeed, benzodiazepine use has been shown to increase the risk of injury in the elderly,[69] and there is pharmacologic evidence that the non-benzodiazepines have a better side-effect profile than the benzodiazepines.[70-71] Studies of relaxation therapy and cognitive/behavioral therapy did not provide adverse event data.

We did not aim to conduct a head-to-head comparison between pharmacological and non-pharmacological treatments for chronic insomnia, in which case we would have required randomized, controlled trials, which directly compare these interventions, in order to control for systematic differences between control and experimental groups. An indirect comparison

between these categories of interventions is not presented here for the following reasons: (1) although our inclusion criteria required blinding for drug and CAM treatments, this criteria was omitted for psychological treatments; (2) the placebo intervention was considered to have no effect for drug and CAM treatments, while it may have had minimal effect for psychological treatments; (3) the pool of participants for psychological interventions was much smaller than for either the benzodiazepines, non-benzodiazepines or antidepressants. Thus, only indirect comparisons between non-psychological intervention categories and between psychological interventions were made.

There was substantial heterogeneity in the pooled estimate for SOL for benzodiazepines, non-benzodiazepines, L-tryptophan, valerian and relaxation therapy. Similarly, there was substantial heterogeneity in the pooled estimate for WASO for benzodiazepines, non-benzodiazepines, melatonin and cognitive/behavioral therapy. The heterogeneity was often due to differences in the magnitude of the point estimate and confidence interval across studies, rather than differences in the directionality of the effect. The exceptions are for estimates of the efficacy of relaxation therapy with respect to SOL and the efficacy of melatonin with respect to WASO. The heterogeneity in the pooled estimates for SOL was explored in sensitivity and sub-group analyses. The results indicate that heterogeneity in the pooled estimate for SOL for relaxation therapy is at least partially due to type of relaxation therapy, length of treatment, age and gender distribution of the study population, and study quality.

There was strong evidence of publication bias in the pooled estimates for SOL for the benzodiazepine and non-benzodiazepine categories of intervention. This finding suggests that the true estimate of efficacy is lower than the estimate calculated in the current analysis.

The results of sub-group analyses of SOL were varied. The efficacy of non-benzodiazepines was greater in participants without a psychiatric illness relative to those with such a disorder. This finding may reflect the strong, poorly understood, complex relationship between psychological or psychiatric disorders and insomnia,[4] which necessitates individualized treatment of insomnia for people suffering from these psychological or psychiatric disorders. The efficacy of relaxation therapy was greater with short-term treatment compared to long-term treatment. There were no salient differences in the design, population, intervention or method of measurement of sleep outcomes between short- and long-term studies that could explain the differences in effect of relaxation therapy with length of treatment. The possibility exists that the subgroup for long-term treatment did not have sufficient power to detect a statistically significant difference between relaxation therapy and placebo. There were too few long-term studies of cognitive/behavioral therapy to arrive at a conclusion regarding the difference in efficacy of this intervention with short- and long-term treatment. There was no evidence to suggest that treatment efficacy is affected by age or gender distribution of the population. It is noteworthy that many of the sub-group analyses were conducted with very few studies in sub-groupings, and some analyses could not be performed at all due to lack of data. Thus, the results of these analyses should be interpreted with caution. It is important that future research examine the role of factors such as psychiatric illness, length of treatment, age and gender in treatment efficacy in chronic insomnia.

We made an *a priori* decision to combine summary estimates of outcomes even if they were measured by different methods i.e. (polysomnography, actigraphy and sleep diary). We assumed that any differences between methods would be cancelled out when absolute differences in the effect of treatment and placebo were obtained. This assumption is correct as long as the differences in measurement between methods were not correlated with the value of the

measurement, which is a reasonable assumption in our view. The sub-group analyses based on method of measurement produced variable results. Of the six comparisons made between polysomnography and sleep diary data, the methods most commonly used in the studies included in this review, only two analyses revealed a significant difference between pooled estimates (benzodiazepines and valerian); in both cases sleep diary overestimated effects relative to polysomnography. However, while four comparisons showed sleep diary to overestimate effects relative to polysomnography (benzodiazepines, non-benzodiazepines, antidepressants, and valerian), two other comparisons showed polysomnography to overestimate effects relative to sleep diary (L-tryptophan and melatonin). These results appear to be inconsistent in terms of the direction of a potential bias and cause us to doubt whether any true relationship between measurement method and effect estimates exists. It is noteworthy that the direction and significance of the estimates were not different between overall and sub-group estimates for the benzodiazepine, non-benzodiazepine and antidepressant categories of interventions. Although some differences were observed in the directionality and significance of overall and sub-group estimates for L-tryptophan, melatonin and valerian, the results may simply reflect the lower power of these sub-group analyses: sub-groups contained only one to three studies of small sample size.

There was no evidence of an effect of barbiturates, hormone therapy, alcohol and low energy emission therapy on sleep onset latency of chronic insomniacs. The lack of evidence may reflect the low number of studies and/or participants encompassed by these categories. It would be worthwhile to explore these interventions in future research on chronic insomnia.

We identified a small sample of studies examining the efficacy of combination treatments in the management of chronic insomnia; some of these studies compared a combination of treatments with placebo, while others compared them with single treatment. Many comparisons did not have data for our primary outcome, sleep onset latency, and the majority of results were non-significant. The latter finding may reflect the low power of these analyses. None of the studies provided data on adverse events. We identified only one study that compared the efficacy of a combined pharmacological and psychological treatment with these treatments administered sequentially. The research agenda for the management of chronic insomnia should include an evaluation of the efficacy and safety of combination treatments and sequential treatments.

Our results regarding the efficacy of benzodiazepines and non-benzodiazepines in the management of chronic insomnia are consistent with those of other meta-analyses.[72-74] Our results regarding the efficacy of melatonin in subsets of the chronic insomnia population are similar to another review.[75] Our results regarding the efficacy of relaxation therapy and cognitive/behavioral therapy in subsets of the chronic insomnia population are similar to a recent meta-analysis reviewing the efficacy of cognitive/behavioral therapy in the management of sleep problems in older adults.[76] Similar to our meta-analysis, the authors restricted the review to randomized, controlled trials. Our results relating to relaxation therapy and cognitive/behavioral therapy are somewhat at odds with three meta-analyses reviewing the efficacy of psychological treatments in the management of chronic insomnia.[74;77-78] The difference in the findings may relate to key differences in the conduct of the reviews. First, we restricted our meta-analysis to a review of placebo-controlled, randomized trials and accounted for placebo effects in our estimations of efficacy. Other meta-analyses have included non-controlled studies, and for these studies, have not accounted for placebo/control effects in their estimation of efficacy. Second, we used clearly defined criteria for chronic insomnia; however, for some studies the criteria for

insomnia was not clear. Third, we separated predominantly cognitive/behavioral approaches from predominantly relaxation approaches in management of insomnia, resulting in distinct meta-analyses for each category of intervention. These interventions have been grouped under the broader heading of psychological/non-pharmacological treatments in other reviews.

Limitations of the Review and Future Research

Additional high quality studies investigating the prevalence of chronic insomnia in outpatients of general practice and clinical populations are needed. Similarly, we found a paucity of data on the natural history and incidence of chronic insomnia, which necessitates further research in these areas. We did not identify any cohort studies that examined the causal relationship between various factors and chronic insomnia; future research should be directed at conducting such studies in order to determine the nature of the relationship between chronic insomnia and its associated factors. Additional studies are needed to examine the relationship between chronic insomnia and race/ethnicity, shift-work, and absenteeism and work performance, since few studies in this area exist. Future research should also examine the relationship between chronic insomnia and accidents and falls in the elderly, and the direct and indirect costs of this disorder, since we did not identify any studies that addressed these issues.

The pooled estimates of efficacy for antidepressants, CAM therapies, relaxation therapy and cognitive/behavioral therapy were based on a small sample size relative to benzodiazepines and non-benzodiazepines. It is necessary that additional large-scale, randomized trials be conducted before firm conclusions can be drawn regarding their efficacy and safety and how they compare to other treatments for chronic insomnia. We found a relatively small number of studies examining the long-term efficacy and safety of various interventions for chronic insomnia: more long-term studies are needed in order to differentiate the short and long-term efficacy and safety of these interventions. It is necessary that an agreed upon criteria be developed to determine what constitutes short- and long- term treatment of chronic insomnia. In addition, research should be conducted to establish a threshold for a clinically significant treatment effect in the management of chronic insomnia, such that statistically significant findings can be put into some clinical context. Future research should report on outcomes in addition to SOL, such as WASO, in order to determine the efficacy of treatments across subsets of the chronic insomnia population; our analysis revealed that studies tend to report SOL much more often than WASO. Quality of life outcomes should also be given more attention. It is necessary that future research be directed at establishing an agreed upon placebo treatment for psychological treatment that is standardized across studies, such that meaningful comparisons can be made across studies of this type. Finally, additional studies are necessary to determine the efficacy and safety of combined pharmacological and psychological treatments, as well as sequential treatments in the management of chronic insomnia.

Many of the sub-group analyses conducted in this review were based on a small number of studies within sub-groupings, and some analyses could not be conducted at all due to lack of data. The paucity of data may reflect a need for future research to determine the efficacy and safety of treatments for chronic insomnia within specific sub-populations stratified by age, gender, and presence or absence of psychiatric illness. There was no evidence of an effect of barbiturates, hormone therapy, alcohol and low energy emission therapy on sleep onset latency of chronic insomniacs, however, there was a small amount of data in these areas, which prevents one from drawing firm conclusions before additional research is conducted.

A number of the six major categories of interventions for chronic insomnia had substantial heterogeneity, suggesting that the studies within these categories were significantly different. In some cases, sub-categorization by type of intervention significantly reduced heterogeneity within some of these categories. The categorization of interventions into classes is reasonable when the goal is to determine the efficacy and safety of a given class of intervention; however, it should be noted that although the interventions of a given class may be similar in some respects, they are in fact unique. For many interventions within these categories, there were few studies that addressed their safety and efficacy, and additional research is required into the efficacy and safety of these various interventions of chronic insomnia.

There was strong evidence of publication bias for the benzodiazepine and non-benzodiazepine categories, which suggests that the pooled estimates of treatment efficacy may be overestimates.

It is noteworthy that research in the area of bright light therapy and physical exercise in the management of insomnia is ongoing; however, we did not identify any studies of these interventions that fulfilled our inclusion criteria.

We restricted our analysis of efficacy and safety to evidence derived from randomized-controlled trials in order to provide the least biased estimate of these parameters. However, it should be noted that the short follow-up period that generally characterizes these types of studies is a limitation when assessing the long-term safety of pharmacological treatments.

Conclusions

- There is evidence that the prevalence of chronic insomnia in outpatient and clinical populations is larger than in the general population.

- There is evidence that chronic insomnia is associated with older age, female gender, present or past psychiatric illness and psychological problems, medical conditions and poor general health, increased healthcare utilization, lower quality of life and social relationships, socioeconomic status (marital separation, unemployment, poorer working conditions and lower social status), and decrements in memory, mood and cognitive function.

- Additional studies are needed to determine the incidence and natural history of chronic insomnia in adults. Similarly, additional studies are needed to explore the relationship between chronic insomnia and race/ethnicity, shift-work, absenteeism and work performance, accidents, falls in the elderly, and the direct and indirect costs of the disorder. It is necessary that longitudinal studies be undertaken to explore the risk factors and consequences of chronic insomnia.

- There is evidence that benzodiazepines and non-benzodiazepines are effective in the management of chronic insomnia. There is some evidence that antidepressants are effective in the management of chronic insomnia: more research is required in this area. There is evidence that benzodiazepines, non-benzodiazepines and antidepressants pose a risk of harm.

- There is some evidence that melatonin is effective in the management of chronic insomnia in subsets of the chronic insomnia population, and there is no evidence that melatonin poses a risk of harm. However, more research is required in this area, given that the results are based on a small number of studies. Similarly, additional large-scale, randomized trials are needed to determine the efficacy of melatonin across subsets of the chronic insomnia population. There is insufficient evidence to conclude on the efficacy and safety of L-tryptophan and valerian in the management of chronic insomnia. Additional large-scale, randomized trials are needed in these areas.

- There is evidence that relaxation therapy and cognitive/behavioral therapy are effective in the management of chronic insomnia in subsets of the chronic insomnia population. Additional large-scale, randomized trials are needed in order to determine their efficacy across subsets of the chronic insomnia population.

- There is evidence that benzodiazepines have a greater risk of harm than non-benzodiazepines.

- There is insufficient evidence to conclude if there are differences between the short-term and long-term efficacy and safety of the various categories of interventions in the management of chronic insomnia; additional long-term studies are needed.

- There is insufficient evidence regarding the efficacy and safety of combined treatments of pharmacological and psychological interventions, and sequential treatments, in the management of chronic insomnia; additional studies are needed in these areas.

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Appendix A: Exact Search Strings

Table A-1. MEDLINE® - Ovid Version: rel9.1.0

1966 to September Week 1 2004 Searched Sept. 15, 2004
1. insomni$.mp.
2. exp "Sleep Initiation and Maintenance Disorders"/
3. (sleep adj initiation adj2 maintenance adj disorder$).mp.
4. (sleep adj onset adj3 (delay$ or latenc$)).mp.
5. dims.mp.
5. (disorder$ adj initiating adj2 maintaining adj sleep).mp.
6. (early adj2 awaken$).mp.
7. (sleeplessness or agrypnia$ or hyposomnia$).mp.
8. or/1-8
9. "analytic stud$".mp.
10. exp case-control studies/ or exp retrospective studies/
11. exp cohort studies/ or exp longitudinal studies/ or exp follow-up studies/ or exp prospective studies/ or comparative study/ or exp Evaluation Studies/
12. exp Cross-Sectional Studies/
13. exp RISK FACTORS/ or exp RISK/ or exp RISK ASSESSMENT/
14. exp Odds Ratio/
15. exp CAUSALITY/
16. exp Logistic Models/
17. exp epidemiologic factors/ or exp age factors/ or exp "bias (epidemiology)"/ or exp comorbidity/ or exp "confounding factors (epidemiology)"/ or exp "effect modifiers (epidemiology)"/ or exp observer variation/ or exp reproductive history/ or exp sex factors/
18. exp morbidity/ or exp incidence/ or exp prevalence/
19. (cohort or observational or correlational or non-experimental or "non experimental" or nonexperimental or control$ or prospectiv$ or volunteer$ or "case series" or "case-series" or "case comparison" or "case-comparison" or "case referent" or "case-referent" or "cross sectional" or "cross-sectional" or risk or "relative risk" or causation or causal$ or "odds ratio$" or etiol$ or aetiol$ or incidence).mp.
20. exp prognosis/ or exp medical futility/ or exp treatment outcome/
21. exp mortality/ or exp "cause of death"/ or exp fatal outcome/ or exp survival rate/
22. exp survival analysis/ or exp disease-free survival/
23. exp disease susceptibility/ or exp genetic predisposition to disease/
24. exp disease progression/ or exp "Severity of Illness Index"/
25. exp Time Factors/
26. exp RECURRENCE/
27. ("natural history" or "inception cohort" or predict$ or prognos$ or outcome$ or course).mp.
28. exp "costs and cost analysis"/ or exp "cost allocation"/ or exp cost-benefit analysis/ or exp "cost control"/ or exp "cost savings"/ or exp "cost of illness"/ or exp "cost sharing"/ or exp "deductibles and coinsurance"/ or exp health care costs/ or exp direct service costs/ or exp drug costs/ or exp employer health costs/ or exp hospital costs/ or exp health expenditures/ or exp capital expenditures/
29. exp "Quality of Life"/ or exp "Activities of Daily Living"/
30. exp "OUTCOME ASSESSMENT (HEALTH CARE)"/ or exp "OUTCOME AND PROCESS ASSESSMENT (HEALTH CARE)"/ or exp Health Status Indicators/ or exp Health Status/ or exp Questionnaires/
31. (cost$ or economic or social or "quality of life" or "life quality" or hrql or well-being or wellbeing or "well being" or "outcome adj assessment$" or "health status").mp.
32. (et or pc or ae or ep or to or ge or ec or in or ut or mo).fs.
33. or/10-33
34. animal/ not human/
35. 34 not 35
36. 9 and 36
37. eng.la.
38. 37 and 38
39. insomni$.mp.
40. exp "Sleep Initiation and Maintenance Disorders"/
41. (sleep adj initiation adj2 maintenance adj disorder$).mp.

Table A-1. MEDLINE® - Ovid Version: rel9.1.0 (continued)

1966 to September Week 1 2004 Searched Sept. 15, 2004
42. (sleep adj onset adj3 (delay$ or latenc$)).mp.
43. dims.mp.
44. "disorder$ of initiating and maintaining sleep".mp.
45. (early adj2 awaken$).mp.
46. (sleeplessness or agrypnia$ or hyposomnia$).mp.
47. (((time-zone or "time zone") adj2 change$) or "jet lag").mp.
48. or/40-48
49. randomized controlled trial.pt.
50. controlled clinical trial.pt.
51. randomized controlled trials/
52. random allocation/
53. double blind method/
54. single blind method/
55. clinical trial.pt.
56. exp Clinical Trials/
57. (clin$ adj25 trial$).ti,ab.
58. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab.
59. placebos/
60. placebo$.ti,ab.
61. random$.ti,ab.
62. research design/
63. or/50-63
64. 64 not 35
65. 49 and 65
66. 66 not 39
67. meta-analysis.pt,sh.
68. (meta-anal$ or metaanal$).mp.
69. ((systematic$ adj3 review$) or (systematic$ adj3 overview$)).mp.
70. ((quantitativ$ adj3 review$) or (quantitativ$ adj3 overview)).mp.
71. ((methodol$ adj3 review$) or (methodol$ adj3 overview$)).mp.
72. (integrative research review$ or research integration$).mp.
73. (quantitativ$ adj (synthes$ or analys$)).mp.
74. (("evidence based" or evidence-based) adj3 (medicine or guideline$ or recommendation$)).mp.
75. guideline.pt.
76. "cochrane database of systematic reviews".mp.
77. cdsr.mp.
78. acp journal club.mp.
79. "health tech$ assess$".mp.
80. hta.mp.
81. "evidence based nursing".mp.
82. "evidence based mental health".mp.
83. "clinical evidence".mp.
84. technolog$ assess$.mp.
85. "evidence report$".mp.
86. or/68-86
87. review.pt. or (review or overview$ or reviews or handsearch or "hand search" or hand-search or "manual search").mp.
88. (medline or medlars or pubmed or embase or "index medicus" or cochrane or scisearch or "Web of Science" or psychinfo or psycinfo or psychlit or psyclit or cinahl or cinhal or "experta medica" or "excerpta medica" or "science citation index" or "sciences citation index" or "biological abstracts" or "current contents").mp.
89. (((electronic or bibliographic) adj3 database$) or "periodical index$").mp.
90. ((pool$ or combined or combining) adj (data or trials or studies or results)).mp.
91. (peto or "der simonian" or dersimonian or "fixed effect$" or "treatment outcome$" or "mantel haenszel").mp.

Table A-1. MEDLINE® - Ovid Version: rel9.1.0 (continued)

1966 to September Week 1 2004 Searched Sept. 15, 2004
92. or/89-92 93. 88 and 93 94. 87 or 94 95. case report.ti,sh. 96. editorial.ti,pt. 97. letter.pt. 98. newspaper article.pt. 99. comment.pt. 100. or/96-100 101. 95 not 101 102. animal/ not human/ 103. 102 not 103 104. eng.la. 105. 104 and 105 106. 9 and 106 107. 107 not (39 or 67)

Table A-2. EMBASE - Ovid Version: rel9.1.0

1988 to 2004 Week 37
Searched September 15, 2004

1. insomni$.mp. or exp insomnia/
2. (sleep adj initiation adj2 maintenance adj disorder$).mp.
3. (sleep adj onset adj3 (delay$ or latenc$)).mp.
4. dims.mp.
5. (disorder$ adj initiating adj2 maintaining adj sleep).mp.
6. (early adj2 awaken$).mp.
7. (sleeplessness or agrypnia$ or hyposomnia$).mp.
8. or/1-7
9. "analytic stud$".mp.
10. exp case-control study/ or exp retrospective study/
11. exp cohort analysis/ or exp longitudinal study/ or exp prospective study/ or exp Comparative Study/ or exp Evaluation/
12. (("follow up" or follow-up) adj stud$).mp.
13. exp GENETIC RISK/ or exp POPULATION RISK/ or exp CORONARY RISK/ or exp HIGH RISK PATIENT/ or exp HIGH RISK PREGNANCY/ or exp RISK FACTOR/ or exp CARDIOVASCULAR RISK/ or exp RISK ASSESSMENT/ or exp RISK/ or exp HIGH RISK POPULATION/ or exp CANCER RISK/ or exp RISK MANAGEMENT/ or exp RISK REDUCTION/ or exp RISK BENEFIT ANALYSIS/ or exp INFECTION RISK/ or exp RECURRENCE RISK/
14. causality.mp.
15. (Logistic adj Model$).mp. or exp Statistical Model/
16. exp COMORBIDITY/ or exp Onset Age/ or exp Observer Variation/ or exp Sex Difference/
17. exp epidemiology/ or exp incidence/ or exp morbidity/ or exp mortality/ or prevalence/
18. (cohort or control$ or correlational or non-experimental or "non experimental" or nonexperimental or prospectiv$ or volunteer$ or "case series" or "case-series" or "case comparison" or "case-comparison" or "case referent" or "case-referent" or "cross sectional" or "cross-sectional" or risk or "relative risk" or causation or causal$ or "odds ratio$" or etiol$ or aetiol$ or incidence).mp.
19. exp prognosis/ or medical futility.mp. or exp treatment outcome/
20. exp "cause of death"/ or exp fatality/ or exp survival rate/
21. exp SURVIVAL RATE/ or exp SURVIVAL/ or exp SURVIVAL TIME/
22. exp Disease Predisposition/ or exp Genetic Predisposition/
23. exp Disease Course/ or "Severity of illness index".mp.
24. exp Recurrent Disease/ or exp Disease Severity/ or exp Chronic Disease/
25. ("natural history" or "inception cohort" or predict$ or prognos$ or outcome$ or course).mp.
26. exp "HOSPITAL COST"/ or exp "COST EFFECTIVENESS ANALYSIS"/ or exp "COST UTILITY ANALYSIS"/ or exp "ENERGY COST"/ or exp "COST CONTROL"/ or exp "DRUG COST"/ or exp "COST BENEFIT ANALYSIS"/ or exp "COST MINIMIZATION ANALYSIS"/ or exp "COST"/ or exp "HEALTH CARE COST"/ or exp "COST OF ILLNESS"/
27. exp "Quality of Life"/ or exp Daily Life Activity/
28. exp Health Status/ or exp Follow Up/ or exp Questionnaire/ or exp Outcomes Research/ or exp Health Care Quality/
29. (cost$ or economic or social or "quality of life" or Hrql or "life quality" or well-being or wellbeing or "well being" or "outcome adj assessment$" or "health status").mp.
30. ((human or "daily living") adj2 activit$).mp.
31. (et or pc or ae or ep or to or ge or ec or in or ut or mo).fs.
32. or/9-31
33. limit 32 to human/
34. Nonhuman/
35. 33 not 34
36. 8 and 35
37. eng.la.
38. 36 and 37
39. insomni$.mp. or exp insomnia/
40. (sleep adj initiation adj2 maintenance adj disorder$).mp.
41. (sleep adj onset adj3 (delay$ or latenc$)).mp.
42. dims.mp.

Table A-2. EMBASE - Ovid Version: rel9.1.0 (continued)

1988 to 2004 Week 37
Searched September 15, 2004

43. (disorder$ adj initiating adj2 maintaining adj sleep).mp.
44. (early adj2 awaken$).mp.
45. (sleeplessness or agrypnia$ or hyposomnia$).mp.
46. exp Jet Lag/
47. (((time-zone or "time zone") adj2 change$) or "jet lag").mp.
48. or/39-47
49. Randomized Controlled Trial/
50. exp Randomization/
51. Double Blind Procedure/
52. Single Blind Procedure/
53. Clinical Trial/
54. (clin$ adj25 trial$).mp.
55. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).mp.
56. exp Placebo/
57. (placebo$ or random$).mp.
58. exp Methodology/
59. or/49-58
60. limit 59 to human/
61. 60 not 34
62. 48 and 61
63. 62 not 38
64. meta-analysis.sh.
65. (meta-anal$ or metaanal$).mp.
66. ((systematic$ adj3 review$) or (systematic$ adj3 overview$)).mp.
67. ((quantitativ$ adj3 review$) or (quantitativ$ adj3 overview)).mp.
68. ((methodol$ adj3 review$) or (methodol$ adj3 overview$)).mp.
69. (integrative research review$ or research integration$).mp.
70. (quantitativ$ adj (synthes$ or analys$)).mp.
71. (("evidence based" or evidence-based) adj3 (medicine or guideline$ or recommendation$)).mp.
72. "cochrane database of systematic reviews".mp.
73. cdsr.mp.
74. acp journal club.mp.
75. "health tech$ assess$".mp.
76. hta.mp.
77. "evidence based nursing".mp.
78. "evidence based mental health".mp.
79. "clinical evidence".mp.
80. technolog$ assess$.mp.
81. "evidence report$".mp.
82. or/64-81
83. review.pt. or (review or overview$ or reviews or handsearch or "hand search" or hand-search or "manual search").mp.
84. (medline or medlars or pubmed or embase or "index medicus" or cochrane or scisearch or "Web of Science" or psychinfo or psycinfo or psychlit or psyclit or cinahl or cinhal or "experta medica" or "excerpta medica" or "science citation index" or "sciences citation index" or "biological abstracts" or "current contents").mp.
85. (((electronic or bibliographic) adj3 database$) or "periodical index$").mp.
86. ((pool$ or combined or combining) adj (data or trials or studies or results)).mp.
87. (peto or "der simonian" or dersimonian or "fixed effect$" or "treatment outcome$" or "mantel haenszel").mp.
88. or/84-87
89. 83 and 88
90. 82 or 89
    91. case report.ti,sh.
91. editorial.ti,pt.
92. letter.pt.
93. note.pt.
94. or/91-94

Table A-2. EMBASE - Ovid Version: rel9.1.0 (continued)

1988 to 2004 Week 37 Searched September 15, 2004
95. 90 not 95 96. Nonhuman/ not human/ 97. 96 not 97 98. eng.la. 99. 98 and 99 100. 8 and 100 101. 101 not (38 or 63)

Table A-3. CINAHL® (Cumulative Index to Nursing & Allied Health Literature) - Ovid Version: rel9.1.0

1982 to September Week 2 2004 Searched September 15, 2004
1. insomni$.mp. or exp INSOMNIA/
2. (sleep adj initiation adj2 maintenance adj disorder$).mp.
3. (sleep adj onset adj3 (delay$ or latenc$)).mp.
4. dims.mp.
5. (disorder$ adj initiating adj2 maintaining adj sleep).mp.
6. (early adj2 awaken$).mp.
7. (sleeplessness or agrypnia$ or hyposomnia$).mp.
8. or/1-7
9. exp Analytic Research/ or (analytic adj (stud$ or research)).mp.
10. exp Nonexperimental Studies/ or exp Case Control Studies/ or exp Hospital-Based Case Control/ or exp Matched Case Control/ or exp Population-Based Case Control/ or exp Correlational Studies/
11. exp Prospective Studies/ or exp concurrent prospective studies/ or exp nonconcurrent prospective studies/ or exp panel studies/ or exp retrospective panel studies/ or exp revolving panel studies/ or exp pseudolongitudinal studies/
12. exp Cross Sectional Studies/
13. exp RELATIVE RISK/ or exp CARDIOVASCULAR RISK FACTORS/ or exp RISK MANAGEMENT/ or exp RISK FACTORS/ or exp FALL RISK ASSESSMENT TOOL/ or exp RISK ASSESSMENT/
14. exp Odds Ratio/ or ("relative odd$" or "rate ratio").mp.
15. exp Causal Attribution/
16. exp professional practice, research-based/ or exp medical practice, research-based/ or exp nursing practice, research-based/
17. exp epidemiological research/ or exp seroprevalence studies/18. exp Age Factors/ or exp "age of onset"/ or exp comorbidity/ or exp disease surveillance/ or exp injury pattern/ or exp Sex Factors/
18. exp morbidity/ or exp incidence/ or exp prevalence/
19. (cohort or comparative or "evaluation stud$" or observational or non-experimental or "non experimental" or nonexperimental or control$ or prospectiv$ or volunteer$ or "case series" or "case-series" or "case comparison" or "case-comparison" or "case referent" or "case-referent" or "cross sectional" or "cross-sectional" or risk or "relative risk" or causation or causal$ or "odds ratio$" or etiol$ or aetiol$ or incidence).mp.
20. exp prognosis/ or exp medical futility/ or exp treatment outcomes/
21. exp mortality/ or exp "cause of death"/ or exp survival/
22. exp survival analysis/
23. exp disease susceptibility/
24. exp disease progression/ or exp "Severity of Illness Indices"/
25. exp Time Factors/
26. exp RECURRENCE/
27. ("natural history" or "inception cohort" or predict$ or prognos$ or outcome$ or course).mp.
28. exp "costs and cost analysis"/ or exp "cost benefit analysis"/ or exp "cost control"/ or exp diagnosis-related groups/ or exp health care costs/ or exp HEALTH FACILITY COSTS/
29. exp "Quality of Life"/ or exp "Activities of Daily Living"/
30. exp "Outcomes (Health Care)"/ or exp Outcome Assessment/ or exp Health Status/ or exp Health Status Indicators/ or exp QUESTIONNAIRES/
31. (cost$ or economic or social or "quality of life" or "life quality" or hrql or well-being or wellbeing or "well being" or "outcome adj assessment$" or "health status").mp.
32. (et or pc or ae or ep or to or ge or ec or in or nu or ut or mo).fs.
33. or/9-33
34. 8 and 34
35. limit 35 to English
36. insomni$.mp. or exp INSOMNIA/
37. (sleep adj initiation adj2 maintenance adj disorder$).mp.
38. (sleep adj onset adj3 (delay$ or latenc$)).mp.
39. dims.mp.
40. "disorder$ of initiating and maintaining sleep".mp.

Table A-3. CINAHL® (Cumulative Index to Nursing & Allied Health Literature) - Ovid Version: rel9.1.0 (continued)

1982 to September Week 2 2004 Searched September 15, 2004
41. (early adj2 awaken$).mp.
42. (sleeplessness or agrypnia$ or hyposomnia$).mp.
43. exp Jet Lag Syndrome/ or (((time-zone or "time zone") adj2 change$) or "jet lag").mp.
44. or/37-44
45. Random Assignment/
46. random sample/
47. Crossover Design/
48. exp Clinical Trials/
49. Double-Blind Studies/
50. Single-Blind Studies/
51. Control Group/ or Factorial Design/ or Quasi-Experimental Studies/ or Community Trials/ or Experimental Studies/ or PRETEST-POSTTEST DESIGN/ or PRETEST-POSTTEST CONTROL GROUP DESIGN/ or SOLOMON FOUR-GROUP DESIGN/
52. clinical trial.pt.
53. (clin$ adj25 trial$).ti,ab.
54. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab.
55. ((clin$ or intervention$ or compar$ or experiment$ or preventive or therapeutic) adj10 trial$).mp.
56. placebos/
57. placebo$.ti,ab.
58. random$.ti,ab.
59. Study Design/
60. or/46-60
61. 45 and 61
62. 62 not 36
63. meta-analysis.sh.
64. (meta-anal$ or metaanal$).mp.
65. ((systematic$ adj3 review$) or (systematic$ adj3 overview$)).mp.
66. ((quantitativ$ adj3 review$) or (quantitativ$ adj3 overview)).mp.
67. ((methodol$ adj3 review$) or (methodol$ adj3 overview$)).mp.
68. (integrative research review$ or research integration$).mp.
69. (quantitativ$ adj (synthes$ or analys$)).mp.
70. (("evidence based" or evidence-based) adj3 (medicine or guideline$ or recommendation$)).mp.
71. guideline$.mp.
72. "cochrane database of systematic reviews".mp.
73. cdsr.mp.
74. acp journal club.mp.
75. "health tech$ assess$".mp.
76. hta.mp.
77. "evidence based nursing".mp.
78. "evidence based mental health".mp.
79. "clinical evidence".mp.
80. technolog$ assess$.mp.
81. "evidence report$".mp.
82. or/64-82
83. review.pt. or (review or overview$ or reviews or handsearch or "hand search" or hand-search or "manual search").mp.
84. (medline or medlars or pubmed or embase or "index medicus" or cochrane or scisearch or "Web of Science" or psychinfo or psycinfo or psychlit or psyclit or cinahl or cinhal or "experta medica" or "excerpta medica" or "science citation index" or "sciences citation index" or "biological abstracts" or "current contents").mp.
85. (((electronic or bibliographic) adj3 database$) or "periodical index$").mp.
86. ((pool$ or combined or combining) adj (data or trials or studies or results)).mp.
87. (peto or "der simonian" or dersimonian or "fixed effect$" or "treatment outcome$" or "mantel haenszel").mp.
88. or/85-88
89. 84 and 89
90. 83 or 90

Table A-3. CINAHL® (Cumulative Index to Nursing & Allied Health Literature) - Ovid Version: rel9.1.0 (continued)

1982 to September Week 2 2004 Searched September 15, 2004
91. "case report".ti. or "case study".pt. 92. editorial.ti,pt. 93. letter.pt. 94. commentary.pt. 95. or/92-95 96. 91 not 96 97. limit 97 to English 98. 8 and 98 99. 99 not (36 or 63)

Table A-4. Ovid MEDLINE® In-Process & Other Non-Indexed Citations - Ovid Version: rel9.1.0

Searched September 14, 2004	
1.	insomni$.mp.
2.	(sleep adj initiation adj2 maintenance adj disorder$).mp.
3.	(sleep adj onset adj3 (delay$ or latenc$)).mp.
4.	(disorder$ adj initiating adj2 maintaining adj sleep).mp.
5.	(early adj2 awaken$).mp.
6.	(sleeplessness or agrypnia$ or hyposomnia$).mp.
7.	(((time-zone or "time zone") adj2 change$) or "jet lag").mp.
8.	or/1-7
9.	"randomized controlled trial$".mp.
10.	"controlled clinical trial$".mp.
11.	"random allocation".mp.
12.	("double blind" adj3 method$).mp.
13.	("single blind" adj3 method$).mp.
14.	(clin$ adj25 trial$).mp.
15.	((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab.
16.	placebo$.ti,ab.
17.	random$.ti,ab.
18.	"research design$".mp.
19.	"clinical research".mp.
20.	or/9-19
21.	8 and 20

Table A-5. Ovid OLDMEDLINE® - Ovid Version: rel9.1.0

1951 to 1965 Searched September 15, 2004
1. insomni$.mp 2. (sleep adj initiation adj2 maintenance adj disorder$).mp. 3. (sleep adj onset adj3 (delay$ or latenc$)).mp. 4. (disorder$ adj initiating adj2 maintaining adj sleep).mp. 5. (early adj2 awaken$).mp. 6. (sleeplessness or agrypnia$ or hyposomnia$).mp. 7. (((time-zone or "time zone") adj2 change$) or "jet lag").mp. 8. or/1-7 9. "randomized controlled trial$".mp. 10. "controlled clinical trial$".mp. 11. "random allocation".mp. 12. ("double blind" adj3 method$).mp. 13. ("single blind" adj3 method$).mp. 14. (clin$ adj25 trial$).mp. 15. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab. 16. placebo$.ti,ab. 17. random$.ti,ab. 18. "research design$".mp. 19. "clinical research".mp. 20. or/9-19 21. 8 and 20

Table A-6. PsycINFO® - Ovid Version: rel9.1.0

1872 to September Week 1 2004 Searched September 15, 2004
1. insomni$.mp. or exp INSOMNIA/
2. (sleep adj initiation adj2 maintenance adj disorder$).mp.
3. (sleep adj onset adj3 (delay$ or latenc$)).mp.
4. dims.mp.
5. (disorder$ adj initiating adj2 maintaining adj sleep).mp.
6. (early adj2 awaken$).mp.
7. (sleeplessness or agrypnia$ or hyposomnia$).mp.
8. or/1-7
9. "analytic stud$".mp.
10. exp Between Groups Design/ or exp Cohort Analysis/ or exp Followup Studies/ or exp Longitudinal Studies/ or exp Repeated Measures/ or empirical methods/ or observation methods/ or exp Causal Analysis/ or exp Cohort Analysis/ or exp Content Analysis/ or exp Data Collection/ or exp Self Report/ or exp QUESTIONNAIRES/
11. prevention/ or exp accident prevention/ or exp preventive medicine/ or exp risk management/ or exp risk perception/
12. exp EPIDEMIOLOGY/ or exp COMORBIDITY/
13. (cohort or observational or correlational or non-experimental or "non experimental" or nonexperimental or control$ or prospectiv$ or volunteer$ or "case series" or "case-series" or "case comparison" or "case-comparison" or "case referent" or "case-referent" or "cross sectional" or "cross-sectional" or risk or "relative risk" or causation or causal$ or "odds ratio$" or etiol$ or aetiol$ or incidence).mp.
14. exp At Risk Populations/ or exp Coronary Prone Behavior/ or exp Age Differences/ or exp Human Sex Differences/ or exp PREDISPOSITION/ or exp DISORDERS/ or exp "SUSCEPTIBILITY (DISORDERS)"/
15. exp ETIOLOGY/ or exp ATTRIBUTION/
16. exp PROGNOSIS/ or exp "DEATH AND DYING"/ or exp Disease Course/ or exp Treatment Effectiveness Evaluation/ or exp Treatment Outcomes/ or exp Psychotherapeutic Outcomes/ or exp "RECOVERY (DISORDERS)"/ or exp "RELAPSE (DISORDERS)"/ or exp "remission (disorders)"/
17. (morbidity or prevalence or mortality or "cause of death" or "survival rate" or "disease progression" or "time factor$" or "disease free survival" or cure$).mp.
18. recurrence.mp.
19. ("natural history" or "inception cohort" or predict$ or prognos$ or outcome$ or course).mp.
20. "costs and cost analysis"/ or exp health care costs/ or exp Resource Allocation/
21. exp "Quality of Life"/ or exp Psychosocial Factors/ or exp Sociocultural Factors/ or exp "Activities of Daily Living"/
22. (cost$ or economic or social or "quality of life" or "life quality" or hrql or well-being or wellbeing or "well being" or "outcome adj assessment$" or "health status").mp.
23. ("empirical study" or "followup study" or "longitudinal study" or "prospective study").fc.
24. or/9-23
25. exp animals/
26. 24 not 25
27. 8 and 26
28. limit 27 to english language
29. insomni$.mp. or exp INSOMNIA/
30. (sleep adj initiation adj2 maintenance adj disorder$).mp.
31. (sleep adj onset adj3 (delay$ or latenc$)).mp.
32. dims.mp.
33. "disorder$ of initiating and maintaining sleep".mp.
34. (early adj2 awaken$).mp.
35. (sleeplessness or agrypnia$ or hyposomnia$).mp.
36. (((time-zone or "time zone") adj2 change$) or "jet lag").mp.
37. or/29-36
38. ("Quantitative Study" or "experimental replication").fc.
39. exp experimental methods/ or exp experimental design/ or exp quantitative methods/

Table A-6. PsycINFO® - Ovid Version: rel9.1.0 (continued)

1872 to September Week 1 2004 Searched September 15, 2004
40. exp Experiment Controls/ 41. treatment/ or alternative medicine/ or interdisciplinary treatment approach/ or "medical treatment (general)"/ or multimodal treatment approach/ or physical treatment methods/ or preventive medicine/ or psychotherapeutic techniques/ or psychotherapy/ or rehabilitation/ or relaxation therapy/ or sociotherapy/ 42. (therapy or treat$).mp. 43. ((clin$ or intervention$ or compar$ or experiment$ or preventive or therap$) adj25 (trial$ or study or studies)).mp. 44. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).mp. 45. exp placebo/ 46. (cross?over or placebo$ or control$ or factorial or sham).mp. 47. "clinical research".mp. 48. random$.mp. 49. or/38-48 50. 49 not 25 51. 37 and 50 52. 51 not 28

Table A-7. EBM Reviews - Cochrane Central Register of Controlled Trials - Ovid Version: rel9.1.0

2nd Quarter 2004 Searched September 15, 2004
1. insomni$.mp. 2. exp "Sleep Initiation and Maintenance Disorders"/ 3. (sleep adj initiation adj2 maintenance adj disorder$).mp. 4. (sleep adj onset adj3 (delay$ or latenc$)).mp. 5. dims.mp. 6. "disorder$ of initiating and maintaining sleep".mp. 7. (early adj2 awaken$).mp. 8. (sleeplessness or agrypnia$ or hyposomnia$).mp. 9. (((time-zone or "time zone") adj2 change$) or "jet lag").mp. 10. or/1-9 11. randomized controlled trial.pt. 12. controlled clinical trial.pt. 13. randomized controlled trials/ 14. random allocation/ 15. double blind method/ 16. single blind method/ 17. clinical trial.pt. 18. exp Clinical Trials/ 19. (clin$ adj25 trial$).ti,ab. 20. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab. 21. placebos/ 22. placebo$.ti,ab. 23. random$.ti,ab. 24. research design/ 25. or/11-24 26. animal/ 27. 25 not 26 28. 10 and 27

Table A-8. International Pharmaceutical Abstracts - Ovid Version: rel9.1.0

1970 to August 2004 Searched September 15, 2004
1. insomni$.mp. 2. (sleep adj initiation adj2 maintenance adj disorder$).mp. 3. (sleep adj onset adj3 (delay$ or latenc$)).mp.4. (disorder$ adj initiating adj2 maintaining adj sleep).mp. 4. (early adj2 awaken$).mp. 5. (sleeplessness or agrypnia$ or hyposomnia$).mp. 6. (((time-zone or "time zone") adj2 change$) or "jet lag").mp. 7. or/1-7 8. "randomized controlled trial$".mp. 9. "controlled clinical trial$".mp. 10. "random allocation".mp. 11. ("double blind" adj3 method$).mp. 12. ("single blind" adj3 method$).mp. 13. (clin$ adj25 trial$).mp. 14. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab. 15. placebo$.ti,ab. 16. random$.ti,ab. 17. "research design$".mp. 18. "clinical research".mp. 19. or/9-19 20. limit 20 to human 21. 8 and 21

Table A-9. AMED (Allied and Complementary Medicine) - Ovid Version: rel9.1.0

1985 to September 2004 Searched September 15, 2004
1. insomni$.mp. 2. exp insomnia/ 3. (sleep adj onset adj3 (delay$ or latenc$)).mp. 4. (disorder$ adj initiating adj2 maintaining adj sleep).mp. 5. (early adj2 awaken$).mp. 6. (sleeplessness or agrypnia$ or hyposomnia$).mp. 7. (((time-zone or "time zone") adj2 change$) or "jet lag").mp. 8. or/1-7 9. "randomized controlled trial$".mp. 10. "controlled clinical trial$".mp. 11. "random allocation".mp. 12. ("double blind" adj3 method$).mp. 13. ("single blind" adj3 method$).mp. 14. (clin$ adj25 trial$).mp. 15. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab. 16. placebo$.ti,ab. 17. random$.ti,ab. 18. "research design$".mp. 19. "clinical research".mp. 20. or/9-19 21. animal/ 22. 20 not 21 23. 8 and 22

Table A-10. HealthSTAR/Ovid Healthstar - Ovid Version: rel9.1.0

1975 to August 2004 Searched September 15, 2004
1. insomni$.mp. 2. exp "Sleep Initiation and Maintenance Disorders"/ 3. (sleep adj initiation adj2 maintenance adj disorder$).mp. 4. (sleep adj onset adj3 (delay$ or latenc$)).mp. 5. dims.mp. 6. (disorder$ adj initiating adj2 maintaining adj sleep).mp. 7. (early adj2 awaken$).mp. 8. (sleeplessness or agrypnia$ or hyposomnia$).mp. 9. or/1-8 10. "analytic stud$".mp. 11. exp case-control studies/ or exp retrospective studies/ 12. exp cohort studies/ or exp longitudinal studies/ or exp follow-up studies/ or exp prospective studies/ or comparative study/ or exp Evaluation Studies/ 13. exp Cross-Sectional Studies/ 14. exp RISK FACTORS/ or exp RISK/ or exp RISK ASSESSMENT/ 15. exp Odds Ratio/ 16. exp CAUSALITY/ 17. exp Logistic Models/ 18. exp epidemiologic factors/ or exp age factors/ or exp "bias (epidemiology)"/ or exp comorbidity/ or exp "confounding factors (epidemiology)"/ or exp "effect modifiers (epidemiology)"/ or exp observer variation/ or exp reproductive history/ or exp sex factors/ 19. exp morbidity/ or exp incidence/ or exp prevalence/ 19. (cohort or observational or correlational or non-experimental or "non experimental" or nonexperimental or control$ or prospectiv$ or volunteer$ or "case series" or "case-series" or "case comparison" or "case-comparison" or "case referent" or "case-referent" or "cross sectional" or "cross-sectional" or risk or "relative risk" or causation or causal$ or "odds ratio$" or etiol$ or aetiol$ or incidence).mp. 20. exp prognosis/ or exp medical futility/ or exp treatment outcome/ 21. exp mortality/ or exp "cause of death"/ or exp fatal outcome/ or exp survival rate/ 22. exp survival analysis/ or exp disease-free survival/ 23. exp disease susceptibility/ or exp genetic predisposition to disease/ 24. exp disease progression/ or exp "Severity of Illness Index"/ 25. exp Time Factors/ 26. exp RECURRENCE/ 27. ("natural history" or "inception cohort" or predict$ or prognos$ or outcome$ or course).mp. 28. exp "costs and cost analysis"/ or exp "cost allocation"/ or exp cost-benefit analysis/ or exp "cost control"/ or exp "cost savings"/ or exp "cost of illness"/ or exp "cost sharing"/ or exp "deductibles and coinsurance"/ or exp health care costs/ or exp direct service costs/ or exp drug costs/ or exp employer health costs/ or exp hospital costs/ or exp health expenditures/ or exp capital expenditures/ 29. exp "Quality of Life"/ or exp "Activities of Daily Living"/ 30. exp "OUTCOME ASSESSMENT (HEALTH CARE)"/ or exp "OUTCOME AND PROCESS ASSESSMENT (HEALTH CARE)"/ or exp Health Status Indicators/ or exp Health Status/ or exp Questionnaires/ 31. (cost$ or economic or social or "quality of life" or "life quality" or hrql or well-being or wellbeing or "well being" or "outcome adj assessment$" or "health status").mp. 32. (et or pc or ae or ep or to or ge or ec or in or ut or mo).fs. 33. or/10-33 34. animal/ not human/ 35. 34 not 35 36. 9 and 36 37. eng.la. 38. 37 and 38

Table A-11. EBM Reviews - Cochrane Database of Systematic Reviews (2nd Quarter 2004); ACP Journal Club (1991 to March/April 2004); Database of Abstracts of Reviews of Effects (2nd Quarter 2004) - Ovid Version: rel9.1.0

Searched September 15, 2004	
1.	insomni$.ti,ab.
2.	(sleep adj initiation adj2 maintenance adj disorder$).mp.
3.	(sleep adj onset adj3 (delay$ or latenc$)).mp.
4.	(early adj2 awaken$).mp.
5.	(sleeplessness or agrypnia$ or hyposomnia$).mp.
6.	or/1-5

Table A-12. Science Citation Index Expanded™ - 1945-September 2004 - ISI Web of Knowledge

Searched September 17, 2004	
☐ #8	#7 NOT #5 *DocType=All document types; Language=All languages; Database=SCI-EXPANDED; Timespan=1945-2004*
☐ #7	#6 AND #3 *DocType=All document types; Language=All languages; Database=SCI-EXPANDED; Timespan=1945-2004*
☐ #6	TS=Analytic Stud* OR TS=Case Control Stud* OR TS=Case-Control Stud* OR TS=Retrospective Stud* OR TS=Cohort OR TS=Longitudinal OR TS=Follow-up Stud* OR TS=Follow up Stud* OR TS=Prospective Stud* OR TS=Comparative Stud* OR TS=Evaluation Stud* OR TS=Cross Sectional Stud* OR TS=Cross-sectional Stud* OR TS=Observational Stud* OR TS=Questionnaire* *DocType=All document types; Language=All languages; Database=SCI-EXPANDED; Timespan=1945-2004*
☐ #5	#4 AND #3 *DocType=All document types; Language=All languages; Database=SCI-EXPANDED; Timespan=1945-2004*
☐ #4	TS=Random* OR TS=Placebo* OR TS=Randomized Controlled Trial* OR TS=Controlled Clinical Trial* OR TS=Clinical Trial* OR TS=Double Blind Method* OR TS=Single Blind Method* *DocType=All document types; Language=All languages; Database=SCI-EXPANDED; Timespan=1945-2004*
☐ #3	#2 OR #1 *DocType=All document types; Language=All languages; Database=SCI-EXPANDED; Timespan=1945-2004*
☐ #2	TS=Sleeplessness OR TS=Agrypnia* OR TS=Hyposomnia* *DocType=All document types; Language=All languages; Database=SCI-EXPANDED; Timespan=1945-2004*
☐ #1	TS=Insomni* *DocType=All document types; Language=All languages; Database=SCI-EXPANDED; Timespan=1945-2004*

Table A-13. Biological Abstracts - WebSPIRS from SilverPlatter, Version 4.3

Searched September 17, 2004	
1.	#1 insomni* or sleeplessness or agrypnia* or hyposomnia*
2.	#2 analytic stud* or case control stud* or case-control stud* or retrospective stud* or cohort or longitudinal or follow up stud* or follow-up stud* or prospective stud* or comparative stud* or evaluation stud* or cross sectional stud* or cross-sectional stud* or observational stud* or questionnaire*
3.	#3 #1 and #2
4.	#4 random* or placebo* or randomized controlled trial* or controlled clinical trial* or clinical trial* or double blind method* or single blind method
5.	#5 #1 and #4

Table A-14. Cochrane Complementary Medicine Field Registry - Reference Web Poster 2001; ISI ResearchSoft

Searched September 20, 2004
1. Insomni or sleeplessness or agrypnia or hyposomnia

Table A-15. CAB Abstracts - WebSPIRS from SilverPlatter, Version 4.3

Searched September 18, 2004
1. Insomni* or agrypnia* or hypsomnia* or sleeplessness 2. Clinical trial* or randomized controlled trial* or random* or cohort or retrospective or prospective or volunteer* or questionnaire*

Table A-16. SIGLE - FIZ Karlsruhe – Version Interhost 3000

Searched September 18, 2004
1. Insomnia or sleeplessness

Table A-17. OCLC Proceedings First - OCLC FirstSearch

Searched September 18, 2004
1. Insomnia or insomniacs

Table A-18. Dissertation Abstracts – ProQuest

Searched September 18, 2004
1. Insomnia

Table A-19. Alt HealthWatch – EBSCOhost

Searched September 18, 2004
1. Insomnia or insomnia – alternative treatment

Table A-20. NLM Gateway

Searched September 18, 2004
1. Searched for insomnia under Meeting Abstracts

Table A-21. PubMed®

Searched September 20, 2004	
1.	A search was conducted for the period of Jan. 01, 2004, to Sept. 20, 2004 for “Sleep Initiation and Maintenance Disorders” [MeSH]

Appendix B: Data Extraction and Quality Assessment Forms

Form B-1: Data extraction form for studies on manifestations of chronic insomnia in adults
Form B-2: Data extraction form for studies on management of chronic insomnia in adults
Form B-3: Quality assessment form for studies on prevalence or incidence of chronic insomnia in adults
Form B-4: Quality assessment form for cohort studies on manifestations of chronic insomnia in adults
Form B-5: Quality assessment form for case-control studies on manifestations of chronic Insomnia in adults
Form B-6: Quality assessment form for studies on management of chronic insomnia in adults

Form B-1: Data extraction form for studies on manifestations of chronic insomnia in adults

To be extracted from all studies, except where indicated.						
Record ID	**Indicate if Relevant to Prevalence**	**Indicate if Relevant to Natural History**	**Indicate if Relevant to Incidence**	**Indicate if Relevant to Associated Factors**	**Reviewer/Date**	**First Author**
Year of Publication	**Study Site**	**Study Setting (if relevant to prevalence)**	**Objective(s)**	**Study Design**	**Sampling Frame and Method of Sampling (if relevant to prevalence)**	**Time Frame for the Study**

To be extracted from all studies, except where indicated.						
Intended Sample Size	**Response/Follow-up Rate**	**Method of Data Collection (if relevant to prevalence)**	**Type of Participants**	**Definition of Cases and Comparison Groups, if applicable**	**Gender Distribution of Population**	**Age Distribution of Population**
Ethnicity of Population	**Co-morbid Conditions of Population at Entry**	**Prevalence of Chronic Insomnia (if relevant to prevalence)**	**Incidence of Chronic Insomnia (if relevant to incidence)**	**Natural History of Chronic Insomnia (if relevant to natural history)**	**Associated Factors of Chronic Insomnia (if relevant to associated factors)**	**Qualitative Summary of Findings (if relevant to associated factors)**

Form B-2: Data extraction form for studies on management of chronic insomnia in adults

Study ID:	**Reviewer Initials:**	**Verifier Initials:**
First Author:		
Title:		
Year of Publication:	**Language of Publication:**	**Country of Corresponding Author:**
Funding: Private Industry ___ Not Specified ___ Government ___ Foundation ___ Internal ___ Other ___		
Role of Funding Organization:		

Study Design:	Parallel ___	Crossover ___	Unclear ___	
Intent to Treat Analysis:	Yes ___	No ___	Unclear ___	N/A ___
Quality Score:				

Number of Participants Enrolled:			
Number of Males Enrolled:	**Number of Females Enrolled:**		
Age of Participants:			
Withdrawals/Dropouts:	Yes ___	No ___	Unclear ___
If yes, state number of withdrawals/ group and reasons for withdrawal:	**Overall:**		
	Treatment Group(s):		
	Control Group:		

Criteria for Insomnia:		
Length of Insomnia:		
Primary Chronic Insomnia:	Yes ___	No ___
If primary chronic insomnia, list any co-morbid conditions:		
Secondary Chronic Insomnia:	Yes ___	No ___
If secondary chronic insomnia, secondary to what condition (if psychiatric, see below)?		
Psychiatric Illness:	Yes ___ If Yes, specify:	No ___
Method used to Assess Outcomes: PSG: ___ Actigraphy: ___ Diary: ___ **If different methods were used for different outcomes OR more than one method was used for one or more outcomes, please specify:**		

Treatment Group	Intervention	Frequency and Duration of Treatment	Timing	Route of Delivery	Number of Participants Allocated/ Analyzed	Length of Follow-up
1						
2						
3						
4						

Did participants have a treatment preference? If so, indicate which treatment was preferred and related information.

	Treatment Group 1	Treatment Group 2	Treatment Group 3	Treatment Group 4
Interventions				
Sleep Onset Latency (SOL)				
Definition of SOL:				
Wakefulness after Sleep Onset (WASO)				
Definition of WASO:				
Sleep Efficiency (SE)				
Definition of SE:				
Total Sleep Time (TST)				
Definition of TST:				
Sleep Quality (SQ)				
Definition of SQ:				

Quality of Life (QOL)				
Definition of QOL:				
Adverse Effects/Events				

Form B-3: Quality assessment form for studies on prevalence or incidence of chronic insomnia in adults

The criteria used to rate studies relevant to the prevalence or incidence of chronic insomnia in adults is outlined below (Loney PL, 1998). One point was assigned for each criterion that was satisfied. The maximum score was eight.

1. Random sample or whole population
2. Unbiased sampling frame (i.e. census data)
3. Adequate sample size
4. Measures were the standard
5. Outcomes measured by unbiased assessors
6. Adequate response rate (70 percent), refusers described
7. Confidence intervals, subgroup analysis
8. Study subjects described

Form B-4: Quality assessment form for cohort studies on manifestations of chronic insomnia in adults (Newcastle-Ottawa scale)

Note: A study could be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars could be awarded for Comparability. Each star was equivalent to one point. The maximum score was nine.

Selection

1) Representativeness of the exposed cohort
a) truly representative of the average _____ (describe) in the community *
b) somewhat representative of the average _____ in the community *
c) selected group of users e.g. nurses, volunteers
d) no description of the derivation of the cohort

2) Selection of the non exposed cohort
a) drawn from the same community as the exposed cohort *
b) drawn from a different source
c) no description of the derivation of the non exposed cohort

3) Ascertainment of exposure
a) secure record (e.g. surgical records) *
b) structured interview *
c) written self report
d) no description

4) Demonstration that outcome of interest was not present at start of study
a) yes *
b) no

Comparability

1) Comparability of cohorts on the basis of the design or analysis
a) study controls for _____ (select the most important factor) *
b) study controls for any additional factor * (This criteria could be modified to indicate specific control for a second important factor.)

Outcome

1) Assessment of outcome
a) independent blind assessment *
b) record linkage *
c) self report
d) no description

2) Was follow-up long enough for outcomes to occur
a) yes (select an adequate follow up period for outcome of interest) *
b) no

3) Adequacy of follow up of cohorts
a) complete follow up - all subjects accounted for *
b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate percent) follow up, or description provided of those lost) *
c) follow up rate < ____% (select an adequate percent) and no description of those lost
d) no statement

Form B-5: Quality assessment form for case-control studies on manifestations of chronic insomnia in adults (Newcastle-Ottawa scale)

Note: A study could be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of two stars could be awarded for Comparability. Each star was equivalent to one point. The maximum score was nine.

Selection

1) Is the case definition adequate?
a) yes, with independent validation *
b) yes, e.g. record linkage or based on self reports
c) no description

2) Representativeness of the cases
a) consecutive or obviously representative series of cases *
b) potential for selection biases or not stated

3) Selection of Controls
a) community controls *
b) hospital controls
c) no description

4) Definition of Controls
a) no history of disease (endpoint) *
b) no description of source

Comparability

1) Comparability of cases and controls on the basis of the design or analysis
a) study controls for _____ (Select the most important factor.) *
b) study controls for any additional factor * (This criteria could be modified to indicate specific control for a second important factor.)

Exposure

1) Ascertainment of exposure
a) secure record (e.g. surgical records) *
b) structured interview where blind to case/control status *
c) interview not blinded to case/control status
d) written self report or medical record only
e) no description

2) Same method of ascertainment for cases and controls
a) yes *
b) no

3) Non-Response rate
a) same rate for both groups *
b) non respondents described
c) rate different and no designation

Form B-6: Quality assessment form for studies on management of chronic insomnia in adults (Jadad scale and allocation concealment for quality assessment of RCTs)

Study # _____ Initials of Assessor: _____

Part 1 (from Jadad – Controlled Clin Trials 1996; 17:1-12)

Score

1. Was the study described as randomized (this includes the use of words such as randomly, random and randomization)?
   Yes = 1 No = 0 _____

2. Was the study described as double-blind?
   Yes = 1 No = 0 _____

3. Was there a description of withdrawals and drop-outs?
   Yes = 1 No = 0 _____

Additional points: Add 1 point if:

Method to generate the sequence of randomization was described and was appropriate (e.g. table of random numbers, computer generated, coin tossing, etc.) _____

Method of double-blinding described and appropriate (identical placebo, active placebo, dummy) _____

Point deduction: Subtract 1 point if:

Method of randomization described and it was **in**appropriate (allocated alternately, according to date of birth, hospital number, etc.) -_____

Method of double-blinding described but it was **in**appropriate (comparison of tablet vs. injection with no double dummy) -_____

OVERALL SCORE (Maximum 5) _____

Part 2 (from Schulz – JAMA 1995; 273:408-12)

Concealment of treatment allocation:

- ☐ Adequate
- ☐ Inadequate
- ☐ Unclear

Adequate: e.g. central randomization; numbered/coded containers; drugs prepared by pharmacy; serially numbered, opaque, sealed envelopes

Inadequate: e.g. alternation, use of case record numbers, dates of birth or day of week; open lists

Unclear: Allocation concealment approach not reported or fits neither above category

Appendix C: Evidence Tables

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults

Abbreviations: **adj** = adjusted; **BA**I = Beck Anxiety Inventory; **BDI** = Beck Depression Inventory; **BMI** = body mass index; **BNZ** = benzodiazepine; **ChI** = chronic insomnia; **CI** = confidence interval; **Com** = community; **CS** = case; **CT** = control group; **DSM-IV** = Diagnostic and Statistical Manual of mental Disorders, 4th edition; **GS** = good sleepers; **Hx** = history; **INS** = drug-free insomnia; **INSBZ** = benzodiazepine use insomnia; **mo** = months; **msec** = mili-seconds; **MSK** = musculoskeletal; **MMPI** = Minnesota Multiphasic Personality Inventory; **NA** = not applicable; **NR** = not reported; **OR** = odds ratio; **p=NS** = not statistically significant; **QoL** = Quality of Life; **TBI** = traumatic brain injury; **VAS** = visual analogue scale; **yrs** = years

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Ancoli-Israel, S / 1999 Moderate (3/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional 18->65 yrs NR NR White:86%(860/1000) Black:8%(80/1000) Hispanic:3%(30/1000) Other:3%(30/1000) 1950 51.2%(1000/1950)	**Prevalence**: **All**: (ChI) 9% (90/1000) 95%CI: 7.23-10.77. No prevalence data by gender. >65 group: 20% (37/183) 95%CI:14.20-25.80 **Associated Factors**: Significant **Socioeconomic status**: (<$50,000/yr vs >$50,000/yr): 42% vs 31%; OR (no insomnia) 0.89; 95%C: 0.55-1.43, p=0.04. Non-significant **Age**: (<65 vs >65): 37% vs 44%; OR (no insomnia) 1.33; 95%CI: 0.83-2.14, p=0.29. **Race/ethnicity**: (White vs non-Caucasian) 38% vs 35%; OR (no insomnia) 1.59; 95%CI: 0.99-2.54, p=0.66; **Socioeconomic status**: Education: (≤ high school vs college): 41% vs 35%; OR (no insomnia) 0.78; 95%CI: 0.54-1.13, p=0.22.
AUTHOR / YEAR QUALITY (score)	**STUDY DESIGN & POPULATION CHARACTERISTICS**		**CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS**
Bastien, CH / 2003 Moderate (5/9)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control >55 yrs X=62.5± 5.8 30 30 60 NR	**Associated Factors**: 3 groups: drug-free insomniacs (INS) vs benzodiazepine use insomniacs (INSBZ) vs good sleepers (GS); mean scores ± SD Significant **Psychiatric illness and psychological problems**: 1) Depression (BDI): INS vs GS: 9.00 ± 4.48 vs 1.75 ± 1.68, p<0.01. INSBZ vs GS: 9.40 ± 7.16 vs 1.75 ± 1.68, p<0.01; 2) Anxiety (BAI): INS vs GS: 9.10 ± 8.38, p<0.01; INSBZ vs GS: 8.60 ± 5.44 vs 1.20 ± 1.47; (p<0.01). 3) Sleep impairment index: INS vs INSBZ vs GS: 17.9 ± 4.85, 16.85 ± 4.55, 1.60 ± 1.88, p<0.01. Non-significant INS vs INSBZ vs GS: 61.7 ± 6.43, 62.3 ± 5.89, 63.35 ± 5.15, p=NS**. Socioeconomic status:** Education: INS vs INSBZ vs GS: 13.6 ± 5.15, 11.65 ± 2.76, 13.35 ± 3.67, p=NS. **Cognitive function:** 1) Folstein Mini-mental State Exam: INS vs INSBZ vs GS: 29.1 ± 1.12, 28.75 ± 1.2, 28.85 ± 1.04, p=NS. 2) Vocabulary: INS vs INSBZ vs GS: 12.65 ± 3.84, 12.0 ± 3.09, 13.30 ± 2.36, p=NS. Information: INS vs INSBZ vs GS: 10.15 ± 3.51, 10.0 ± 3.01, 11.5 ± 3.40, p=NS.
AUTHOR / YEAR QUALITY (score)	**STUDY DESIGN & POPULATION CHARACTERISTICS**		**CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS**
Bixler, EO / 2002 Moderate (3/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional > 20 yrs 57.4%(1000/1741) 42.6%(741/1741) NR 1741 66.6%(1160/1741)	**Prevalence**: Insomnia ≥1 year: 7.5% (131/1741), 95%CI: 6.27-8.73. **Associated Factors**: Significant **Age**: CS vs CT: 50.4 ± 1.0 vs 46.9 ± 0.7 yrs, p=0.02. **Gender**: M vs F: 5.9% vs 9%; OR=1.6, 95%CI: 1.1-2.4, p<0.01. **Race/ethnicity**: Non-Caucasian vs Caucasian 12.9% vs 6.6%; OR: 2.1; 95%CI: 1.3-3.2, p<0.002. **Psychiatric illness and psychological problems**: Depression: adj OR: 5.5; 95%CI: 3.6-8.4, p<0.0001. **Medical conditions**: 1) Colitis: adj OR: 1.3; 95%CI: 1.0-6, p<0.02. 2) Hypertension: adj OR: 1.2; 95%CI: 1.1-1.3, p<0.0001. 3) Anemia: adj OR: 1.2; 95%CI: 1.1-1.4, p=0.004. Non-significant None reported

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Bixler, EO / 1979 Moderate (3/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional > 18 yrs 56%(563/1006) 44%(443/1006) NR 1006 NR	**Prevalence**: **Life-time prevalence**: (Current or past insomnia): 42.5% (428/1006), 95%CI: 39.4-45.5. Current chronic insomnia: 32.2% (324/1006), 95%CI: 29.3-35.0. **Gender**: M vs F: 39% (172/443), 95%CI: 34.5-43.5 vs 61% (343/563), 95%CI: 57-65. **Associated Factors**: Significant **Age**: >51yr (higher prevalence) 39.8%, 95%CI: 34.6-45.3, p<0.05. **Psychiatric illness and psychological problems**: 1) Tension: 29.2%, p<0.01. 2) Depression: 19.4%, p<0.05. 3) Loneliness: 12.9%, p<0.01. **Medical conditions**: 1) Presence of a persistent or recurring health problem: 50%, p<0.01. 2) Multiple health problems: 17.3%, p<0.05, 3) Hospitalizations during the past year: 15.7%, p<0.01. Non-significant **Gender**: reported NS difference. **Other factors**: Marital/family problems: 17.8%, Alcohol related problems: 2.8 % & Mental Healthcare utilization: 9.2%, all p=NS.

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Bliwise, NG / 1992 Low (1/9)	**Study Design**: **Age Group (years)**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 68.4 ± 8.7, 49-82 (CS) 67.5 ± 9.9, 52-95 (CT) 38 0 NS 38 total 16 (CS) 22 (CT) NR	**Associated Factors**: Significant **Psychiatric illness and psychological problems**: (SCL-90-R Revised Symptom Checklist) CS vs CT: 1) Somatization: 0.66 ± 0.54 vs 0.26 ± 0.30, p<0.05. 2) Obsessive-compulsive: 1.06 ± 0.48 vs 0.68 ± 0.66, p<0.10. 3) Anxiety: 0.55 ± 0.68 vs 0.21 ± 0.26, p<0.10. 4) Phobic anxiety: 0.15 ± 0.25 vs 0.02 ± 0.05, p<0.05. 8) Paranoid ideation: 0.50 ± 0.49 vs 0.18 ± 0.23, p<0.05. 5) Psychoticism: 0.31 ± 0.27 vs 0.12 ± 0.23, p<0.05. 6 Geriatric Depression Scale (total score): 8.10 ± 7.64 vs 4.42 ± 0.47, p<0.10. Non significant **Psychiatric illness and psychological problems**: 1) Interpersonal: 0.44 ± 0.33 vs 0.31 ± 0.38; 2) Depression: 0.75 ± 0.63 vs 0.54 ± 0.54; 3) Hostility: 0.33 ± 0.36 vs 0.16 ± 0.17. **Other factors**: Chronic illness, Psychosocial (widowed/divorced), Age, Socioeconomic status, Exercise, Alcohol and Caffeine intake all reported p=NS.

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Bonnet, MH / 1995 High (7/9)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional matched case-control 18-50 yrs NR NR NR 40 total 20 (CS) 20 (CT) 50%, 10/20 (CS) 50%, 10/20 (CT)	**Associated Factors**: Significant **Psychiatric illness and psychological problems**: (Profile of Mood States scale): 1) Confusion: 5.4 ± 4.2 vs 3.1 ± 3.2, p<0.01. 2) Tension: 6.0 ± 5.8 vs 4.0 ± 3.8, p<0.05. 3) Depression: 9.0 ± 11.8 vs 4.1 ± 5.3, p<0.05. 4) Vigor: 16.4 ± 6.7 vs 21.5 ± 7.5, p<0.001. **Memory and cognitive function**: 1) Low results on short-term memory (# words): 5.7 ± 3.7 vs 7.2 ± 2.7, p=0.02. 2) Low results on MAST test (# correct): 53.2 ± 24 vs 60.5 ± 19, p<0.001. Non Significant: (cases vs controls): **Memory and cognitive function**: 1) Proofread lines: 246 ± 71 vs 258 ± 75; 2) Vigilance: 0.88 ± 0.15 vs 0.87 ± 0.16. **Psychiatric illness and psychological problems**: 1) Fatigue: 5.7± 5.7 vs 3.6 ± 4.3; 2) Anger: 5.6 ± 9.0 vs 3.8 ± 4.7. 2) MMPI scores: Hypochondriasis: 57 ± 13 vs 51 ± 6.6; Psychopathic deviate: 72 ± 12 vs 62 ± 14; M/F: 50 ± 7.7 vs 56 ± 12; Paranoia: 60 ± 6.5 vs 56 ± 7.4; Psychasthenia: 58 ± 10 vs 54 ± 6.4; Schizophrenia: 59 ± 12 vs 57 ± 7.1; Hypomania: 60 ± 16 vs 64 ± 12; Social introversion: 52 ± 12 vs 48 ± 9.3, all p=NS.

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Braga-Neto. P / 2004 Low (2/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional 34-86 yrs 36% (31/86) 64% (55/86) NR 86 NR	**Co-Morbidity**: Medically ill (Parkinson's disease). **Prevalence**: **One-month prevalence**: 53.3% (49/86) (95%CI: 42.8-63.8). No prevalence data by gender.
AUTHOR / YEAR QUALITY (score)	**STUDY DESIGN & POPULATION CHARACTERISTICS**		**CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS**
Broman, JE / 1996 High (6/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional 20-64 yrs 53.1% (210/396) 46.9% (186/396) NR 583 68% (396/583)	**Prevalence**: **Three-month prevalence**: (ChI): 12% (47/396) 95%CI: 8.8-15.2. **Associated Factors**: Groups 1) M vs F; 2) Age: 20-34 (reference group), 35-49 and 50-64 Significant (Basic Nordic Sleep Questionnaire scores) **Medical conditions**: 1) Personal illness (age): p<0.05. **Quality of life**: 1) Leisure activities (age): p<0.0001. 2) Having too little time (age): p<0.0001, 3) Watching TV (age): p<0.0001. **Social relationships**: 1) Relatives' illness (gender): p<0.05, 2) Children's sleeping pattern (age): p<0.0001. **Cognitive function**: (age) p<0.001; Somatic factor (age): p <0.05; Sleepiness (age): p<0.01; Non-Significant (Basic Nordic Sleep Questionnaire scores) **Quality of life**: Working conditions/hours, low capacity for sleep both p=NS.
AUTHOR / YEAR QUALITY (score)	**STUDY DESIGN & POPULATION CHARACTERISTICS**		**CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS**
Broman, JE / 1992 Moderate (5/9)	**Study Design**: **Age Group** mean ± SD: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 45.8 ± 11.5 yrs (CS) 45.0 ± 10.2 yrs (CT) 15 (CS), 15 (CT) 5 (CS), 5 (CT) NR 40 total 20 (CS), 20 (CT) NR	**Associated Factors**: Significant **Psychiatric illness and psychological problems**: 1) Mood, anxiety and cognitive performance: (VAS for Tiredness): 61.0 vs 43.4, p<0.01. 2) State anxiety (State-Trait Anxiety Inventory): 39.9 ± 9.5 vs 32.6 ± 7.6, p<0.05. Non-Significant **Objective performance**: Reaction time dominant hand 1) Speed (ms:) 225.9 ± 42.3 vs 230.1 ± 43.3; 2) Variability: 64.1 ± 44.3 vs 54.3 ± 25.4; Word recognition 1) # correct: 19.5 ± 2.6 vs 19.8 ± 2.5; 2) Latency (s): 2.66 ± 1.01 vs 2.86 ± 0.87; Figure recognition 1) # correct: 12.9 ± 3.1 vs 12.2 ± 3.1; 2) Latency (s): 3.55 ± 1.46 vs 3.24 ± 1.07; Finger tapping dominant hand 1) # taps 61.0 ± 7.6 vs 61.7 ± 8.9; 2) Variability 3.9 ± 2.9 vs 4. ± 2.8, all p=NS. **Psychiatric illness and psychological problems**: VAS for Tension: 47.5 vs 38.5, Excitement 46.4 vs 41.7, Stress 40.9 vs 35.4, Concentration 53.6 vs 858.1; all p=NS. Behavior: (Jenkins Activity scale) all subscales p=NS.

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Chambers, MJ / 1993 Low (1/9)	**Study Design**: **Age Group** mean ± SD: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 47.5 ± 10.9 yrs (CS) 45.9 ± 16.0 yrs (CT) 64.5%, 20/31 (CS) 60%, 21/35 (CT) 35.5%, 11/31 (CS) 40%, 14/35 (CT) NR 66 total 31 (CS), 35 (CT) NR	**Associated Factors**: Significant **Psychiatric illness and psychological problems**: Anxiety 1) State anxiety: 39.1 ± 10.3 vs 31.7 ± 7.3, p<0.001. 2) Trait anxiety: 44.8 ± 9.8 vs 32.3 ± 7.7, p<0.001. Non-Significant None reported

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Coursey, RD / 1975 High (7/9)	**Study Design**: **Age Group** mean ± SD: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 44.7 ± 16.8 yrs 5 (CS), 5 (CT) 13 (CS), 13 (CT) NR 36 total 18 (CS), 18 (CT) NR	**Associated Factors**: Significant **Psychiatric illness and psychological problems**: 1) Anxious worriers (Byrne's Repression-Sensitization scale): 72.7 ± 19.2 vs 50.4 ± 20.9, p<0.01; Taylor Manifest Anxiety scale: 22.5 ± 9.5 vs 13.3 ± 11.6, p<0.01; Edward's Social Desirability scale: 25.4 ± 6.1 vs 30.1 ± 5.8, p<0.05; Eysenck's Neuroticism scale: 12.1 ± 4.5 vs 5.7 ± 4.6, p<0.001; Time competence: 28.4 ± 7.8 vs 19.8 ± 3.5, p<0.001; Zung's Depression scale: 53.0 ± 11.5 vs 35.7 ± 6.2, p<0.001; MMPI Psychastenia scale: 31.24 ± 7.06 vs 25.94 ± 3.75, p<0.01. 2) Concern with internal vs external stimuli (MMPI Hysteria scale): 20.0 ± 7.1 vs 21.5 ± 4.1, p<0.01, MMPI Hypochondriasis scale: 19.0 ± 5.3 vs 12.5 ± 3.1, p<0.001; Zuckerman Sensation-Seeking scale: 7.2 ± 3.2 vs 11.4 ± 3.7, p<0.001. **Memory and cognitive function**: Wechsler Adult Intelligence Scale 1) Low scores: Block Completion: 9.2 ± 2.2 vs 11.5 ± 2.6, p<0.05, Object Assembly: 8.4 ± 3.4 vs 11.4 ± 3.4, p<0.05 and Performance IQ: 107.1 ± 13.5 vs 118.2 ± 12.6, p<0.05. Non-significant **Psychiatric illness and psychological problems**: 1) MMPI *K:* 14.24 ± 4.43 vs 16.33 ± 5.39; 2) MMPI Introversion scale: 29.24 ± 9.88 vs 24.39 ± 9.47; 3) Depression Adjective Checklist: 8.94 ± 6.78 vs 7.0 ± 6.32; 4) MMPI extroversion scale: 19.94 ± 4.71 vs 20.83 ± 4.51; 5) Eysenck's Extraversion: 11.82 ± 3.13 vs 11.56 ± 4.18; all p=NS. All Test honesty and other MMPI neurotic scales NS differences. **Memory and cognitive function**: Wechsler Adult Intelligence Scale NS difference in scores for: Information, Comprehension, Arithmetic, Similarities, Digit span, Vocabulary, Digit symbol, Picture arrangement, Verbal IQ, Full scale IQ.

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Crenshaw, MC / 1999 Moderate (3/9)	**Study Design**: **Age Group** mean ± SD: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 67.7 ± 4.8 yrs (CS) 67.5 ± 5.7 yrs (CT) 16 (CS), 16 (CT) 16 (CS), 16 (CT) NR 64 total 32 (CS), 32 (CT) NR	**Co-Morbidity**: Stable medical conditions: 3.2 ± 2.4 vs 2.3 ± 1.7, p>0.10. CS vs CT: hypertension 43.8% (14/32) vs 34.4% (11/32); diabetes 9.4% (3/32) vs 3.1% (1/32), asthma 6.3% (2/32) vs 6.3% (2/32). **Associated Factors**: Significant None detected Non-significant **Cognitive function**: Performance measures: 1) SRT- latency (ms): 256.9 ± 77.1 vs 265.4 ± 92.7; 2) SRT - mean SD (ms): 57.6 ± 29.7 vs 67.9 ± 37.5; 3) CPT-mean latency (ms): 381.6 ± 60.0 vs 373.9 ± 60.0; 4) CPT-mean SD (ms): 60.5 ± 18.6 vs 60.9 ± 20.7; 5) SWAT - Part I: mean latency (ms): 306.9 ± 63.8 vs 293.0 ± 57.3; 6) SWAT - Part I: mean SD (ms): 64.3 ± 26.9 vs 68.3 ± 26.0; 7) SWAT - Part II: mean latency (ms): 472.8 ± 93.3 vs 478.2 ± 77.4; 8) SWAT - Part II: mean SD (ms): 99.7 ± 38.6 vs 111.8 ± 43.2. For all, p >0.10. SRT = simple reaction time; CPT = continuous performance test; SWAT = Switching attention test.

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Dorsey, CM / 1997 Low (2/9)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 18-25 yrs 14 17 NR 31 total 18 (CS), 13 (CT) NR	**Associated Factors**: Non-significant **Psychiatric illness and psychological problems**: Objective Insomnia vs Subjective Insomnia vs CTs: 1) Eysenck Personality Inventory Extraversion scale: 10.2 ± 3.9 vs 12.7 ± 3.9 vs 14.4 ± 3.7, p<0.058; 2) Neuroticism: 9.7± 3.4 vs 13.7 ± 4.4 vs 9.9 ± 4.3, p=0.062, 3) Sociability 5.0 ± 3.0 vs 6.8 ± 2.3 vs 7.7 ± 3.1 p >0.05.

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Edinger, JD / 2000A Moderate (4/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 40-59 yrs (CS) 40-59 yrs (CT) 55.6%, 15/27 (CS) 51.6%, 16/31 (CT) 44.4%, 12/27 (CS) 48.4%, 15/31 (CT) NR 32 (CS), 32 (CT) 84.4%, 27/32 (CS) 96.9%, 31/32 (CT)	**Associated Factors**: Significant **Cognitive function**: Performance measures - mean latencies (ms): 1) SWAT Part II: 406.7 ± 70.2 vs 464.5 ± 130.8, p=0.05; 2) SWAT-Part III-B-direction: 611.9 ± 110.0 vs 689.8 ± 177.9, p=0.05. Non-significant **Cognitive function**: Performance measures - mean latencies (ms): 1) Simple reaction time: 222.0 ± 36.5 vs 229.5 ± 40.4, p=NS; 2) Continuous performance test: 353.8 ± 37.3 vs 362.7 ± 45.2, p=NS; 3) SWAT - Part I: 257.7 ± 38.0 vs 280.4 ± 53.0, p=NS; 4) SWAT - Part III-A-side: 459.7 ± 138.7 vs 543.2 ± 192.0, p=NS. SWAT = Switching attention test

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Edinger, JD / 2000B High (8/9)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 40-79 yrs 32 (CS), 31 (CT) 32 (CS), 31 (CT) NR 128 total 64 (CS), 64 (CT) 100%, 64/64 (CS) 95.3%, 61/64 (CT)	**Associated Factors**: Significant **Psychiatric illness and psychological problems**: Objective Insomnia CS vs Objective normal sleepers: 1) Elevation in dysfunctional beliefs and attitudes about sleep control: 37.7 ± 11.6 vs 18.5 ± 10.9; p<0.05. Subjective Insomnia CS vs Subjective normal sleepers: 2) High scores on Trait portion of the State-Trait Anxiety Inventory (STAI-2): 37.0 ± 7.3 vs 28.9 ± 6.5; p<0.05. 3) High scores on the Beck Depression Inventory: 8.6 ± 5.2 vs 3.5 ± 3.3; p<0.05. 4) High scores on Dysfunctional beliefs and attitudes about sleep effects: 44.6 ± 18.6 vs 26.9 ± 20.4; p<0.05. 5) High scores on Dysfunctional beliefs and attitudes about sleep control: 33.6 ± 11.4 vs 18.3 ± 10.8; p<0.05. 6) High scores on Dysfunctional beliefs and attitudes about sleep needs: 46.3 ± 24.4 vs 30.6 ± 15.9; p<0.05. Non-significant **Psychiatric illness and psychological problems**: Objective Insomnia CS vs Objective normal sleepers: 1) Elevation in dysfunctional beliefs and attitudes about sleep [a] *Effects*: 41.5 ± 19.9 vs 33.2 ± 15.6, [b] *Cause*: 27.0 ± 18.5 vs 29.6 ± 18.2, [c] *Needs*: 38.3 ± 15.9 vs 37.2 ± 11.9, [d] *Habits*: 25.7 ± 13.9 vs 27.0 ± 11.1, all p>0.05. 2) High scores on Trait portion of the State-Trait Anxiety Inventory (STAI-2): 34.9 ± 6.7 vs 30.7 ± 6.1, p>0.05. 3) High scores on the Beck Depression Inventory: 6.8 ± 4.0 vs 4.6 ± 3.7, p>0.05. Subjective Insomnia CS vs Subjective normal sleepers: 1) High scores on Dysfunctional beliefs and attitudes about sleep [a] *Cause*: 30.6 ± 17.0 vs 23.0 ± 15.4, p>0.05; [b] *Habits:* 27.2 ± 13.3 vs 25.1 ± 12.7, p>0.05.
AUTHOR / YEAR QUALITY (score)	**STUDY DESIGN & POPULATION CHARACTERISTICS**		**CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS**
Fichtenberg, NL / 2002 Moderate (4/8)	**Study Design**: **Age Group** mean ± SD: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional 36.5 ± 14.5 yrs (TBI) 38.2 ± 13.5 yrs (SCI) 47.3 ± 12.2 yrs (MSK) 44%, 22/50 (TBI) 24%, 6/25 (SCI) 80%, 20/25 (MSK) 56%, 28/50 (TBI) 76%, 19/25 (SCI) 20%, 5/25 (MSK) NR 100 total 50 (TBI), 25 (SCI), 25 (MSK) 100%	**Co-Morbidity**: Traumatic back injury, spinal cord injury, or muskuloskeletal injury. **Prevalence**: **DSM-IV Criteria**: 30% (15/50) 95%CI: 27.3-42.7% of TBI patients. **PSQI Criteria**: 28% (14/50) 95%CI: 15.6-40. 4) of TBI patients. 56% (14/25) 95%CI: 36.5-75.5 for SCI patients. 56% (14/25) 95%CI: 36.5-75.5 for MSK patients.

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Hajak, G / 2001 High (6/8) - cross sectional High (7/9) - case control	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control Over 18 yrs Cross-sectional: 53.1% (1016/1913) 46.8% (897/1913) NR 1913 Cross-sectional 368 Case-control: 206 (CS), 162 (CT) NR	**Prevalence**: **One-month prevalence**: (Sleep disturbances) 45% (784/1913), 95%CI: 42.7-47.2%. (Severe insomnia): 4% (81/1913), 95%CI: 3.2-4.8%. **Male**: 3% (26/897), 95%CI: 1.89-4.11%. **Female**: 5% (51/1016), 95%CI: 3.66-6.34%. **Associated Factors**: Significant Cross-sectional data: **Gender**: 1) Female: OR: 1.77; 95%CI: 1.09-2.86; p=0.04. **Social relationships:** 1) Separated or divorced: OR: 3.45; 95%CI: 1.84-6.47, p<0.01; 2) Living in cities > 20,000: OR: 12.88; 95%CI: 6.90-24.05, p=0.004. Case-control: **Healthcare utilization**: 1) Regular medication use: OR: 1.63; 95%CI: 1.06-2.52; 2) # medical tests performed in ≤ 6 mo.: OR: 1.54; 95%CI: 1.02-2.34. Cross-sectional: **Quality of life**: 1) Bad/Very Bad QoL (SF-36) OR: 8.49; 95%CI: 3.28-21.97. Non-significant **Age**: <65 vs > 65: OR 1.06; 95%CI: 0.60-1.89. **Social Relationships:** # in household, # children <15 yrs; **Socioeconomic status:** working status, type of employment; all p=NS. **Healthcare utilization**: 1) Consult physician any reason: OR 1.31; 95%CI: 0.78-2.18; 2) Hospitalizations in <12 m: OR 1.38; 95% C!: 0.71-2.65. **Quality of life**: QoL dimensions (severe insomnia vs no sleep complaints; SF-36 scores); Vitality scale: 41.17 vs 62.7; Social functioning scale: 66.7 vs 90.23; Role emotional scale: 55.17 vs 87.57; Mental health scale: 50.35 vs 73.61; all p=NS.

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Han, SY / 2002 Low (2/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional 27-78 yrs 39% (32/82) 61% (50/82) NR 82 NR	**Co-Morbidity**: Diabetes requiring hemodyalisis. **Prevalence**: **Point prevalence**: (Sleep difficulties ≥2 months): 68.2% (56/82), 95%CI: 58.2-78.2; **Male**: 72% (36/50), 95%CI: 59.5-84.4. **Female**: 62.5% (20/32), 95%CI: 45.7-79.2. **Associated Factors**: Significant **Psychiatric illness and psychological problems**: 1) Depression (Center for Epidemiologic Studies of Depression scale - CES-D) score ± SD; insomnia vs non-insomnia: 25.2 ± 12.1 vs 18.9 ± 10.3; p=0.02. **Medical conditions**: 1) Dialysis adequacy: adj OR: 0.80; 95%CI: 0.67-0.98; p=0.028. Non-significant **Age**: Older vs younger: CS vs CT: 60.5 ± 9.0 vs 56.1 ± 9.6; p=0.053. **Gender**: M/F: OR 1.54; 95%CI: 0.06-3.92. **Socioeconomic status**: 1) Education (>12yr vs ≤12yrs): OR 0.81; 95%CI: 0.25-2.63; 2) Job (yes/no) OR: 0.44; 95%CI: 0.17-1.13, p=NS. **Medical conditions**: Duration of diabetes, frequency of somatic symptoms, p=NS. **Other factors:** Smoking and Alcohol, p=NS.

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Harvey, AG / 2003 Moderate (3/9)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 20.4 ± 4.7 yrs (CS) 22.3 ± 8.9 yrs (CT) 60%, 18/30 (CS) 63.3%, 19/30 (CT) 40%, 12/30 (CS) 36.7%, 11/30 (CT) NR 60 total 30 (CS), 30 (CT) NR	**Associated Factors**: Significant **Psychiatric illness and psychological problems**: Measures of Psychopathology 1) Sleep concern (scale: 0 "Not at all" to 8 "Very much") 3.7 ± 1.8 vs 0.1 ± 0.3, p<0.001. **Quality of life**: Cost (scale: 0 "There is no cost, sleeping badly does not effect me at all" to 10 "Sleeping badly is extremely costly and significantly disrupts my life") 5.5 ± 1.8 vs 3.9 ± 2.4, p<0.01. **Psychiatric conditions**: 1) Beck Anxiety Inventory 13.6 ± 9.6 vs 7.3 ± 7.2, p<0.01. 2) Penn State Worry Questionnaire 57.4 ± 15.1 vs 41.2 ± 14.9, p<0.001. Non-significant **Age**: Insomnia vs good sleeper: (mean ± SD): 20.4 ± 4.7 vs 22.3 ± 8.9, p=NS. **Psychiatric illness and psychological problems**: 1) Beck Depression Inventory 10.3 ± 7.3 vs 7.0 ± 6.6, p=0.07.

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Hauri, PJ / 1997 High (7/9)	**Study Design**: **Age Group** mean ± SD: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 47.7 ± 11.8 yrs 19 (CS), 19 (CT) 7 (CS), 7 (CT) NR 52 total 26 (CS), 26 (CT) NR	**Associated Factors**: Significant **Memory and cognitive function**: (CS vs CT) Performance: 1) Simple reaction tasks: *Sway Forward/backward (sec):* 43.4 vs 41.2, p<0.02; *Initiation time (*msec): 486 ± 614 vs 330 ± 115, p<0.01; *Total time (*msec): 662 ± 683 vs 485 ± 16, p<0.02; 2) Complex reaction tasks: *Initiation time* (msec): 489 ± 218 vs 401 ± 98, p<0.02; *Total time* (msec): 740 ± 289 vs 633 ± 146, p<0.03; 3) Performance on Digit Span test (*Number remembered)*: 21.4 vs 24.5; p<0.01), 4) *Sleepiness throughout the day* (Stanford Sleepiness scale mean scores: 3.67 vs 2.33; p<0.0001). Non-significant **Memory and cognitive function**: Performance: 1) *Sway sideward* (sec) 43.4 vs 49.7; 2) Simple reaction tasks: *Movement time* (msec) 188 ± 150 vs 156 ± 79; 3) Complex reaction tasks: *Initiation time* (msec) 259 ± 157 vs 230 ± 102; 3) Performance on Digit Span test: Divided Attention: *Sum of squares* 2711 vs 1826; *Reaction time (msec)* 2746 vs 2771; Digit symbol substitution: # attempted 58.9 vs 62.1, all p=NS.

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Healey, ES / 1981 High (8/9)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 19-63 yrs (CS) 18-63 yrs (CT) 22 (CS), 22 (CT) 9 (CS), 9 (CT) NS 62 total 31 (CS), 31 (CT) NS	**Associated Factors**: Significant **Psychiatric illness and psychological problems**: Childhood variables 1) Nightmares (1-5 scale); 1 = never: 2.19 vs 1.58; p<0.05, 2) Sleeping problems (1-5 scale); 1 = never: 1.90 vs 1.48; p<0.05, 3) Sleep quality in childhood (1-5 scale); 1 = excellent: 1.90 vs 1.45; p<0.01, 4) Reporting of eating problems: 1.77 vs 1.35; p<0.05. Self concept (Adjective Checklist): 1) Affiliation: 42.3 vs 48.2; p<0.05, 2) Abasement: 54.4 vs 47.8; p<0.05, 3) Aggression: 55.9 vs 49.6; p<0.05, 4) Counseling readiness: 55.9 vs 47.4; p<0.01, 5) Low defensiveness: 43.1 vs 52.4; p<0.01, 6) Low self-control: 44.7 vs 50.3; p<0.05, 7) Low personal adjustment: 41.4 vs 50.9; p<0.01, 8) Low achievement: 46.1 vs 52.7; p<0.05, 9) Low dominance: 45.0 vs 52.6; p<0.05, 10) Low affiliation: 39.9 vs 49.7; p<0.001, 11) Poor self-perception: 59.3% vs 4.5%; p<0.01, 12) "Weak" self-perception: 65.2% vs 21.7%; p<0.01, 13) Passive traits: 60% vs 20%; p<0.05, 14) Nervousness (Health Questionnaire): 61.3% vs 31.8%; p<0.05, 15) Suicidal thoughts: Health Questionnaire: 35.5% vs 9.7%; p<0.05, 16) Incidence of emotional/mental disturbance (Health Questionnaire): 38.7% vs 6.5%; p<0.01. **Medical conditions**: 1) Total # illnesses (Health Questionnaire): 3.19% vs 1.84%; p<0.001, 2) Incidence of allergies (Health Questionnaire): 45.2% vs 12.9%; p<0.05. **Socio-economic status**: 1) Change in financial status (Social Readjustment Rating Scale): 53.23 vs 40.48 ± 69.37; p<0.05, 2) Change to different line of work: 56.13 vs 41.61; p<0.05. **Healthcare utilization** 1) More hospitalizations two years prior to onset of insomnia to evaluation time (Health Questionnaire): 1.55% vs 0.34%; p<0.01, 2) Major hospitalizations ≥ 3 days during same period (Health Questionnaire): 1.07% vs 0.26%; p<0.05. **Quality of life**: 1) Satisfaction with parent relationship (Life Satisfaction scale mean subscores; 1 = satisfied): 4.07 vs 2.85; p<0.01, 2) Satisfaction with social life (Life Satisfaction scale mean subscores; 1 = satisfied): 3.74 vs 2.94; p<0.05, 3) Satisfaction with leisure time (Life Satisfaction scale mean subscores; 1 = satisfied): 4.16 vs 3.16; p<0.05, 4) Satisfaction with living arrangements (Life Satisfaction scale mean subscores; 1 = satisfied): 3.26 vs 2.32; p<0.01, 5) Satisfaction with oneself (Life Satisfaction scale mean subscores; 1 = satisfied): 3.94 vs 2.48; p<0.01, 6) Satisfaction with health prior to sleep problem (Life Satisfaction scale mean subscores; 1 = satisfied): 2.90 vs 1.90; p<0.05, 7) Satisfaction with health in the present (Life Satisfaction scale mean subscores; 1 = satisfied): 3.84 vs 1.97; p<0.001, 8) Total number of health complaints (Health Questionnaire): 9.55 vs 5.87; p<0.001, 9) Lack of energy (Health Questionnaire): 64.5% vs 25.8%; p<0.05. **Social relationships**: 1) Mean # losses from social field: 1.19 ± 1.01 vs 0.52 ± 1.03; p<0.01. **Memory and cognitive function**: 1) Trouble concentrating (Health Questionnaire): 51.6% vs 12.9%; p<0.05. **Other factors**: Life events: 1) Life events year of insomnia onset (Life Change Unit scale): 157.52 ± 65.96 vs 91.90 ± 69.37; p<0.0), 2) Recent experiences during year of insomnia onset (Schedule of Recent Experience interview): 345.56 ± 148.08 vs 197.78 ± 158.64; p<0.01, 3) Mean # personal events experienced: 2.71 ± 1.97 vs 1.58 ± 1.95; p<0.05, 4) Mean # undesirable events: 2.68 ± 2.12 vs 1.03 ± 1.33; p<0.001. Non-significant **Social relationships**: Area of activity: 1) mean # life events: work, financial, legal, family, desirable, ambiguous, deaths; all p=NS. 2) Mean # entrances into social field 0.32 ± 0.60 vs 0.19 ± 0.48; p=NS.
AUTHOR / YEAR QUALITY (score)	**STUDY DESIGN & POPULATION CHARACTERISTICS**		**CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS**
Hetta, J / 1999 Low (0/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional Over 18 yrs NS NS NS 1,996 total 25%, 499/1996	**Prevalence**: **One-month prevalence**: 31% (155/499) (95%CI: 27-35). No prevalence data by gender.

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Hidalgo, MP / 2002 Moderate (5/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional 18-35 yrs 41.8%, 143/342 58.2%, 199/342 NS 342 total NS	**Prevalence**: **One-year prevalence**: (Sleep difficulties ≥ 1 mo): 26% (89/342) 95%CI: 21.3-30.6. No prevalence data by gender. **Associated Factors**: Significant **Psychiatric illness and psychological problems**: 1) Minor psychiatric disorders and insomnia: adj OR: 2.45; 95%CI: 1.32-4.56; p<0.05. Non-significant **Gender**: (F vs M) OR 0.87; 95%CI: 0.56-0.65; p=NS. **Psychiatric illness and psychological problems**: Hx psychopathologies: OR 0.99, 95%CI: 0.5 -1.96; p=NS.
AUTHOR / YEAR QUALITY (score)	**STUDY DESIGN & POPULATION CHARACTERISTICS**		**CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS**
Hohagen, F / 1993 Moderate (4/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional 18-65 yrs 55.3%, 1389/2512 44.7%, 1123/2512 NS 2,512 total 97.9%, 2459/2512	**Prevalence**: **Six-month prevalence**: (Severe, moderate, mild insomnia): 45.9% (1152/2512) 95%CI: 44-48. Severe: 18.7% (469/2512) 95%CI: 17.1-20.2. No prevalence data by gender. **Associated Factors**: Significant **Psychiatric illness and psychological problems**: 1) Depression (mild chronic insomnia): n = 23, 8.0%; p<0.01; moderate ChI: n = 18, 7%; p<0.001; severe ChI: n = 85, 21.7%; p<0.001, 2) Neurosis/personality disorders (severe chronic insomnia): n = 28, 7.2%; p<0.001, 3) Acute psychological distress (moderate chronic insomnia): n = 20, 7.8%; p<0.001; severe ChI: n = 40, 10.2%; p<0.001, 4) Alcohol drug abuse (severe ChI): n = 18, 4.6%; p<0.001, 5) Psychosomatic disorders (severe ChI): n = 22, 5.6%; p<0.001. Non-significant **Psychiatric illness and psychological problems**: 1) Neurosis/personality disorders - moderate ChI: n = 10, 3.9%; p=NS.
AUTHOR / YEAR QUALITY (score)	**STUDY DESIGN & POPULATION CHARACTERISTICS**		**CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS**
Hohagen, F / 1994 Moderate (4/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional Over 65 yrs 72%, 237/330 8%, 93/330 NS 338 97.5%, 330/338	**Prevalence**: **Point prevalence**: (All DSM-III-R insomnia): 56.3% (186/330) 95%CI: 50.9-61.6. Severe DSM-III-R insomnia: 23% (17/75) 95%: 18.4-27.5. No prevalence data by gender. **Associated Factors**: Significant **Gender**: severe insomnia F/M 29.1 vs 7.9, p <0.001. **Healthcare utilization**: 1) Prescribed hypnotics - patient report: OR: 6.19; 95%CI: 3.19-12.0; p<0.001; physician report: OR: 2.09; 95%CI: 2.09-12.6; p<0.001. **Psychiatric illness and psychological problems**: Depression OR 2.93; 95%CI: 1.51-5.71; p <0.01. Mental disorders (Total) OR 1.71; 95%CI: 1.07-2.74 p <0.01. Non-significant **Medical conditions** (acute/chronic): reported NS.

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Ishigooka, J / 1999 Moderate (5/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional 15-65 yrs 58.1%, 3645/6277 41.9%, 2632/6277 All Asian (Japanese) 7112 total 88.3%, 6277/7112	**Prevalence**: **Point prevalence**: (Insomnia lasting ≥ 1 mo): 11.7% (735/6277), 95%CI: 10.9-12.4. **Male**: 11.2% (295/2632), 95%CI: 10-12.4. **Female**: 12% (440/3645), 95%CI: 10.9-13. **Associated Factors**: **Significant** **Age**: 1) Older age group (45-54 yrs): OR 1.42; p<0.001; 55-64 yrs OR: 1.81; p<0.0001; 65+ OR: 1.64; p<0.001. **Gender**: Female/male: OR 1.12; p<0.05. **Healthcare utilization**: 1) Neurology service: OR: 1.73; p<0.01), 2) Psychiatry service: OR: 3.85; p<0.0001. **Other factors**: 1) Living alone: OR: 1.18; p<0.05), 2) Dissatisfaction with sleep environment: OR: 1.58; p<0.0001. Non-significant **Other factors:** Occupation, Residential area, Season, Alcohol consumption, Smoking, Caffeine intake, Regularity of living; all p=NS. (no data)
AUTHOR / YEAR QUALITY (score)	**STUDY DESIGN & POPULATION CHARACTERISTICS**		**CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS**
Kageyama, T / 2001 Moderate (5/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional study 24-59 yrs NS NS Japanese 555 total NS	**Prevalence**: **Point prevalence**: 29.2% (162/555) 95%CI: 28.7, 29.7. **Associated Factors**: Significant **Age**: (40-49 yrs reference group): <24 yrs: 34% (62/184), adj OR = 2.34; 95%CI: 1.19-4.62. **Work performance**: (CS vs CT, mean score ± SE): 1) Workload: 2.47 ± 0.06 vs 2.30 ± 0.004, p<0.05; 2) Mental workload: 2.41 ± 0.05 vs 2.25 ± 0.04, p<0.05; 3) Problem in personal relationships: 2.18 ± 0.06 vs 2.00 ± 0.03, p<0.05; 4) Job satisfaction: 2.51 ± 0.07 vs 2.67 ± 0.04, p<0.05; 5) Support from colleagues and superiors: 2.66 ± 0.05 vs 2.82 ± 0.03, p<0.01; 7) Severity of patients' illness: 2.79 ± 0.06 vs 2.57 ± 0.04, p<0.01. 8) # non-working days in ≤ 3mo: (≤ 6 days/mo): OR 2.62; 95%CI: 1.27-5.42; 9) # night shifts in ≤ 3mo. (≥ 9 nights/mo is reference gr): (1-3 nights/mo) OR 3.32; 95%CI: 1.0-11.16. **Socioeconomic status**: # working days in last 3 mo (<10 vs ≥10) p<0.05 Non-significant **Age**: (40-49 yrs reference group): 25-29 yrs: 26% (37/143), adj OR = 1.45; 95%CI: 0.69-30.2), 30-39 yrs: 29% (30/103), adj OR = 1.48; 95%CI: 0.71-3.11; 50-59 yrs: 33% (14/43), adj OR = 2.41; 95%CI: 0.96-6.05, all p=NS. **Healthcare utilization**: Undergoing medical treatment (no vs yes): 27% (119/441) vs 36% (37/104), p=NS. **Work performance**: (CS vs CT, mean score ± SE): 1) Job control: 2.36 ± 0.05 vs 2.45 ± 0.03, p=NS). 2) # non-working days in ≤ 3mo: 7-9 days/mo): OR 1.14; 95%CI: 0.74-1.76; 3) # night shifts in ≤ 3mo. (≥ 9 nights/mo is reference gr): (4-5 nights/mo) OR 2.75; 95%CI: 0.87-8.64; (6-8 nights/mo): OR 1.80; 95%CI: 0.54-6.02. **Relationships**: 1) Marital status OR 1.31; 95%CI: 0.89-1.94; 2) Difficulty in patient-nurse relationship: 1.94 ± 0.04 vs 2.10 ± 0.06. 3) # Children < 6: OR 0.95; 95%CI: 0.51-1.76, 4) # life events in ≤ 6 mo (≤ 1 vs ≥ 2): OR 0.74, 95%CI: 0.49-1.12. **Medical conditions**: Current OR 0.67, 95%CI: 0.43-1.05.

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Kageyama, T / 1997 High (6/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional 20 - 80 yrs 3600 0 Japanese 3600 total Varied between district 51-59%	**Prevalence**: **Point prevalence**: 11.2% (403/3600) 95%CI: 10.2, 12.2. **Associated Factors**: Significant **Age**: (% ± SE, reference group 30-39 yr): 70+ years: 14.2% (46/322) ± 1.9, adj OR = 2.1; 95%CI: 1.1-3.8. **Medical conditions**: 1) Sleep apnea-like symptoms (absent vs present, absent is reference category): adj OR = 2.7; 95%CI: 1.6-4.8; 2) Heart Disease: OR = 2.4, p<0.01. **Relationships:** 1**)** Children ≤ 6 in home: OR 1.5; 95%CI: 1.0-2.1; 2) Major life event ≤6 mo: OR 1.4; 95%CI 1.1-1.9. **Healthcare utilization**: 1) Consulting a physician or other specialist (insomniacs vs non-insomniacs, % ± SE): Current: 11.4% ± 1.6 (46/403) vs 1.3% ± 0.2 (42/3197), OR = 9.68; 95%CI: 6.28-14.92; Past: 17.4% ± 1.9 (70/403) vs 4.9% ± 0.4 (157/3197), OR = 4.07; 95%CI: 3.00-5.51; Never: 71.2% ± 2.3 (287/403) vs 93.8% ± 0.4 (2999/3197), OR = 0.16; 95%CI: 0.13-0.21; 2) Undergoing medical treatment (yes vs no, no is reference category) adj OR = 2.1; 95%CI: 1.6-2.8. **Work performance**: (insomniacs vs non-insomniacs % ± SE): 1) Inefficiency in work: 17.2% ± 1.9 (69/403) vs 8.6% ± 0.5 (275/3197), p<0.001, OR = 2.20; 95%CI: 1.65-2.93; 2) Tardiness: 10.2% ± 1.5 (41/403) vs 4.4% ± 0.4 (141/3197), p<0.001, OR = 2.45; 95%CI: 1.71-3.53; 3) Prone to errors in work (8.9% ± 1.4 (36/403) vs 3.5% ± 0.3 (112/3197), p<0.001, OR = 2.70; 95%CI: 1.83-3.99. Non-significant **Age**: (% ± SE, reference group 30-39 yr): 20-29 yrs: 13.3% (45/337) ± 1.8, adj OR = 1.5; 95%CI: 0.9-2.5; 40-49 yrs: 9.2% (90/982) ± 0.9, adj OR = 1.1; 95%CI: 0.7-1.7, 50 - 59 yrs: 12.6% (107/852) ± 1.1, adj OR = 1.1; 95%CI: 0.8-2.0, 60-69 yrs 13.1% (66/501) ± 1.5, adj OR = 1.6; 95%CI: 0.9-2.6; all p=NS. **Socio-economic status**: (% with insomnia ± SE): employed: 10.5% (183/1739) ± 0.7, unemployed: 11.9% (195/1639) ± 0.8; p=NS. **Social relationships**: Marital Status: Married: 10.7% (291/2722) ± 0.2, Single 13.0% (94/721) ± 1.3, p=NS. **Other factors**: Exercise, Smoking, Alcohol, Caffeine all reported NS (no data).

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Kales, AK / 1983 Moderate (4/9)	**Study Design**: **Age Group** mean ± SD: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 43.1 ± 0.9 (CS) 40.9 ± 1.5 (CT) 59%, 177/300 (CS) 59%, 59/100 (CT) 41%, 123/300 (CS) 41%, 41/100 (CT) NS 400 total 300 (CS), 100 (CT) 93%, 279/300 (CS) 97%, 97/100 (CT)	**Associated Factors**: Significant **Psychiatric illness and psychological problems**: (MMPI) (mean ± SE): 1) *F Scale:* 7.4 ± 0.2 vs 4.2 ± 0.3, p<0.01; 2) *K Scale:* 13.9 ± 0.3 vs 15.8 ± 0.5, p<0.01; 3) *Hypochondriasis Scale*: 63.2 ± 0.8 vs 50.2 ± 0.8, p<0.01); 4) *Depression Scale:* 71.6 ± 1.0 vs 52.8 ± 1.1, p<0.01; 5) *Conversion Hysteria Scale*: 66.8 ± 0.7 vs 54.8 ± 0.8, p<0.01; 6) *Psychopathic Deviate Scale*: 65.0 ± 0.7 vs 56.2 ± 1.1, p<0.01; 9) *Paranoia Scale*: 60.7 ± 0.6 vs 55.4 ± 0.9, p<0.01; 10) *Psychasthenia Scale*: 67.7 ± 0.8 vs 53.7 ± 0.9, p<0.01; 11) *Schizophrenia Scale*: 66.4 ± 0.9 vs 54.5 ± 1.0, p<0.01. Non-significant **Psychiatric illness and psychological problems**: (MMPI) (mean ± SE): 1) *L Scale*: 50.1 ± 0.4 vs 49.1 ± 0.7, p=NS; 2) *Masculine-Feminine Scale:* Male 65.5 ± 0.9 vs 62.3 ± 1.7, p=NS. Female 45.2 ± 0.7 vs 45.5 ± 1.3, p=NS. 3) *Hypomania Scale*: 57.2 ± 0.7 vs 55.0 ± 1.0, p=NS. MMPI = Minnesota Multiphasic Personality Inventory Scale

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Kales, AK / 1982 Low (2/9)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 18-78 yrs (CS) 18-74 yrs (CT) 118 (CS), 59 (CT) 82 (CS), 41(CT) NS 300 total 200 (CS), 100 (CT) NS	**Associated Factors**: Significant **Psychiatric illness and psychological problems**: (CSs with sleep apnea vs CTs with sleep apnea; mean ± SE): 1) Elevation in MMPI Psychopathic deviate scale: 64.5 ± 2.2 vs 52.4 ± 2.7; p<0.01. 2) Elevation in MMPI Psychasthenia scale: 66.2. ± 3.1 vs 55.7 ± 2.1; p<0.01. 3) Elevation in MMPI Schizophrenia scale: 64.4. ± 2.9 vs 53.8 ± 1.8; p<0.01. 4) Elevations in at least one MMPI scale: 68.4% vs 36.4%; p<0.01. 5) Mean # elevated MMPI scales: 1.9 ± 0.5 vs 0.4 ± 0.2; p<0.05. (CSs with nocturnal myoclonic activity vs CTs with nocturnal myoclonic activity; mean ± SD): 1) Elevation in MMPI Depression scale: 68.6 ± 3.9 vs 50.5 ± 3.2; p<0.01. 2) Elevation in MMPI Conversion hysteria scale: 64.3. ± 2.8 vs 55.6 ± 2.2; p<0.05. 3) Elevation in MMPI Psychopathic deviate scale: 65.8. ± 2.6 vs 54.8 ± 2.8; p<0.01. 4) Elevation in MMPI Psychasthenia scale: 66.9. ± 3.3 vs 50.9 ± 2.4; p<0.01. 5) Elevation in MMPI Schizophrenia scale: 64.2. ± 2.6 vs 50.6 ± 2.7; p<0.01. 6) Elevation in MMPI Hypomania scale: 62.2. ± 3.1 vs 51.4 ± 2.1; p<0.01. 7) Elevations in at least one MMPI scale: 83.3% vs 36.4%; p<0.05. 5) Mean number elevated MMPI clinical scales: 2.1 ± 0.5 vs 0.4 ± 0.2; p<0.01. Non-significant **Psychiatric illness and psychological problems**: 1) CSs with sleep apnea vs CTs with sleep apnea; mean ± SD: No difference in frequency: 9.1± 1.3 vs 9.5 ± 2.2 or duration of episodes (sec): 16.2 ± 1.0 vs 13.8 ± 0.7. 2) CSs with nocturnal myoclonic activity vs CTs with nocturnal myoclonic activity; mean ± SE: *Prevalence*: 5% (n=10) vs 6% (n=6), p=NS; *Frequency* 106.5 ± 16.9 vs 171.3 ± 41.2, p=NS. 3) Elevation in MMPI Hypochndriasis scale: 60.9 ± 3.8 vs 53.4 ± 2.0; p=NS. 4) Elevation in MMPI Paranoia scale: 56.4 ± 2.3 vs 53.2 ± 2.5; p=NS. MMPI = Minnesota Multiphasic Personality Inventory Scale

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Kales, JD / 1984 Low (1/9)	**Study Design**: **Age Group** mean ± SD: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 43.1± NS (CS) 48.2 ± 1.5 (CT) 58.9%, 126/214 (CS) 59%, 59/100 (CT) 41.1%, 88/214 (CS) 41%, 41/100 (CT) NS 314 total 214 (CS), 100 (CT) NS (CS) 94%, 94/100 (CT)	**Associated Factors**: Significant **Psychiatric illness and psychological problems**: 1). Mental Health: a) More nervous than others 50% (107/214) vs 12% (11/94), p<0.01 (OR = 7.55, 95%CI: 3.81-14.95), b) Ready to go to pieces 51% (109/214) vs 12% (11/94), p<0.01 (OR = 7.83, 95%CI: 3.95-15.52), c) Feeling life is a strain 46% (99/214) vs 7% (7/94), p<0.01 (OR = 10.70, 95%CI: 4.73-24.19), d) Less happy than others 52% (111/214) vs 20% (19/94), p<0.01 (OR = 4.25, 95%CI: 2.40-7.53), e) Lacking self-confidence 44% (94/214) vs 20% (19/94), p<0.01 (OR = 3.09, 95%CI: 1.75-5.47), f) Lonely much of the time 43% (92/214) vs 7% (7/94), p<0.01 (OR = 9.37, 95%CI: 4.14-21.20), g) Brood a great deal 41% (88/214) vs 8% (8/94), p<0.01 (OR = 7.51, 95%CI: 3.46-16.28), h) Feeling blue 35% (75/214) vs 2% (2/94), p<0.01 (OR = 24.82, 95%CI: 5.95-103.59), i) Feeling future is hopeless 17% (36/214) vs 0, p<0.01), j) "take things hard" 65% (139/214) vs 34% (32/94), p<0.01 (OR = 3.59, 95%CI: 2.15-5.98), k) Have not lived "the right kind of life" 31.8% (68/214) vs 11.7% (11/94), p<0.01 (OR = 3.51, 95%CI: 1.76-7.02), l) Thought there was something "wrong with their mind" 21.5% (46/214) vs 2.1% (2/94), p<0.01 (OR = 12.60, 95%CI: 2.99-53.07), m) Feeling worried 81.3% (174/214) vs 38.3% (36/94), p<0.01 (OR = 7.01, 95%CI: 4.09-12.02), n) Feeling anxious 50.5% (108/214) vs 7.4% (7/94), p<0.01 (OR = 12.66, 95%CI: 5.60-28.62), o) Feeling "high strung" 59.8% (128/214) vs 17.0% (16/94), p<0.01 (OR = 7.26, 95%CI: 3.97-13.27), p) Not usually feeling calm 43.5% (93/214) vs 11.7% (11/94), p<0.01 (OR = 5.80, 95%CI: 2.92-11.50). **Medical conditions**: a) Poor currently 43% (43/100) vs 3% (3/100), p<0.01 (OR = 24.39, 95%CI: 7.24-82.23), b) Under a doctor's care 55% (55/100) vs 11% (11/100), p<0.01 (OR = 9.89, 95%CI: 4.72-20.73), c) "Psychosomatic" illnesses 59% (126/214) vs 31% (29/94), p<0.01 (OR = 3.21, 95%CI: 1.92-5.37), d) Work limited by illness 49% (49/100) vs 17% (17/100), p<0.01 (OR = 4.69, 95%CI: 2.44-9.01), e) Hospitalizations (means only) 2.7 vs 1.4, p<0.01, f) Headaches 19.2% (41/214) vs 1.1% (1/94), p<0.01 (OR = 22.04, 95%CI: 2.98-162.81), g) Diarrhea 28.0% (60/214) vs 9.6% (9/94), p<0.01 (OR = 2.93, 95%CI: 1.40-6.15), h) Stomach discomfort 28.5% (61/214) vs 3.2% (3/94), p<0.01 (OR = 12.09, 95%CI: 3.69-39.67), i) Palpitations 40.7% (87/214), 16.0% (15/94), p<0.01 (OR = 3.61, 95%CI: 1.95-6.68), j) Non-specific pain 34.6% (74/214) vs 13.8% (13/94), p<0.01 (OR = 3.29, 95%CI: 1.72-6.31), k) Tiredness 64.0% (137/214) vs 12.8% (12/94), p<0.01 (OR = 12.16, 95%CI: 6.24-23.69), l) Weakness 26.2% (56/214) vs 3.2% (3/94), p<0.01 (OR = 10.75, 95%CI: 3.27-35.33). **Health care Utilization**: Hospitalizations (mean #) 2.7 vs 1.4 times, p<0.01). **Quality of life**: a) "I believe that my home life is as pleasant as that of most people I know" 64.5% (138/214) vs 94.7% (89/94), p<0.01 (OR = 0.08, 95%CI: 0.03- 0.23), b) "I seem to make friends about as quickly as others do" 69.2% (148/214) vs 91.5% (86/94), p<0.01 (OR = 0.21, 95%CI: 0.10-0.46), c) "I like children" 79.9% (171/214) vs 95.7% (90/94), p<0.01 (OR = 0.18, 95%CI: 0.06-0.51), d) "My sex life is satisfactory" 52.8% (113/214) vs 81.9% (77/94), p<0.01 (OR = 0.16, 95%CI: 0.09-0.29). **Mood**: Behavioural correlates (CS vs CT): 1) Feelings before going to sleep: a) "Mind racing" 48% (48/100) vs 15% (15/100), p<0.01 (OR = 5.23, 95%CI: 2.66-10.27), b) Tense/anxious 44% (44/100) vs 2% (2/100), p<0.01 (OR = 38.50, 95%CI: 8.99, 164.89), c) Worried 35% (35/100) vs 6% (6/100), p<0.01 (OR = 8.44, 95%CI: 3.36-21.21), d) Depressed 24% (24/100) vs 2% (2/100), p<0.01 (OR = 15.47, 95%CI: 3.55-67.52), e) Desperate 10% (10/100) vs 0%, p<0.01, f) Mentally tired 56% (56/100) vs 39% (39/100), p<0.01 (OR = 1.99, 95%CI: 1.13-3.50), g) Sleepy 31% (31/100) vs 71% (71/100), p<0.01 (OR = 0.18, 95%CI: 0.10-0.34). 2) Thoughts before going to sleep: a) About getting enough sleep 77% (77/100) vs 12% (12/100), p<0.01 (OR = 24.55, 95%CI: 11.46-52.60), b) About personal problems 49% (49/100) vs 30% (30/100), p<0.05 (OR = 2.24, 95%CI: 1.25-4.00), c) About work 47% (47/100) vs 29% (29/100), p<0.05 (OR = 2.17, 95%CI: 1.21-3.89), d) About health 36% (36/100) vs 16% (16/100), p<0.01 (OR = 2.95, 95%CI: 1.51-5.79), e) About death 14% (14/100) vs 3% (3/100), p<0.05 (OR = 5.26, 95%CI: 1.16-18.94), f) "Most nights I go to sleep without thoughts or ideas bothering me" 23.8% (51/214) vs 80.9% (76/94), p<0.01 (OR = 0.07, 95%CI: 0.04-0.14), g) Being frightened in the middle of the night 25.2% (54/214) vs 5.3% (5/94), p<0.01 (OR = 6.01, 95%CI: 2.32-15.57). Non-significant **Medical conditions**: a) Poor in childhood 19% (19/100) vs 11% (11/100), OR = 1.90; 95%CI: 0.85-4.23; b) Attempts at suicide: 11% vs 3%, p=NS. Smoking and Caffeine consumption reported NS.

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Kappler, C / 2003 Low (2/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional 18-65 yrs 50.1%, 1257/2512 49.9%, 1253/2512 NS 2512 total 37.6%, 945/2512	**Prevalence**: **Six-month prevalence**: (DSM-III severe/moderate insomnia): 27.3% (258/945) (95%CI: 24.5-30.1). No prevalence data by gender. **Associated Factors**: Significant **Age**: 1) Older (OR: 18.17; p<0.001). **Psychiatric illness and psychological problems**: (95%CI: not reported) 1) Psychiatric disorder (OR: 7.38; p=0.007). **Socio-economic status**: 1) Social status (OR: 1.64; p=0.0009). **Quality of life**: 1) Overload housekeeping (OR: 11.02; p=0.01). **Social relationships**: 1) Conflicts with relatives (OR: 16.44; p=0.0002), 2) Illness of relatives (OR: 1.7; p=0.04), 3) Overload profession (OR: 11.02; p=0.0003). Non-significant None reported

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Kawada, T / 2003 High (6/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional 20-80 yrs 1286 0 All Asian (Japanese) 1286 50.4%, 648/1286	**Prevalence**: **Point prevalence**: (DSM-IV criteria for at least 1 month): 8.8% (57/648) (95%CI: 6.6-10.9). No prevalence data by gender. **Associated Factors**: Significant **Psychiatric illness and psychological problems**: 1) Depressive state (adj OR: 1.2; 95%CI: 1.1-1.3; p<0.01). **Medical condition**: 1) Poor self-rated health (adj OR: 3.2; 95%CI: 1.0-10.1; p<0.05). 2) Medical treatment: OR: 2.15; 95%CI: 1.23-3.76. **Other factors**: 1) Experiencing a major life event (adj OR: 4.4; 95%CI: 1.7-11.4; p<0.01). 2) Child ≤ 6yrs: OR: 2.08; 95%CI: 1.13-3.84. Non-significant **Age**: (<50 vs >50) adj OR: 2.7; 95%CI: 0.9-7.9. **Social Relationships**: (Married vs not married) OR: 1.01; 95%CI: 0.51-2.03. **Socioeconomic status**: (Employed vs other) OR: 0.97; 95%CI: 0.26-1.7. **Other factors**: 1) Smoking: OR: 1.24; 95%CI: 0.62-2.5; 2) Alcohol (yes vs no) OR: 1.42; 95%CI: 0.76-2.66; 3) Regular exercise: OR: 0.67; 95%CI: 0.32-1.41.

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Leger, D / 2000 High (6/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional Over 18 yrs 53%, 6772/12,778 47%, 6006/12,778 NS 14,998 85.2%, 12778/14,997	**Prevalence**: **One-month prevalence**: (Insomnia) 19% (2376/12,778) (95%CI: 18.3-19.6). **Associated Factors**: Significant **Gender**: *Male*: 14% (841/6006), 95%CI: 13.1-14.80). *Female*: 23% (1542/6772), 95%CI: 22-24. (Severe/chronic insomnia): 9% (1192/12,778), 95%CI: 8.51-9.49. *Male*: 6.3% (377/6006), 95%CI: 5.4-6.6. *Female*: 12% (815/6772), 95%CI: 11.2-12.7. **Age**: Severe insomnia increased significantly both sexes $p<10^{-4}$. **Socio-economic status**: 1) Retired: 18.3%; p <0.0001, 2) White-collar worker: 20.8%; p<0.03. **Social Relationships**: Singles less insomnia than other states 13% $p<10^{-4}$. Non-significant **Other factors**: Urban vs rural p=NS

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Leppavuori, A / 2002 Moderate (4/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional 55-85 yrs 49.1%, 136/277 50.9%, 141/277 NS 277 NS	**Co-Morbidity**: Medically ill (stroke). **Prevalence**: **Point prevalence**: (DSM-IV criteria of insomnia): 37.6% (104/277) (95%CI: 31.9-43.3). (Insomnia complaints): 56.7% (157/277) (95%CI: 50.9-62.5). (Before-stroke insomnia complaints): 38.6% (107/277) (95%CI: 32.9-44.3). (Post-stroke insomnia complaints): 18.1% (50/277) (95%CI: 13.6-22.6). (Before-stroke DSM-IV insomnia): 69.2% (74/107) (95%CI: 60.5-77.9). (Post-stroke DSM-IV insomnia): 60% (30/50) (95%CI: 46.5-73.5). No prevalence data by gender. **Associated Factors**: **Significant** **Age**: 1) Age (mean ± SD years) (71.1 ± 7.1 vs 72.6 ± 7.2 (p<0.01) vs 71.6 ± 7.8 (p<0.05) vs 69.5 ± 6.8). **Gender**: 1) Female (Prestroke insomniacs vs New insomniacs vs All insomniacs vs Non-insomniacs: 52.3% vs 60% vs 54.8% (p<0.05) vs 41.7%). **Psychiatric illness and psychological problems**: 1) History of depression (29.9% vs 16% vs 25.5% (p<0.01) vs 11.7%) and anxiety disorders (32.7% (p<0.001) vs 8.0% vs 24.8% (p<0.01) vs 11.7%), 2) Any depression (51.4% (p<0.00001) vs 52% (p<0.001) vs 51.6% (p<0.00001) vs 25%), 3) Major depression (34.6% (p<0.001) vs 34% (p<0.01) vs 34.4% (p<0.001) vs 15.0%), 4) Organic depression (3.7% vs 18% (p<0.01) vs 8.3% vs 4.2%), 5) Any anxiety disorder (31.8% (p<0.00001) vs 30.0% (p<0.001) vs 31.2% (p<0.00001) vs 9.2%), 6) Generalized anxiety (21.5% (p<0.00001) vs 6.0% vs 16.6% (p<0.01) vs 4.2%), 7) Organic anxiety (9.3% vs 22.0% (p<0.001) vs 13.4% (p<0.01) vs 4.2%), 8) Dementia (18.1% vs 38.0% (p<0.001) vs 24.2% (p<0.05) vs 13.3%), 9) High scores on Beck Depression Inventory (mean score ± SD: 11.6 ± 8.3 (p<0.00001) vs 10.2 ± 5.2 (p<0.01) vs 11.2 ± 7.6 (p<0.00001) vs 7.1 ± 5.9) 10) High scores on Montgomery-Åsberg Depression Rating Scale (MADRS): 9.9 ± 8.0 (p<0.00001) vs 10.3 ± 8.6 (p<0.00001) vs 10.1 ± 8.2 (p<0.00001) vs 4.9 ± 6.3), 11) High scores on Zung depression scale (40.7 ± 10.0 (p<0.00001) vs 41.7 ± 9.3 (p<0.00001) vs 41.0 ± 9.7 vs 35.0 ± 9.2), 12) High scores on Zung anxiety scale (30.9 ± 7.8 (p<0.00001) vs 30.5 ± 7.1 (p<0.00001) vs 30.8 ± 7.6 (p<0.00001) vs 26.2 ± 5.8), 13) Low score on Global Assessment of Functioning scale (GAF) after stroke (58.6 ± 13.1 (p<0.00001) vs 56.6 ± 17.9 (p<0.00001) vs 58.0 ± 14.8 (p<0.00001) vs 65.3 ± 11.1), 14) Low score on Global Assessment of Functioning scale (GAF) before stroke: 69.8 ± 9.5 (p<0.00001) vs 72.6 ± 8.8 vs 70.7 ± 9.3 (p<0.00001) vs 74.8 ± 7.3). **Medical conditions**: 1) Major dominant stroke syndrome (14.2% vs 26.0% (p<0.05) vs 17.9% vs 12.5%, 2) Stroke severity (Scandinavian Stroke Scale mean score ± SD: 54.9 ± 6.4 vs 49.9 ± 12.3 (p<0.01) vs 53.3 ± 9.0 vs 54.8 ± 8.1). 3) Migraine (17.8% vs 10.0% vs 15.3% (p<0.05) vs 5.8%). **Quality of life**: 1) Being dependent (34.6% vs 56.0% (p<0.001) vs 41.4% (p<0.01) vs 25.8%), 2) Activities of daily living (Barthel's Index mean score ± SD: 72.4 ± 15.4 vs 61.6 ± 23.1 (p<0.00001) vs 68.9 ± 18.9 (p<0.01) vs 74.4 ± 13.7). **Memory and cognitive function**: 1) Cognition (Mini Mental Status Examination mean score ± SD: 25.7 ± 4.0 vs 23.8 ± 5.4 (p<0.00001) vs 25.1 ± 4.6 (p<0.01) vs 26.6 ± 3.0). **Prestroke insomniacs vs New insomniacs vs All insomniacs vs Non-insomniacs**: (reference group: Non-insomnia): 1) Sleep-promoting drug use (86.9% (p<0.0001) vs 78% (p<0.0001) vs 84.1% (p<0.0001) vs 0.0%), 2) Anxiolytics (32.7% (p<0.0001) vs 22% (p<0.0001) vs 29.3% (p<0.0001) vs 1.7%), 3) Antidepressants use (28% vs 42% (p<0.0001) vs 32.5% (p<0.0001) vs 10.8%), 4) Antipsychotics use (8.4% (p<0.05) vs 14.0% (0.01) vs 10.2% (p<0.01) vs 1.7%). Non-significant Non reported

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Levitt, H / 2004 Low (2/9) - case control Low (0/9) - cohort	**Study Design**: **Age Group**: mean ± SD: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 20-30 yrs 24.1±3.4 (CS) 23.3±1.9 (CT) 85.7%, 6/7 (CS) 87.5%, 7/8 (CT) 14.3%, 1/7 (CS) 12.5%, 1/8 (CT) NS 15 total 7 (CS), 8 (CT) 100%	**Associated Factors**: Significant **Psychiatric illness and psychological problems** (CS vs CT): 1) Hamilton Rating Scale for Anxiety: 5.9 ± 1.8 vs 0.0 ± 0.0, t = -8.74, p<0.001. 2) Inventory of depressive symptomatology: 11.6 ± 3.0 vs 1.9 ± 2.2, t = -7.01, p<0.001. 3) Pittsburgh Sleep Quality Index: 8.9 ± 1.0 vs 1.4 ± 1.1, t = -6.33, p<0.001. 4) SF-36 Vitality Index: 52.9 ± 21.4 vs 78.1 ± 7.0, t = 2.97, p<0.05. **Cognitive function**: 1) Subjective alertness morning: 46.59 ± 5.28 vs 80.86 ± 4.27, p=0.003. 2) Energy morning: 58.05 ± 5.12 vs 84.08 ± 5.11, p=0.003; noon: 73.28 ± 5.45 vs 87.68 ± 4.10, p=0.052. 3) Concentration morning: 54.75 ± 5.43 vs 82.17 ± 5.23, p=0.003; night: 53.01 ± 4.78 vs 68.21 ± 4.93, p=0.045. **Mood** (CS vs CT, mean ± SE) morning: 66.22 ± 4.23 vs 87.40 ± 4.49, p=0.004. Non-significant **Psychiatric illness and psychological problems** (CS vs CT): 1) Perceived Stress Scale: 12.6 ± 8.8 vs 9.0 ± 3.4, t = -1.01,p= NS. 2) SF-36 General Health Perceptions Index: 84.4 ± 9.3 vs 91.0 ± 8.5, t = 1.42, p=NS. **Cognitive function**: 1) Subjective alertness noon: 75.88 ± 4.62 vs 88.34 ± 4.69, p=0.08; evening: 74.32 ± 3.96 vs 83.04 ± 4.29, p=0.16; night: 43.47 ± 5.35 vs 45.65 ± 3.87, p=0.74. 2) Energy evening: 72.17 ± 4.26 vs 84.08 ± 5.21; p=0.098; night: 51.40 ± 5.77 vs 55.28 ± 4.50, p=0.60. 3) Concentration noon: 69.96 ± 6.67 vs 83.17 ± 5.42, p=0.15; evening: 70.20 ± 5.53 vs 81.67 ± 5.50, p=0.16. **Mood** (CS vs CT, mean ± SE) noon: 77.43 ± 3.83 vs 86.99 ± 3.75, p=0.10; evening: 77.02 ± 4.30 vs 86.16 ± 3.43, p=0.12; night: 74.11 ± 4.86 vs 83.25 ± 3.95, p=0.17.

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Lichstein, KL / 2001 Moderate (5/9)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control Over 58 yrs 58 (CS) primary 23 (CS) secondary 35 (CT) 24 (CS) primary 23 (CS) secondary 23 (CT) NS 189 total 82 (CS) primary 46 (CS) secondary 61 (CT) NS	**Co-Morbidity**: Among secondary insomnia: Depression (n = 13), Anxiety (n = 8), Chronic pain (n = 10), Prostate disease (n = 7), Neurological disorders (n = 5), Respiratory disease (n = 3). **Associated Factors**: Significant **Psychiatric illness and psychological problems**: (primary insomnia vs secondary insomnia vs CT; mean ± SD): 1) Self-reported anxiety (State-Trait Anxiety Inventory -Form Y Trait Scale (STAI): 33.6 ± 7.7 (p<0.001) vs 40.9 ± 12.1 (p<0.001) vs 29.8 ± 7.1; 2) Depression (Geriatric Depression Scale (GDS): 5.4 ± 4.3 (p<0.001) vs 11.6 ± 7.9 (p<0.001) vs 3.1 ± 3.7. **Quality of life**: 1) Mental health (SF-36 Mental health subscale: 80.7 ± 14.0 vs 56.0 ± 21.0 (p<0.001) vs 90.1 ± 26.5; 2) Physical functioning (SF-36 Physical functioning subscale: 78.1 ± 18.5 vs 52.4 ± 24.3 (p<0.001) vs 77.7 ± 21.7. Non-significant **Age**: 68.1 ± 7.0 vs 68.4 ± 6.4 vs 71.4 ± 6. **Socioeconomic status**: Education years (primary insomnia 14.7 ± 3.0 vs CTs 15.0 ± 2.2). **Gender**: 70%; 95%CI: 60-80 vs 57%; 95%CI: 36-64 vs 57%; 95%CI: 45-69; all reported NS.

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Linzmayer, L / 2002 Low (1/9)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 22-63 yrs 51.1%, 93/182 (CS) 52.2%, 131/251 (CT) 48.9%, 89/182 (CS) 47.8%, 120/251 (CT) NS 433 total 182 (CS), 251 (CT) NS	**Co-Morbidity**: **Group A**: nonorganic insomnia (psychophysiological insomnia in ICSD' primary insomnia in DSM-IV) (N = 8 CS, 32 CT). **Group B**: bipolar affective disorder (N = 16 CS, 32 CT). **Group C**: depressive episode (N = 13 CS, 26 CT). **Group D**: recurrent depressive disorder (N = 31 CS, 31 CT). **Group E**: dysthymia (N = 30 CS, 30 CT). **Group F**: generalized anxiety disorder (N = 41 CS, 41 CT). **Group G**: mixed anxiety and depressive disorder (N = 16 CS, 27 CT). **Group H**: adjustment disorders (N = 16 CS, 32 CT). **Associated Factors**: Significant **Cognitive function**: *Intelligence* (IQ): Group A: 100-112, Group B: 100-118, Group C: 100-118, Group D: 100-112, Group E: 100-112, Group F: 100-118, Group G: 100-107, Group H: 100-112). IQ not ascertained in controls. IQ surpassing normative values found in Groups B, C and F. **Memory**: 1) *Visual Memory*: differed significantly (>2 points) from age- and intelligence-dependent expected values only for Group F. 2) *Numerical Memory* (GVG): Group B (5.6 ± 1.7 vs 6.9 ± 1.6. p ≤ 0.05), Group C (4.9 ± 1.4 vs 6.4 ± 1.7, p ≤ 0.01), Group D (5.3 ± 1.5 vs 6.2 ± 1.8, p ≤ 0.05). 3) *Total Verbal Memory* (GVG) Group C (24.0 ± 6.3 vs 27.8 ± 6.4, p ≤ 0.05), Group D (25.3 ± 7.6 vs 28.7 ± 6.7, p ≤ 0.05). **Mood**: 1) *Thymopsychic Variables* (CS vs CT, mean ± SD): Drive: Group C (70.8 ± 22.3 vs 34.7 ± 27.0, p ≤ 0.01), Group D (51.4 ± 24.9 vs 24.4 ± 19.9, p ≤ 0.01); Group E (46.2 ± 21.5 vs 23.9 ± 20.9, p ≤ 0.01) 2) *Mood (VAS):* Group C (35.9 ± 18.1 vs 69.4 ± 25.1, p ≤ 0.01) Group D (47.4 ± 24.7 vs 75.0 ± 19.1, p ≤ 0.01), Group E (47.8 ± 18.0 vs 66.7 ± 22.7, p ≤ 0.01). 3) *Affectivity (VAS):* Group C (49.8 ± 28.4 vs 77.7 ± 19.8, p ≤ 0.01), Group D (57.9 ± 19.6 vs 83.5 ± 14.0, p ≤ 0.001), Group E (60.1 ± 14.9 vs 81.9 ± 18.8, p ≤ 0.01), Group G (69.0 ± 14.7 vs 77.8 ± 22.9, p ≤ 0.01). 4) *Wakefulness* (VAS): Group A (48.7 ± 21.0 vs 31.0 ± 21.9, p ≤ 0.05), Group C (73.5 ± 26.9 vs 32.3 ± 26.7, p ≤ 0.01), Group D (54.3 ± 30.0 vs 22.2 ± 19.9, p ≤ 0.01), Group E (55.9 ± 28.4 vs 28.4 ± 25.6, p ≤ 0.01), Group G (46.1 ± 30.2 vs 29.0 ± 25.8, p ≤ 0.05), Group H (43.1 ± 26.9 vs 25.2 ± 25.0, p ≤ 0.05). 5) *Well-being* (Bf): Group B (24.3 ± 14.5 vs 9.8 ± 8.3, p ≤ 0.01), Group C (32.5 ± 13.6 vs 12.6 ± 10.4, p ≤ 0.01), Group D (29.1 ± 11.6 vs 9.9 ± 8.1, p ≤ 0.01), Group E (24.0 ± 10.5 vs 13.6 ± 10.5, p ≤ 0.01), Group G (20.5 ± 12.0 vs 13.0 ± 12.1, p ≤ 0.01), Group H (19.1 ± 7.1 vs 14.0 ± 11.5, p ≤ 0.05). 6) *State Anxiety*: Group B (49.3 ± 13.9 vs 35.7 ± 7.1, p ≤ 0.01), Group C (54.3 ± 13.8 vs 37.0 ± 9.3, p ≤ 0.01), Group D (51.2 ± 12.1 vs 33.6 ± 5.8, p ≤ 0.01), Group E (45.5 ± 9.9 vs 38.9 ± 8.7, p ≤ 0.05), Group G (45.1 ± 8.4 vs 35.5 ± 8.5, p ≤ 0.01). 7) *Trait Anxiety:* Group B (58.5 ± 6.7 vs 34.6 ± 9.2, p ≤ 0.01), Group C (53.5 ± 11.2 vs 38.6 ± 12.3, p ≤ 0.01), Group D (55.3 ± 10.7 vs 34.7 ± 8.2, p ≤ 0.01), Group E (50.4 ± 9.0 vs 39.9 ± 12.0, p ≤ 0.01), Group G (49.6 ± 8.0 vs 37.7 ± 13.4, p ≤ 0.01). Non-significant **Cognitive function**: 1) *Intelligence* (IQ): Daytime Nonpsychic performance (cases vs controls, mean ± SD): 2) *General Verbal Memory*: Group A: (8.7 ± 1.9 vs 9.9 ± 2.1, p ≤ 0.10), Group B: (8.8 ± 1.5 vs 8.8 ± 2.5, p=NS), Group C: (7.3 ± 2.8 vs 8.4 ± 2.6, p=NS), Group D: (7.9 ± 2.4 vs 8.5 ± 2.6, p=NS), Group E: 8.3 ± 2.2 vs 8.4 ± 2.6, p=NS), Group F: (9.0 ± 2.2 vs 8.5 ± 2.7, p=NS), Group G: 7.6 ± 2.7 vs 8.5 2.5, p ≤0.10), Group H: (8.1 ± 1.3 vs 8.0 ± 2.6, p=NS). 3) *Associative verbal memory* (Gruenberger Verbal Memory): Memory Test: Group A (14.9 ± 2.7 vs 16.2 ± 3.2, p ≤ 0.10), Group B (13.5 ± 3.2 vs 14.4 ± 4.1, p=NS), Group C (11.9 ± 3.8 vs 13.2 ± 4.3, p=NS), Group D (12.1 ± 5.1 vs 14.1 ± 4.3, p=NS), Group E (12.9 ± 3.8 vs 14.2 ± 4.0, p=NS), Group F (15.1 ± 3.6 vs 13.5 ± 4.3, p ≤ 0.10), Group G (11.9 ± 5.2 vs 14.1 ± 4.3, p ≤ 0.10), Group H (12.6 ± 5.0 vs 14.0 ± 4.3, p=NS). 4) *Numerical Memory* (GVG): Group A (6.1 ± 2.2 vs 6.1 ± 1.9, p=NS), Group E (6.2 ± 2.0 vs 6.2 ± 1.9, p=NS), Group F (6.0 ± 2.0 vs 6.1 ± 1.9, p=NS), Group G (6.2 ± 1.7 vs 6.4 ± 1.7, p=NS), Group H (5.8 ± 1.5 vs 6.4 ± 1.6, p=NS),5) *Total Verbal Memory* (GVG): Group A (29.8 ± 5.6 vs 32.8 ± 5.1, p ≤ 0.10), Group B (27.9 ± 4.3 vs 30.0 ± 6.3, p=NS), Group E (27.4 ± 6.0 vs 28.5 ± 6.5, p=NS), Group F (30.1 ± 6.2 vs 28.3 ± 7.0, p=NS), Group G (25.7 ± 8.3 vs 28.9 ± 6.5, p ≤ 0.10), Group H (26.5 ± 6.0 vs 28.4 ± 6.9, p ≤ 0.10). **Mood**: 1)*Thymopsychic Variables* (cases vs controls, mean ± SD): 1) Drive (VAS): Group A (43.9 ± 11.9 vs 35.0 ± 24.8, p ≤ 0.10), Group B (41.1 ± 31.5 vs 26.7 ± 21.2, p=NS), Group F (23.8 ± 17.4 vs 29.1 ± 23.4, p=NS), Group G (36.0 ± 25.7 vs 31.6 ± 26.3, p=NS), Group H (30.4 ± 19.5 vs 25.6 ± 24.4, p=NS). 2) *Mood (VAS):* Group A (66.3 ± 17.0 vs 71.3 ± 18.5. p=NS), Group B (59.3 ± 29.3 vs 73.1 ± 21.0, p=NS), Group F (69.1 ± 17.7 vs 67.4 ± 23.3, p=NS), Group G (73.5 ± 10.8 vs 71.6 ± 24.5, p=NS), Group H (71.3 ± 20.5 vs 67.3 ± 26.2, p=NS). 3) *Affectivity (VAS):* Group A (61.9 ± 23.0 vs 76.1 ± 19.1, p ≤ 0.10), Group B (64.3 ± 27.2 vs 78.8 ± 18.4, p ≤ 0.10), Group F (77.8 ± 16.6 vs 77.7 ± 19.9, p=NS), Group H (77.7 ± 15.4 vs 77.1 ± 22.7, p=NS). 4) *Wakefulness* (VAS): Group B (46.4 ± 34.8 vs 25.0 ± 21.4, p ≤ 0.10), Group F (41.5 ± 28.5 vs 29.6 ± 25.7, p ≤ 0.10). 5) *Well-being* (Bf): Group A (13.7 ± 5.8 vs 11.1 ± 9.2, p ≤ 0.10), Group F (15.4 ± 10.6 vs 13.4 ± 11.2, p=NS). 6) *State Anxiety*: Group A (33.4 ± 7.2 vs 37.2 ± 7.1, p ≤ 0.10), Group F (40.7 ± 12.6 vs 37.5 ± 8.5, p=NS), Group H (42.0 ± 13.1 vs 36.0 ± 7.9, p ≤ 0.10). 6) *Trait Anxiety:* Group A (32.5 ± 5.8 vs 36.9 ± 10.4, p=NS), Group F (41.8 ± 11.2 vs 37.9 ± 10.2, p ≤ 0.10), Group H (42.9 ± 9.4 vs 39.3 ± 12.5, p ≤ 0.10).

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Lundh, LG / 1997 Moderate (5/9)	**Study Design**: **Age Group** mean ± SD: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 20-65 yrs 46.5 ± 11.3 (CS) 45.5 ± 11.1 (CT) 16 (CS) 16 (CT) 4 (CS) 4 (CT) NS 40 total 20 (CS), 20 (CT) NS	**Associated Factors**: Significant **Psychiatric illness and psychological problems**: (CS vs CT; mean scores): 1) Depression (Beck Depression Inventory scores; 8.5 vs 3.7; p<0.01). **Memory and cognitive function**: 1) Verbal ability (WAIS-R vocabulary scores; 46.9 vs 55.8; p<0.05). 2) Cued recall (Emotional Stroop test scores: 0.37 vs 0.47; p<0.005). Non-significant **Psychiatric illness and psychological problems**: (CS vs CT; mean scores): Spielberger Trait State Anxiety Inventory: 36.5 vs 35.4; p=NS.

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Martikainen, K / 2003 Moderate (5/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional 41-55 yrs 57.8%, 362/626 42.2%, 264/626 NS 1190 52.6%, 626/1190	**Prevalence**: **Three-month prevalence**: 14% (88/626) 95%CI: 11.3-16%. **Male**: 9.8% (26/264) 95%CI: 6.2-13.3%. **Female**: 17.0% (62/362) 95%CI: 13.1-20.8%. **Associated Factors**: Significant (CS vs CT) **Age:** (> 55 yrs): p<0.01. **Psychiatric illness and psychological problems**: 1) Depression: adj OR: 2.78; 95%CI: 1.22-6.33; p=0.023. 2) Nervousness and tension: adj OR: 3.05; 95%CI: 1.66-5.63; p<0.001. **Medical conditions**: 1) Fatigue: adj OR: 2.24; 95%CI: 1.22-4.12; p<0.001, 2) Hypertension: adj OR: 2.05; 95%CI: 1.10-3.82; p=0.026. 3) Heart conditions (arrhythmias, heart failure): 14 vs 4%, p=<0.001. 4) Allergic rhinitis: 18.6%; p=0.006. **Socio-economic status**: 1) Poorer job: adj OR: 6.10; 95%CI: 1.82-20.5; p<0.001; Unemployed: 83.9 vs 91.7%; p=0.019. **Healthcare utilization**: Hospital treatment: 42.5 vs 27.1%; p=0.003 **Other factors**: 1) Moving house: adj OR: 0.19; 95%CI: 0.04-0.83; p=0.003. 2) Insomniacs less often current smokers: 8 vs 17.1%; p=0.032; 3) Insomniacs less caffeine/day (mean cups coffee): 4.16 vs 4.76; p=0.014. Non-significant **Other factors**: Marital status, BMI, Exercise, Snoring, Alcohol consumption all reported p=NS. **Medical conditions**: Heart conditions (Angina, myocardial or brain infarction) p=NS

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Mendelson, WB / 1984 Moderate (4/9)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 22-44 yrs 9 (CS), 9 (CT) 1 (CS), 1 (CT) NS 20 total 10 (CS), 10 (CT) NS	**Associated Factors**: Significant **Psychiatric illness and psychological problems**: (CS vs CT; mean scores ± SD): 1) Depression (MMPI Depression scale: 62.0 ± 9.3 vs 49.0 ± 6.5; p<0.009). 2) Social introversion (MMPI Social introversion scale: 56.3 ± 11.2 vs 44.7 ± 6.2; p<0.009). **Memory and cognitive function**: (CS vs CT; number of responses ± SD): 1) Long-term semantic/knowledge memory (per time of day) (11 am: 10.4 ± 3.3 vs 12.9 ± 3.6. 2 pm: 11.3 ± 3.9 vs 13.8 ± 2.7. 5 pm: 10.6 ± 3.6 vs 13.3 ± 3.3. 8 pm: 11.3 ± 3.3 vs 13.9 ± 3.3). Non-significant **Psychiatric illness and psychological problems**: (CS vs CT; mean scores ± SD): MMPI subscales L, HS, HY, PD, MF, PA, PT, SC, MA all p=NS. **Psychomotor functioning:** On 12 tasks no significant differences. **Cognitive Function**: Attention, Vigilance, Learning and Memory no significant difference.

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Millar, A / 2004 High (6/9)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 26-68 yrs (CS) 27-67 yrs (CT) 11 (CS), 11 (CT) 8 (CS), 8 (CT) NS 51 total 32 (CS), 19 (CT) Follow-up rate: 59.3%, 19/32 (CS) NS (CT)	**Prevalence**: Percentage of reported longstanding sleep disturbances (Sleep History Questionnaire): **Cases**: 100% (19/19). **Controls**: 21% (4/19) (95%CI: 2.7-39.3). No data by gender.

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Niemcewicz, S / 2001 Low (2/9)	**Study Design**: **Age Group** mean ± SD: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Case-control 21-55 yrs 40.8 ± 11.3 56%, 9/16 (CS) 56%, 9/16 (CT) 44%, 7/16 (CS) 44%, 7/16 (CT) NS 32 total 16 (CS), 16 (CT) 100%	**Associated Factors**: Significant **Psychiatric illness and psychological problems**: (MMPI scale, CS vs CT, mean ± SD): 1) Hypochondria (55.93 ± 8.94 vs 49.00 ± 6.65, t = -2.489, df = 30, p = 0.019). 2) Depression (57.31 ± 10.44 vs 45.53 ± 7.79, t = -3.645, df = .0, p = 0.001). 3) Hysteria (58.62 ± 8.77 vs 50.50 ± 6.34, t = -3.001, df = 30, p = 0.005). 4) Psychasthenia (51.18 ± 9.23 vs 42.50 ± 5.86, t = -2.999, df = 30, p = 0.005). 5) Hamilton score (6.4 ± 2.4 vs 0.5 ± 1.0, U = 2.5, p<0.001). 6) Beck score (6.8 ± 4.6 vs 2.2 ± 3.6, U = 42.5, p = 0.001). 6) Hyperarousal score (65.0 ± 7.54 vs 55.12 ± 8.74, U = 49.0, p = 0.003). **Memory**: (CS vs CT, mean ± SD: 1) (Selective Reminding Test) # of presentations needed to memorize all items (10.06 ± 4.31 vs 6.56 ± 2.25, U = 68.5, p=0.02). 2) Reaction time (514.60 ± 69.24 msec vs 577.44 ± 78.25 msec, U=65.0, p = 0.02). Non-significant **Memory:** 1) False target detections (Continuous Attention Test) (2.81 ± 3.10 vs 2.16 ± 4.19, U=80.5, p=0.07).

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Ohayon, MM / 2003 High (7/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional Over 15 yrs 52.1% 7771/14,915 47.9% 7144/14,915 NS 18,972 78.6%, 14,915/18,972	**Prevalence**: **Point prevalence**: (Chl > 6 mo): 17.6% (2625/14,915), 95%CI: 16.9-18.21. **Male**: 13.5% (965/7144), 95%CI: 12.71-14.29. **Female**: 22.3% (1733/7771), 95%CI: 21.38-23.22. (Insomnia ≥ month): 18.4% (2744/14,915), 95%CI: 17.78-19.02. **Associated Factors**: Significant **Psychiatric illness and psychological problems**: 1) Previous psychiatry hx: adj OR: 5.8; 95%CI: 2.4-14.0. Non-significant None reported

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Ohayon, MM / 2002A High (8/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional Over 15 yrs 51.8%, 2055/3470 48.2%, 1916/3470 NS 4442 89.4%, 3970/4442	**Prevalence**: **One-year prevalence** (Insomnia symptoms): 27.6% (1096/3970) (95%CI: 26.2-28.9). **Male**: 24.5% (469/1916) (95%CI: 22.5-26.4). **Female**: 30.5% (627/2055) (95%CI: 28.5-32.4). (Insomnia disorder diagnoses): 7% (278/3970) (95%CI: 6.2-7.7). **Male**: 4.2% (80/1916) (95%CI: 3.3-5.1). **Female**: 9.2% (189/2055) (95%CI: 8.0-10.4). **Associated Factors**: Significant **Gender** (DSM-IV insomnia diagnoses): 1) Gender: OR: 9.2; 95%CI: 8.0-10.4; p<0.001. Non-significant **Healthcare utilization**: (95%CI not reported) 1) Use of sleep-enhancing medication (Having one insomnia symptom: OR: 2.2; Having two insomnia symptoms: OR: 3.4; Having three or four insomnia symptoms: OR: 2.9. **Other factors**: (Risk factors for sleep dissatisfaction) Marital status, BMI, MSK disease, heart disease, hypertension, snoring, daily stress level all p=NS

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Ohayon, MM / 2002B High (8/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional Over 18 yrs 51.8%, 509/982 48.2%, 473/982 NS 1256 78.2%, 982/1256	**Prevalence**: **Point prevalence**: Insomnia disorder diagnoses: 11.7% (115/982). No prevalence data by gender.

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Ohayon, MM / 2002C High (8/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional 15-90 yrs 50.5%, 1877/3719 49.5%, 1842/3719 NS 4067 91.4%, 3719/4067	**Prevalence**: **Point prevalence**: 5% (186/3719) (95%CI: 4.3, 5.7). **Associated Factors**: Significant **Age**: Elderly (>65yr) 8.2% (26/314) vs other age groups (4.2 to 5%), p<0.05. Non-significant **Gender**: Male 4.7% (87/1842) vs Female 5.1% (96/1877), OR = 0.92 (0.68, 1.24).

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Ohayon, MM / 2001A High (7/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional 19-24 yrs 50.5%, 731/1447 49.5%, 716/1447 NS 1447 NS	**Co-Morbidity**: **Psychiatric illness and psychological problems**: 12.6% (182/1447) had ICDS dyssomnia or sleep disturbances associated with a mental disorder. **Prevalence**: **Point prevalence**: 8.1% (117/1447) (95%CI: 7.4, 8.8).

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Ohayon, MM / 2001B High (8/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional Over 15 yrs 51%, 12665/24600 49%, 11936/24600 NS 24,600 total (France=5622, UK=4972, Germany=4115, Italy=3970, Portugal=1856) 81.0% overall (Germany=68.1, all others over 80%)	**Prevalence**: **Point prevalence**: 6.1% (1,501/24,600) (95%CI: 5.8, 6.4).

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Ohayon, MM / 2001C High (8/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional Over 15 yrs 52.1%, 6791/13,057 47.9%, 6266/13,057 NS 16,738 78%, 13,057/16,738	**Prevalence**: No prevalence estimates for DSM-IV insomnia disorder overall. Data for each insomnia symptom: 1) Difficulties initiating sleep: 13.11% (1712/13,057) 95%CI: 12.6-13.6%, 2) Disrupted sleep: 21.3% (2792/13,057) 95%CI: 20.6-22%, 3) Early morning awakenings: 13.1% (1712/13,057) 95%CI: 12.6-13.6%, 4) Nonrestorative sleep: 14.4 (1890/13,057) 95%CI: 13.8-15% (data extracted from graphs). No prevalence data by gender. **Associated Factors**: Significant ***For difficulties initiating sleep***: **Gender**: 1) Female (adj OR: 1.4; 95%CI: 1.2-1.6; p<0.001). **Medical conditions**: 1) Physical illness (adj OR: 1.9; 95%CI: 1.7-2.2; p<0.001). **Psychiatric illness and psychological problems**: 1) Mental disorder (adj OR: 3.5; 95%CI: 3.1-4.1; p<0.001). **Quality of life**: Satisfaction with life (adj OR: 0.4; 95%CI: 0.2-0.7; p<0.01). ***For disrupted sleep***: **Gender**: 1) Female (adj OR: 1.3; 95%CI: 1.2-1.5; p<0.001). **Psychiatric illness and psychological factors**: 1) Mental disorder (adj OR: 3.0; 95%CI: 2.6-3.4; p<0.001). **Quality of life**: Satisfaction with life (adj OR: 0.4; 95%CI: 0.2-0.7; p<0.01). ***For early morning awakening***: **Gender**: 1) Female (adj OR: 1.3; 95%CI: 1.1-1.4; p<0.001). **Medical conditions**: 1) Physical illness (adj OR: 1.6; 95%CI: 1.4-1.8; p<0.001). ***For nonrestorative sleep***: **Gender**: 1) Female (adj OR: 1.3; 95%CI: 1.1-1.4; p<0.001). Medical conditions: 1) Physical illness (adj OR: 1.9; 95%CI: 1.6-2.2; p<0.001). **Psychiatric illness and psychological factors**: 1) Mental disorder (adj OR: 3.6; 95%CI: 3.2-4.2; p<0.001). **Quality of life**: Satisfaction with life (adj OR: 0.4; 95%CI: 0.2-0.9; p<0.01). Non-significant None reported

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Ohayon, MM / 2000 High (7/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional 19 - 24 yrs 50.8%, 1102/2169 49.2%, 1067/2169 NS 2169 NS	**Co-Morbidity**: Psychiatric disorders: 1) adjustment disorders (20, 0.9%, 95%CI: 0.5-1.3), 2) anxiety disorders (163, 7.5%, 95%CI: 6.4-8.6): 2a) panic disorder (37, 1.7%, 95%CI: 1.2-2.2), 2b) generalized anxiety (24, 1.1%, 95%CI: 0.7-1.5), 2c) obsessive-compulsive disorder (11, 0.5%, 95%CI: 0.2-0.8), 2d) posttraumatic stress disorder (30, 1.4%, 95%CI: 0.9-1.9), 2e) social phobia (20, 0.9%, 95%CI: 0.5-1.3), 2f) specific phobia (46, 2.1%, 95%CI: 1.5-2.7), 2g) agoraphobia (9, 0.4%, 95%CI: 0.1-0.7), 3) depressive disorders (52, 2.4%, 95%CI: 1.8-3.0). **Prevalence**: **Point prevalence**: 5.4% (117/2169), 95%CI: 4.5, 6.4.

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Ohayon, MM / 1999 Moderate (5/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional Over 15 yrs 55.5%, 6555/11,810 44.5%, 5255/11,810 NS 11,810 NS	**Prevalence**: **Point prevalence**: (Complaint of insomnia symptoms accompanied with sleep dissatisfaction): 16.0% (1890/11,810, 95%CI: 15.3--16.7. No prevalence data by gender.

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Ohayon, MM / 1997 High (8/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional Over 15 yrs 52.1%, 2929/5622 47.9%, 2693/5622 NS 6966 80.7%, 5622/6966	**Prevalence**: **Point prevalence**: (Insomnia complaints lasting for at least 1 month): 15.3% (860/5622) (95%CI: 14.36-16.24).

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Pallesen, S / 2002 High (7/9)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 60-84 yrs (CS) 63-83 yrs (CT) - Gs 60-86 yrs (CT) - Com 49 (CS), 32 (CT) - Gs 41 (CT) - Com 11 (CS), 9 (CT) - Gs 19 (CT) - Com NS 187 total 60 (CS), 41 (CT) - Gs, 60 (CT) - Com NS (CS), NS (CT) - Gs, 82.6% (CT) - Com	**Associated Factors**: Significant **Psychiatric illness and psychological problems**: (CS vs GS vs CT; mean ± SD): 1) Sleep impairment (Sleep Impairment Index scale: 23.1 ± 4.8 vs 10.1 ± 2.7 vs 14.6 ± 6.0; F(1,96) = 237.6), 2) Somatization (Symptom Checklist 90-Revised: CS vs GS: 0.78 ± 0.59 vs 0.32 ± 0.28 F(1, 97) = 20.3), 3) Obsessive-compulsive traits (Symptom Checklist 90-Revised: CS vs GS: 0.95 ± 0.80 vs 0.44 ± 0.31; F(1, 95) = 14.0), 4) Interpersonal sensitivity (Symptom Checklist 90-Revised: CS vs GS): 0.56 ± 0.58 vs 0.25 ± 0.28; F(1, 97) = 9.4), 5) Depression (Symptom Checklist 90-Revised: CS vs GS): 0.74 ± 0.56 vs 0.37 ± 0.26; F(1, 95) = 14.7), 6) Anxiety (Symptom Checklist 90-Revised: CS vs GS): 0.46 ± 0.47 vs 0.09 ± 0.12; F(1, 96) = 22.6), 7) Hostility (Symptom Checklist 90-Revised: CS vs GS): 0.32 ± 0.33 vs 0.11 ± 0.16; F(1, 96) = 12.4), 8) Phobic anxiety (Symptom Checklist 90-Revised: CS vs GS): 0.17 ± 0.27 vs 0.03 ± 0.07; F(1, 97) = 10.4). 9) Mental health global measures (GSI CS vs GS: 0.61 ± 0.39 vs 0.23 ± 0.15; F(1, 92) = 31.0; Positive Symptom Distress Index: 1.75 ± 0.49 vs 1.21 ± 0.20; F(1, 92) = 39.6; Positive Symptom Total: 31.4 ± 16.8 vs 16.6 ± 9.6; F(1, 99) = 25.8; PSWQ: 44.8 ± 10.9 vs 35.7 ± 8.0; F(1, 92) = 18.8, TAS-20: 49.8 ± 9.4 vs 42.6 ± 8.8; F(1, 91) = 14.2) 10) Difficulties identifying feelings (TAS-20 subscale CS vs GS: 15.2 ± 5.8 vs 11.4 ± 4.3; F (1, 93) = 11.7). **Socioeconomic status:** Education: CS vs GS (p=0.001) vs community controls (p=0.26). Non-significant **Age:** CS vs GS (p=0.48) vs CT (p=0.23). **Gender:** CS vs GS (p=0.65) vs community controls (p=0.09). **Psychiatric illness and psychological problems**: (CS vs GS vs CT; mean ± SD): 1) Paranoid ideation: 0.35 ± 0.49 vs 0.13 ± 0.18 vs .033 ± 0.41; F=NS; 2) Psychoticism: 0.21 ± 0.27 vs 0.09 ± 0.14 vs 0.19 ± 0.26; p=NS; 3) Difficulty describing feelings: 13.1 ± 3.4 vs 11.8 ± 3.7 vs 12.6 ± 3.9; p=NS; 4) Externally oriented thinking: 21.2 ± 4.1 vs 19.3 ± 4.7 vs 21.0 ± 4.3; p=NS; 5) # life events: 3.5 ± 3.36 vs 3.1 ± 1.7 vs 4.55 ± 4.21; p=NS; 6) Subjective impact Life events: 8.52 ± 9.44 vs 7.31 ± 5.32 vs 10.7 ± 10.8; p=NS.

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Pavlova, M / 2001 Moderate (4/9)	**Study Design**: **Age Group** mean ± SD: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 45.9 ± 14 yrs (CS) 44.6 ± 15 yrs (CT) NS NS NS 532 total 256 (CS), 139 (CT) NS	**Associated Factors**: Significant **Psychiatric illness and psychological problems**: (CS vs CT; mean scores for scales/subscales ± SD): 1) Introspectiveness (Introspectiveness score from the Hyperarousal scale): 40.5 ± 0.3 vs 37.1 ±0.4; p<0.002. **Memory and cognitive function**: (CS vs CT) 1) Hyperarousal (Hyperarousal scale mean total score ± SD, 95%CI: 41.1 ± 10.2 (95%CI: 39.9-42.3) vs 32.6 ± 7.3 (95%CI: 31.4-33.8); p<0.0001). 2) Reaction type (Median React score from the Hyperarousal scale ± range: 4.5 (6-23) vs 2 (0-12). Non-significant None reported

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Perlis, ML / 2001 Moderate (5/9)	**Study Design**: **Age Group** mean ± SD: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 30.6 ± 8.9 yrs (CS) 32.3 ± 11.5 yrs (CT) 3 (CS), 2 (CT) 2 (CS), 2 (CT) NS 9 total 5 (CS), 4 (CT) NS	**Associated Factors**: Significant **Memory**: (CT vs CS, mean ± SD): 1) First trial: 46.2 ± 12.6 vs 75.8 ± 12.7, p=0.01. Non-significant **Memory**: (CT vs CS, mean ± SD): 1) number of words encoded (43 ± 20.0 vs 49 ± 18.3, p=0.61), 2) recognition (false-positive %) (8.9 ± 7.2 vs 20 ± 19.1, p=0.27), 3) free recall (all trials, %) (4.6 ± 3.2 vs 9.8 ± 10.7, p=0.35), 4) recognition: all trials (%) (45.2 ± 11.8 vs 68.6 ± 19.9, p=0.08), Second trial (42.0 ± 17.6 vs 58.0 ± 38.1, p=0.55), Third trial (42.5 ± 26.9 vs 59.7 ± 25.5, p=0.38), Fourth trial (51.6 ± 8.6 vs 59.3 ± 29.9, p=0.69), 5) Recognition speed (true-positive, msec) (2753 ± 820 vs 2137 ± 761, p=0.29), 6) Recognition speed (false-positive, msec) (3358 ± 510 vs 2664 ± 903, p=0.19), 7) Speed (false/true-positive) (1.259 ± 0.20 vs 1.261 ± 0.17, p = 0.99).

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Riedel, BW / 2004 High (6/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional 20-98 yrs 50.7%, 390/769 49.3%, 379/769 53.6%, 536/769 (White) 28.6%, 220/769 (Black) 0.7%, 6/769 (Asian) 10.8%, 7/769 (NS) 1769 43.4%, 769/1769	**Prevalence**: **Point prevalence**: 32.1% (247/769) (95%CI: 28.8-35.3). No prevalence data by gender. **Associated Factors**: Significant (3 groups: Nonsmokers, Light smokers (<15/day) Heavier smoker (≥15/day). **Race/ethnicity:** (non-smoker vs <15/day vs ≥15/day) p<0.01. **Psychiatric illness and psychological problems**: 1) Depression (Beck depression inventory OR: 2.03, 95%CI: 1.45-2.83), 2) Anxiety (Trait Anxiety Inventory OR: 8.45, 95%CI: 3.21-22.28; p<0.05). **Other factors:** 1) Heavy smoking among females (OR: 2.31; p<0.05), 2) Light smoking (adj OR: 2.75; 95%CI: 1.17-6.49; p<0.05). **Medical conditions**: 1) Physical health problems (Cancer OR: 2.45; 95%CI: 1.14-5.27; p<0.05), 2) High blood pressure (OR: 1.53, 95%CI: 1.11-2.69; p<0.05), 3) Breathing problems (OR: 3.01, 95%CI: 1.68-5.40; p<0.05), 4) Gastrointestinal problems (OR: 2.00, 95%CI: 1.22-3.28; p<0.05). Non-significant None reported

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Robbins, L / 1995 Moderate (4/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Retrospective cross-sectional 18-60 yrs 79.6%, 393/494 20.4%, 101/494 NS 494 100%	**Co-Morbidity**: Migraines. **Prevalence**: Sleep onset insomnia: 27% (133/494), 95%CI: 23.1-30.9. Difficulty maintaining sleep insomnia: 26% (128/494), 95%CI: 22.1-29.9.

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Rocha, FL / 2002A High (7/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional Over 60 yrs 61.1%, 926/1516 38.9%, 590/1516 NS 1742 87%, 1516/1742	**Prevalence**: **One-month prevalence**: (Insomnia): 38.9% (590/1516), 95%CI: 34.6-41.3. **Male**: 28.8% (170/590), 95%CI: 25.1-32.4. **Female**: 45.3% (419/916), 95%CI: 42.0-48.5. **Associated Factors**: Significant **Gender**: 1) Female (adj OR: 1.78; 95%CI: 1.41-2.24). **Medical condition**: 1) Self-rated reasonable (adj OR: 2.02; 95%CI: 1.50-2.72) and very bad health (adj OR: 3.12; 95%CI: 2.21-4.39), 2) History of previous medical diagnosis of a chronic condition (adj OR: 1.38; 95%CI: 1.10-1.73), 3) Inability to perform routine activities due to a health problems in the last 2 weeks (adj OR: 1.54; 95%CI: 1.10-2.15). **Other factors**: 1) Staying in bed in the last 2 weeks (adj OR: 1.61; 95%CI: 1.04-2.48), 2) Dissatisfaction with free time arrangements (adj OR: 1.88; 95%CI: 1.28-2.77). **Healthcare utilization**: 1) Use of sleeping pills: OR: 1.74 (95%CI: 1.38-2.21). **Social Relationships:** Social support Unsatisfied OR 1.88; (95%CI: 1.28-2.77). Non-significant **Age**: 60-69yr: 60.9 vs 59.2%, OR 1; 70-79yr: 29.1 vs 30.6% OR 0.92; 95%CI: 0.73-1.16); ≥80yrs: 10.0 vs 10.1%, OR 0.96; 95%CI: 0.68-1.37. **Social Relationships:** 1) Married/live together vs single: OR 1.05; 95%CI: 0.73-1.53. 2) Social support Indifferent OR 0.95; 95%CI: 0.62-1.43.

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Rocha, FL / 2002B High (7/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional Over 18 yrs 55.7%, 594/1066 44.3%, 472/1066 53.6%, 572/1066 (White) 2.4%, 26/1066 (Black) 43.8%, 467/1066 (Other) 0.2%, 1/1066 (Unknown) 1221 87.3%, 1066/1221	**Prevalence**: **One-month prevalence**: 35.4% (377/1066), 95%CI: 32.5-38.3. **Male**: 20.7% (98/472), 95%CI: 17.0-24.3. **Female**: 46.9% (279/594), 95%CI: 42.9-50.9. **Associated Factors**: Significant **Socioeconomic status**: 1) Low education: (1-3 years): males adj OR: 2.2; 95%CI: 1.1-4.1; females adj OR: 1.8; 95%CI: 1.1-3.0; no years of education: females adj OR: 2.6; 95%CI: 1.3-5.1. **Age**: 1) Age group over 60 years (females) adj OR: 1.8; 95%CI: 1.1-3.3. **Healthcare utilization**: 1) Use of sleeping pills in the previous 30 days: OR: 3.5; 95%CI: 2.4-4.9. Non-significant **Race/Ethnicity: white vs other:** p=0.751. **Relationships:** Religion: p=0.35

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Roth, T / 1999 Moderate (3/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional 18-65 yrs NS NS 86%, 860/1000 (White) 8%, 80/1000 (Black) 3%, 30/1000 (Hispanic) 3%, 30/1000 (Other) 1950 51.2%, 1000/1950	**Associated Factors**: Significant **Memory and cognitive function**: 1) Impaired concentration (ChI vs non-insomnia); "little trouble": 68% vs 93%; p=0.01). 2) Difficulties remembering things; "very often or sometimes": 53% vs 29%; p=0.0). **Social relationships**: 1) Ability to enjoy relationships; "good or excellent": 64% vs 89%; p=0.01. 2) Relationships with spouse; "good or excellent": 70% vs 81%; p=0.01. Medical condition 1) Self-perceived health; "good or excellent": 53% vs 86%; p=0.01. **Psychiatric illness and psychological problems**: Ability to handle minor irritations; "good or excellent": 57% vs 81%; p = 0.0). Non-significant **Accidents**: (Had an automobile accident due to being tired; ChI vs non-insomnia): 5% vs 2% (p=NS). **Quality of life**: (ChI vs non-insomnia; "good or excellent": 70% vs 96%; p = NS). **Psychiatric illness and psychological problems**: 1) Self-perceived mental health; "good or excellent": 67% vs 90%; p=NS).

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Sabbatini, M / 2002 Moderate (3/8)	**Study Design**: **Age Group** mean ± SD: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional 61.0 ± 14.4 yrs 44.5%, 309/694 55.5%, 385/694 NS 694 NS	**Co-Morbidity**: Medically Ill (Renal disorders). **Prevalence**: **Point prevalence**: 45% (311/694), 95%CI: 41.3-48.7. **Male**: 40.5% (156/385), 95%CI: 35.6-45.4. **Female**: 50.1% (155/309), 95%CI: 44.5-55.6. **Associated Factors**: Significant **Psychiatric illness and psychological problems**: (insomnia vs non-insomnia): 1) Anxiety (45% vs 33.2%; p<0.04). **Medical conditions**: 1) Longer time on dialysis (13-48 months adj OR: 1.7; 95%CI: 1.1-2.8; p=0.03; 49-84 months adj OR: 1.8; 95%CI: 1.2-2.8; p=0.006; ≥ 85 months adj OR: 1.7; 95%CI: 1.2-2.7; p=0.01), 2) Having dialysis in the morning (adj OR: 1.6; 95%CI: 1.2-2.2; p=0.003), 3) High levels of parathyroid hormone (> 149 pg/ml) (adj OR: 1.5; 95%CI: 1.0-2.2; p=0.05). 4) Pruritus (% insomnia vs non-insomnia; 19.9% vs 13.1%; p<0.04). Non-significant **Other factors:** BMI, Blood pressure, Smoking, Alcohol, Caffeine intake all p=NS

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Saletu-Zyhlarz, G / 1997 Low (1/9)	**Study Design**: **Age Group**: mean ± SD: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 24-65 yrs 43.2 ± 11.7 yrs (CS) 43.0 ± 11.7 yrs (CT) 56.8%, 25/44 (CS) 54.5%, 24/44 (CT) 43.2%, 19/44 (CS) 45.5%, 20/44 (CT) NS 88 total 44 (CS), 44 (CT) 100%, 44/44 (CS) 77.3%, 34/44 (CT)	**Co-Morbidity**: **Cases**: all CS have generalized anxiety disorder (GAD). **Controls**: normal. **Associated Factors**: Significant **Psychiatric illness and psychological problems**: Mood: (CS vs CT, median, mean ± SD): 1) Evening well-being score (18, 19 ± 12 vs 7, 11 ± 10, p<0.01), 2) Morning well-being score (16, 18 ± 12 vs 7, 11 ± 10, p<0.05), 3) Drive (mm) (51, 50 ± 26 vs 37, 38 ± 25, p<0.05), 4) Mood (mm) (63, 62 ± 18 vs 74, 75 ± 17, p<0.01), 5) Drowsiness (mm) (59, 58 ± 27 vs 45, 42 ± 26, p<0.01). **Cognitive function**: (psychometry) (cases vs controls, median, mean ± SD): 1) Fine-motor activity, right (37, 37 ± 11 vs 52, 49 ± 9, p , 0.01), 2) Fine-motor activity, left (27, 28 ± 9 vs 41, 40 ± 11, p<0.01), 3) Fine-motor activity, right + left (65, 66 ± 18 vs 91, 86 ± 17, p , 0.01), 4) Reaction time (mean score) (534, 545 ± 108 vs 473, 478 ± 113, p , 0.01). Non-significant **Psychiatric illness and psychological problems**: Mood**:** Affectivity (mm) (68, 63 ± 23 vs 71, 71 ± 21, p=NS). **Cognitive function**: (psychometry) (CS vs CT, median, mean ± SD): 1) Attention score (522, 536 ± 145 vs 520, 519 ± 145, p=NS), 2) Concentration (% errors) (3, 4 ± 3 vs 3, 5 ± 5, p=NS), 3) Attention variability score (15, 16 ± 9 vs 15, 15 ± 5, p=NS), 4) Numerical memory (6, 6 ± 2 vs 6, 6 ± 2, p=NS 5) Reaction time, variability (mean score) (109, 107 ± 30 vs 105, 97 ± 37, p=NS), 6) Reaction time, errors of omission (n) (1, 2 ± 2 vs 1, 3 ± 3, p=NS), 7) Reaction time, errors of omission (n) (0, 0 ± 1 vs 0, 0 ± 1, p=NS).

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Savard, J / 2001 Moderate (4/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional 28-90 yrs 339 0 All White (Caucasian) 339 88%, 300/339	**Co-Morbidity**: Medically ill (Metastatic breast cancer). **Prevalence**: **Point prevalence**: (Insomnia symptoms): 51.3% (154/300) (95%CI: 45.7-56.9); (Insomnia syndrome): 19% (56/300) (95%CI: 14.6-23.4); (Chronic Insomnia syndrome): 17.6% (53/300) (95%CI: 13.3-21.9). **Associated Factors**: Significant ***For insomnia symptoms***: **Medical conditions**: 1) Cancer stage at diagnosis (I-III) (OR: 0.46; 95%CI: 0.24-0.88; p<0.05), 2) Lumpectomy (OR: 5.2; 95%CI: 1.5-18.1; p<0.01), 3) Chemotherapy (OR: 4.3; 95%CI: 1.7-10.7; p<0.01). **Social Relationships**: 1) Widowhood (OR: 4.7; 95%CI: 1.5-15.2; p<0.01). **Other factors**: 1) Antecedents of insomnia symptoms (OR: 0.18; 95%CI: 0.06-0.52; p<0.01). ***For insomnia syndrome***: **Socioeconomic factors**: **Socioeconomic status**: 1) University degree (OR: 4.0; 95%CI: 1.1-15.0; p<0.05). **Social Relationships**: Separated/divorced (OR: 4.2; 95%CI: 1.4-13.1; p<0.05). 3) Widowhood (OR: 0.08; 95%CI: 0.01-0.64; p<0.05). **Direct and indirect costs**: 1) Sick leave: (OR: 14.1; 95%CI: 1.1-173.8; p<0.05), 2) Unemployment (OR: 3.8; 95%CI: 1.1-13.6; p<0.05). Non-significant None reported

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Schneider-Helmert, D / 1987 High (7/9)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 32-61 yrs (CS) 28-61 yrs (CT) 9 (CS), 9 (CT) 7 (CS), 7 (CT) NS 32 total 16 (CS), 16 (CT) NS	**Associated Factors**: Significant **Psychiatric illness and psychological problems**: (CS vs CT; mean scores ± SD): 1) Personality patterns (MMPI): Hypochondriasis: 62.3 ± 9.5 vs 48.1 ± 7.2,; p<0.00001; Depression: 64.0 ± 12.7 vs 45.9 ± 7.5, p<0.00001; Hysteria: 65.3 ± 7.6 vs 52.7 ± 9.2, 0.0001; Psychopatic deviate: 62.9 ± 9.2 vs 49.2 ± 7.4, p<0.0001; Paranoia: 61.3 ± 12.6 vs 49.3 ± 11.1, p<0.01; Psychasthenia: 47.3 ± 8.2 vs 62.0 ± 9.6, p<0.0001; Schizophrenia: 60.6 ± 11.0 vs 49.1 ± 7.1; p<0.005; Ego strength: 44.4 ± 12.5 vs 56.5 ± 5.1, p<0.001; Impulsivity: 52.8 ± 8.8 vs 45.6 ± 5.6, p<0.01; Control: 54.8 ± 9.7 ± 44.1 ± 12.3; Anxiety: 57.3 ± 11.6 vs 45.2 ± 9.9, 0.005; Internalization: 55.2 ± 10.1 vs 48.8 ± 7.6, p<0.05. **Cognitive function**: 1) Auditory function: 7.9 vs 10.5, p<=0.001; 2) Line judgment all sessions p =0.01; 3) Line tracing (3 errors) 20.3 vs 13.6, p=0.005. Non-significant **Psychiatric illness and psychological problems**: (CS vs CT; mean scores ± SD): 1) Scale L: 49.6 ± 8.1 vs50.3 ± 10.4; 2) Scale K: 50.8 ± 8.3 vs 54.6 ±8.1; 3) Masculinity-femininity: 45.5 ± 10.3 vs 48.3 ± 11.0; 4) Hypomania: 46.8 ± 13.3 vs 42.1 ± 12.3; 5) Social introversion: 56.9 ± 12.2 vs 52.3 ± 12.3. All p=NS. **Cognitive function**: (3 sessions @ 0945, 1245, & 1500) # correct responses: Logical reasoning, Addition, Digit symbol substitution, Word detection, Visual Search All p=NS.

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Seidel, WF / 1984 High (6/9)	**Study Design**: **Age Group** mean ± SD: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 29 ± 5 yrs 23 (CS), 23 (CT) 15 (CS), 15 (CT) NS 76 total 38 (CS), 38 (CT) NS	**Associated Factors**: Significant Laboratory measures (CS vs CT; mean min. ± SD): 1) Objective total sleep time: 402.8 ± 50.5 vs 445.8 ± 42.4, p<0.001; 2) Subjective total sleep time: 352.2 ± 94.9 vs 441.2 ± 44.7, p<0.001. Non-significant **Psychiatric illness and psychological problems:** 1) Profile of mood state (POMS): *Fatigue:* 6.6 ± 6.2 vs 3.9 ± 4.5; *Depression*: 2.3 ± 3.6 vs 1.2 ± 1.9; *Anger/hostility:* 3.2 ± 5.9 vs 1.2 ± 2.2; *Tension/anxiety:*1.1 ± 3.8 vs -0.7 ± 2.8; *Vigor:* 9.5 ± 6.5 vs 11.7 ± 7.8; *Total mood disturbance*: 5.2 ± 19.3 vs -5.9 ± 16.9; all p=NS. 2) MMPI scale: *Scale L:* 48.1 ± 7.8 vs 45.5 ± 5.7; *Scale F:* 56.5 ± 8.7 vs 53.8 ± 10.2; *Scale K:* 54.3 ± 8.1 vs 56.5 ± 8.8; *Hypochondriasis:* 53.3 ± 7.6 vs 47.8 ± 9.2; *Depression:* 56.8 ± 9.8 vs 53.0 ± 8.1; *Hysteria:* 59.2 ± 7.2 vs 55.5 ± 8.5; *Psychopathic deviate:* 61.1 ± 8.0 vs 59.7 ± 8.8; *Paranoia:* 61.1 ± 6.7 vs 57.7 ± 6.8; *Psychasthenia:* 59.9 ± 7.7 vs 55.1 ± 6.8; *Schizophrenia:* 57.4 ± 7.4 vs 58.1 ± 8.7; *Hypomania*: 65.2 ± 10.7 vs 61.6 ± 11.1. All p=NS.

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Sharpley, AL / 1997 Moderate (5/9)	**Study Design**: **Age Group** (mean, range) **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 54.7, 40-69 yrs (CS) 53.9, 40-68 yrs (CT) 50% (CS), 50% (CT) 50% (CS), 50% (CT) NS 40 total 20 (CS), 20 (CT) 100% in both groups	**Associated Factors**: Significant **Psychiatric illness and psychological problems**: (CS vs CT): 1) Past psychiatric disorder 45% (9/20) vs 10% (2/20), P<0.01; OR = 7.36, 95%CI: 1.34, 40.55, 2) Major depression 35% (7/20) vs 5% (1/20), p<0.01, 3) Past alcohol dependence 20% (4/20) vs 0, p<0.05,. Non-significant **Psychiatric illness and psychological problems**: (CS vs CT): 1) Panic disorder 5% (1/20) vs 0, p=NS; 2) Eating disorder 5% (1/20) vs 0, p=NS; 3) Past alcohol abuse 5% (1/20) vs 5% (1/20), p=NS; 4) Past drug dependence 5% (1/20) vs), p=NS.

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Shaver, JLF / 2002 High (6/9)	**Study Design**: **Age Group**: mean ± SD: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control PP-type: 46.7±3.3 yrs (CS) SO-type: 46.1±4.4 yrs (CS) 44.4±3.5 yrs (CT) 131 0 ***Cases***: PP-type: White 76.2%, African American 9.5%, unknown 14.3%. ***Cases***: SO-Type: White 72.2%, Asian/Pacific Islander 5.6%, African American 11.1%, Native American 5.6%, unknown 5.6%. ***Controls***: White 92.9%, Asian/Pacific Islander 7.1% 101 (CS), 30 (CT) NS	**<u>Associated Factors</u>**: Significant **Psychiatric illness and psychological problems:** Psychological Distress Scores (PP-type vs SO-type insomnia vs CT, mean ± SD): 1) Somatization: 0.65 ± 0.61 vs 0.54 ± 0.47 vs 0.27 ± 0.31, p = 0.03; 2) Global severity: 0.60 ± 0.64 vs 0.50 ± 0.38 vs 0.28 ± 0.28, p = 0.04, 3) Positive symptom distress: 1.6 ± 0.40 vs 1.4 ± 0.20 vs 1.1 ± 0.40, p = 0.01. Non-significant **Psychiatric illness and psychological problems**: Stress Exposure (PP-type vs SO-type insomnia vs CT, mean ± SD): 1) Daily diary: the sum of items, how stressful: (a) felt today, (b) relationship with closest friends, (c) family life, (d) work; rated 1 = not at all to 6 = very much (2.4 ± 0.6 vs 2.4 ± 0.5 vs 2.2 ± 0.76, p=NS), 2) Daily hassles, Daily Hassles and Uplifts Scale: Number (23.9 ± 15.1 vs 19.8 ± 13.9 vs 16.7 ± 15, p=NS), Severity (29.6 ± 26.2 vs 28 ± 22.4 vs 20.3 ± 23.1, p=NS), Index of Severity (1.1 ± 0.32 vs 0.89 ± 0.47 vs 0.95 ± 0.32, p=NS). 3) Stressful life events, Stressful Life Events Questionnaire: Positive (4.8 ± 3.1 vs 4.6 ± 3.4 vs 6.2 ± 3.2, p=NS), Negative: (5.3 ± 3.9 vs 5.2 ± 4.8 vs 4.8 ± 3.9, p=NS), 4) Small life events, Inventory of Small Life Events: Positive (27.9 ± 10 vs 27.6 ± 8.9 vs 30.2 ± 7.9, p=NS), Negative: (11.8 ± 7.4 vs 10.6 ± 7.3 vs 12.1 ± 6.0, p=NS). Psychological Distress Scores 1) Obsessive compulsive (0.78 ± 0.85 vs 0.64 ± 0.57 vs 0.44 ± 0.59, p = 0.24), 2) Interpersonal sensitivity (0.67 ± 0.64 vs 0.46 ± 0.43 vs 0.42 ± 0.54, p = 0.21), 3) Depression (0.79 ± 0.83 vs 0.69 ± 0.63 vs 0.42 ± 0.37, p = 0.26), 4) Anxiety (0.47 ± 0.76 vs 0.39 ± 0.39 vs 0.16 ± 0.24, p = 0.11), 5) Hostility (0.38 ± 0.67 vs 0.32 ± 0.43 vs 0.27 ± 0.32, p = 0.98), 6) Psychoticism (0.31 ± 0.63 vs 0.25 ± 0.29 vs 0.07 ± 0.11, p = 0.10), 7) Phobic anxiety (0.21 ± 0.58 vs 0.12 ± 0.20 vs 0.06 ± 0.13, p = 0.52), 8) Paranoid ideation (0.43 ± 0.61 vs 0.37 ± 0.45 vs 0.29 ± 0.32, p = 0.85), 9) Positive symptom total (31.7 ± 20.8 vs 30.1 ± 17.7 vs 19.1 ± 16.7, p = 0.10. PP-type = psychophysiologic type insomnia; SO-type = subjective only type insomnia;

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Shochat, T / 1999 Low (1/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional 18-87 yrs 58%, 166/286 42%, 120/286 White 52%, Asian 28%, African-American 2.8%, Hispanic 4.5%, Other 12.2% 286 NS	**Prevalence**: **Point prevalence**: 19% (54/286) (95%CI: 14.5, 23.5). **Associated Factors**: Significant For all factors (GS vs occasional insomniac vs ChI). **Psychiatric illness and psychological problems**: Mood: 1) General mood Excellent p<0.0010 (25.3% (22/88) vs 11.3% (16/141) vs 11.3% (6/54)) Good (62.1% (55/88) vs 57.4% (81/141) vs 49.1% (27/54) Fair (10.3% (9/88) vs 24.8% (35/141) vs 35.8% (19/54) Poor (1.1% (1/88) vs 6.4% (9/141) vs 3.8% (3/54). 2) Ability to handle minor irritations p = 0.0060 Excellent (15.9% (14/88) vs 9.3% (13/141) vs 11.3% (6/54)) Good (58.0% (51/88) vs 43.6% (61/141) vs 45.3% (24/54)) Fair (21.6% (19/88) vs 36.4% (51/141) vs 30.2% (16/54)) Poor (2.3% (2/88) vs 10.7% (15/141) vs 13.2% (7/54). **Cognitive function**: 1) Ability to concentrate p = 0.0010 Excellent (19.3% (17/88) vs 9.3% (13/141) vs 13.2% (7/54) Good (68.2% (60/88) vs 57.9% (82/141) vs 52.8% (29/54) Fair (11.4% (10/88) vs 30.0% (42/141) vs 30.2% (16/54) Poor (1.1% (1/88) vs 2.1% (3/141) vs 3.8% (2/54). **Memory**: 1) Having trouble remembering p = 0.0370 Very often (4.5% (4/88) vs 9.3% (13/141) vs 11.1% (6/54) Sometimes (34.1% (30/88) vs 43.6 (61/141) vs 50.0% (71/141) Not very often (45.5% (40/88) vs 37.9% (53/141) vs 20.4% (11/54) Never (13.6% (12/88) vs 7.9% (11/141) vs 16.7% (9/54). **Social relationships**: 1) Personal relationship with spouse p = 0.0030 Excellent (44.9% (40/88) vs 26.3% (37/141) vs 23.8% (13/54) Good (38.5% (34/88) vs 43.2% (61/141) vs 40.5% (22/54) Fair (14.1% (12/88) vs 18.6% (26/141) vs 28.6% (15/54) Poor (2.6% (2/88) vs 11.9% (17/141) vs 7.1% (4/54). 2) Ability to enjoy family/social life p = 0.0050 Excellent (29.5% (26/88) vs 16.3% (23/141) vs 17.0% (9/54)) Good 48.9% (43/88) vs 48.2% (68/141) vs 35.8% (19/54)) Fair (14.5% (13/88) vs 27.7% (39/141) vs 34.0% (18/54)) Poor (4.8% (4/88) vs 7.8% (11/141) vs 13.2% (7/54). **Quality of life**: 1) General quality of life p = 0.0060 Excellent (18.2% (16/88) vs 10.7% (15/141) vs 9.6% (5/54)) Good (67.0% (59/88) vs 61.4% (87/141) vs 51.9% (28/54)) fair (11.4% (10/88) vs 25.7% (36/141) vs 34.6% (19/54)) Poor (2.3% (2/88) vs 0.7% (1/141) vs 1.9% (1/54)). **Work performance**: 1) Ability to accomplish things during the day p<0.0010 Excellent (29.5% (26/88) vs 15.7% (22/141) vs 11.3% (6/54)) Good (59.1% (52/88) vs 53.6% (75/141) vs 56.6% (31/54)) Fair (6.8% (6/88) vs 27.1% (38/141) vs 22.6% (12/54)) Poor (3.4% (3/88) vs 3.6% (5/141) vs 7.5% (4/54)). Non-significant None reported

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Sugerman, JL / 1985 High (6/9)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 21-55 yrs 6 (CS)-objective 6 (CS)-subjective, 6 (CT) 2 (CS)-objective 2 (CS)-subjective, 2 (CT) NS 24 total 16 (CS), 8 (CT) NS	**Associated Factors**: Significant **Memory and cognitive function**: (Objective vs Subjective insomnia vs CT): 1) Waking function (Auditory Vigilance Task number of misses: 7.73 vs 29.95 vs 6.68, p<0.05). Non-significant None reported

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Taylor, DJ / 2003 High (6/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional 20-98 yrs 50.6%, 391/772 49.4%, 381/772 Caucasians 69.8% (539/772), African Americans 28.9% (223/772), Asian 0.9% (7/772), Hispanic 0.1% (1/772) 1769 49%, 859/1,769	**Prevalence**: **Prevalence parameters**: 19.6% (151/772), 95%CI: 16.8, 22.4. **Associated Factors**: Significant **Age**: (no insomnia vs insomnia, mean ± SD): 50.41 ± 19.1 vs 61.49 ± 19.68, F = 35.73, p<0.001. **Gender**: (no insomnia vs insomnia, % female): 45.3 (174/384) vs 60.0 (90/150), p<0.01, OR = 0.55 (0.38, 0.81. **Medical conditions**: (% no insomnia vs % insomnia): 1) Heart 9.1 (35/384) vs 23.3 (35/150), F = 19.15, p<0.001, OR = 0.32 (0.20, 0.55), 2) Cancer 4.2 (16/384) vs 9.3 (14/150), F = 5.43, p<0.05, OR = 0.42 (0.20, 0.89), 3) HTN 18.2 (70/384) vs 44 (66/150), F = 37.74, p<0.001, OR = 0.28 (0.19, 0.43), 4) Neurological 1.3 (5/384), vs 7.3 (11/150), F = 13.50, p<0.001, OR = 0.17 (0.06, 0.49), 5) Respiratory 5.7 (22/384) vs 24.7 (37/150), F = 39.36, p<0.001, OR = 0.19 (0.11, 0.33), 6) Urinary 9.6 (37/384) vs 18 (27/150),). **Race/Ethnicity**: (no insomnia vs insomnia, % African American): 25 (96/384) vs 28 (42/150), p=NS, OR = 0.86 (0.56, 1.31). F== 7.154, p<0.01, OR = 0.49 (0.28, 0.83), 7) Diabetes 3.6 (14/384) vs 12.7 (19/150), F = 15.14, p<0.001, OR = 0.26 (0.13, 0.54), 8) Pain 19 (73/384) vs 48 (72/150), F = 45.83, p<0.001, OR = 0.25 (0.17, 0.38), 9) Gastrointestinal 9.4 (36/384) vs 32.7 (49/150), F = 43.77, p<0.001, OR = 0.21 (0.13, 0.35). **Healthcare Utilization**: 1) Number of medications 1.68 ± 1.93 vs 3.44 ± 2.79, F = 68.20, p<0.001.2) Psychiatric Conditions: Beck Depression Inventory 5.72 ± 5.37 vs 13.08 ± 8.93 (means adjusted for ethnicity and gender: 6.63 ± 7.19 vs 12.42 ± 6.79, p<0.001, adjusted for neurological problems, PLMD/RLS and cigarette use, OR = 8.96 (3.97, 20.19, p<0.001, reference group people with insomnia). Psychological Conditions: 33.14 ± 9.33 vs 42.26 ± 11.70, p<0.001. Non-significant **Race/Ethnicity**: (no insomnia vs insomnia, % African American): 25 (96/384) vs 28 (42/150), p=NS, OR = 0.86 (0.56, 1.31). **Other factors:** Alcohol (drinks/wk): 2.74 ±5.19 vs 2.0 ± 4.93, p=NS; Caffeine drinks/day: 2.36 ± 2.46 vs 2.21 ± 2.67, p=NS. Smoking and BMI p=NS.

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Terzano, MG / 2004 Moderate (4/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional > 18 yrs 60.9% 39.1% NS 3284 NS	**Co-morbidity**: **Medically ill**: [1) Cardiovascular (1149; 35%), 2) MSK and connective (921; 28%), 3) Digestive (624; 19%), 4) Endocrine, nutritional, metabolic, immunity (556, 16.9%), 5) Brain, nervous system and sense organs (495, 15.1%), 6) Respiratory (460, 14%), 7) Genitourinary (362, 11%), 8) Infectious and parasitic (74, 2.3%), 9) Other (1008, 30.7%)]. **Prevalence**: **Point prevalence** (Sleep difficulties ≥ one month): 63.7% (2093/3284) (95%CI: 62-65). **Male**: 59.6% (766/1284) (95%CI: 56.9-62.2). **Female**: 66.3% (1327/2000) (95%CI: 64.2-68.3). **Associated Factors**: Significant **Age**: Older (adj OR: 1.02; 95%CI: 1.02-1.03). **Gender**: 1) Female (adj OR: 1.19; 95%CI: 1.01-1.40). **Psychiatric illness and psychological problems**: 1) Depression (adj OR: 2.70; 95%CI: 2.31-3.15). **Medical condition**: 1) Involvement of > 1 organ system (adj OR: 1.24; 95%CI: 1.06-1.48). **Socioeconomic status**: 1) < junior high (adj OR: 1.18; 95%CI: 1.00-1.40). **Healthcare utilization**: 1) Use of prescribed drugs (OR: 2.26; 95%CI: 1.95-2.62), 2) > 1 hospitalization (OR: 1.61; 95%CI: 1.11-2.32), 3) > 1 GP home visit (OR: 2.31; 95%CI: 1.30-4.09), 4) > 1 GP office visit (OR: 1.81; 95%CI: 1.56-2.10), 5) > 1 call to a GP (OR: 1.48; 95%CI: 1.27-1.73), 6) > 1 laboratory test (OR: 1.43; 95%CI: 1.23-1.65), 7) > 1 drug prescription (OR: 1.81; 95%CI: 1.56-2.09). **Quality of life**: 1) SF-36 mean scores ± SD); No insomnia vs Level I vs Level II insomnia; (data extracted from graphs): Physical functioning (90.01 vs 81.11 vs 79.34), Role limitations physical (82.3 vs 76.0 vs 63.3), Bodily pain (74.4 vs 69.8 vs 61.8), Health perception (69.8 vs 61.6 vs 55.9), Energy/fatigue (64.7 vs 62.3 vs 50.0), Social functioning (81.4 vs 78.1 vs 64.0), Role limitations emotional (83.9 vs 78.5 vs 56.7), Mental health (71.6 vs 67.7 vs 52.7)). **Work Performance:** Direct and indirect costs: 1) > 1 sick leave day (OR: 1.54; 95%CI: 1.17-2.01; N = 1389 employed patients). Non-significant **Other factors:** BMI, Smoking, and Caffeine intake p=NS.

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Vgontzas, AN / 1995 Low (2/9)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 18-86 yrs (CS) 16-80 yrs (CT) 50.1%, 188/375 (CS) 58.7%, 88/150 (CT) 49.9%, 187/375 (CS) 41.3%, 62/150 (CT) NS 525 total 375 (CS), 150 (CT) NS	**Co-Morbidity**: Psychiatric illness in cases recruited from the sleep clinic: 98.3% (172/175) had at least one psychiatric illness as a secondary disorder: 1) depression 58.3% (102/175): 1a) major depression 10.3% (18/175), 1b) dysthymia 36.6% (64/175), 1c) other minor depression (atypical depression) 10.9% (19/175), 1d) bipolar disorder 5.7% (1/175). **Associated Factors**: Non-Significant **Medical conditions**: (CS vs CT) 1) sleep apnea 2.3% 8/375) vs 1.3% (2/150), OR = 1.61 (0.34, 7.69), 2) sleep apneic activity 13.9% (52/375) vs 14.7% (22/150), OR = 0.94 (0.55, 1.61), 3) nocturnal myoclonus/nocturnal myoclonic activity 11.5% (43/375) vs 8.5% (11/150), OR = 1.63 (0.82, 3.27).

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Vignola, A / 2000 Moderate (5/9)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control Over 55 yrs 10-ChI/BNZ (CS) 11-drug-free ChI (CS) 9 (CT) 10-ChI/BNZ (CS) 9-drug-free ChI (CS) 11 (CT) NS 60 total 20 – ChI/BNZ (CS), 20 drug-free ChI (CS), 20 (CT) NS	**Associated Factors**: Significant **Psychiatric illness and psychological problems**: (drug-free ChI vs insomnia using benzodiazepines vs CT; mean ± SD): 1) Depression (Beck Depression Inventory): 9.00 ± 4.48 vs 9.40 ± 7.16 vs 1.75 ± 1.6, p<0.01. 2) Anxiety (Beck Anxiety Inventory): 9.10 ± 8.38 vs 8.60 ± 5.4 vs 1.20 ± 1.47, p<0.01. 3) Global security (Brief symptom inventor): 0.57 ± 0.35 vs 0.62 ± 0.42 vs 0.13 ± 0.15, p<0.01. 4) Subjective measures related to neuropsychological performance (Visual Analogue Scale-VAS for Energy): 49.80 ± 19.35 vs 46.10 ± 23.23 vs 24.25 ± 12.23, p<0.01. VAS for Mood: 35.63 ± 16.99 vs 38.85 ± 20.94 vs 15.75 ± 9.94, p<0.01. VAS for Tiredness: 51.50 ± 20.77 vs 47.70 ± 17.14 vs 21.55 ± 11.16, p<0.01. VAS for Stress/Tension: 38.50 ± 18.70 vs 39.60 ± 17.90 vs 16.85 ± 8.77, p<0.01. VAS for Motivation: 68.60 ± 20.24 vs 80.60 ± 20.38 vs 84.80 ± 15.7, p<0.05. **Memory and cognitive function**: 1) Attention and concentration (Digit Span Forward (percentiles): 33.60 ± 27.23 vs 41.80 ± 28.89 vs 63.95 ± 25.64, p< 0.01; Digit Span Backward (percentiles): 42.55 ± 30.60 vs 45.80 ± 21.43 vs 65.45 ± 23.32, p<0.05. 2) Subjective measures related to neuropsychological performance (Visual Analogue Scale-VAS for alertness: 44.20 ± 22.52 (p<0.01) vs 37.55 ± 22.72 (p<0.05) vs 21.55 ± 13.01, VAS for performance expectancy: 57.85 ± 17.22 (p<0.01) vs 73.55 ± 16.98 vs 83.90 ± 12.78, VAS for Performance: 61.40 ± 13.95 (p<0.05) vs 61.75 ± 12.58 (p<0.05) vs 71.07 ± 13.56). Non-significant **Memory and cognitive function:** 1) Mini-mental state: 29.1 ± 1.12 vs 28.75 ± 1.25 vs 28.85 ± 1.04. 2) Vocabulary: 17.9 ± 3.84 vs 12.0 ± 3.09 vs 13.3 ± 2.36. 3) Information: 10.15 ± 3.51 vs 10.0 ± 3.01 vs 11.5 ± 3.4, all p=NS. No difference on visual and verbal memory, p>0.19; psychomotor speed, p> 0.23; and executive functions, p>0.9.

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Vincent, NK / 2000 Moderate (4/9)	**Study Design**: **Age Group** mean ± SD: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 46.91±10.04 yrs (CS) 39.6 ±11.49 yrs (CT) 72%,23/32 (CS), NS(CT) 28%, 9/32 (CS), NS (CT) 30/32 Caucasian (CS) 58 total 32 (CS), 26 (CT) NS	**Co-Morbidity**: **Cases**: 39% (12/32) had at least one secondary co-morbidity: generalized anxiety disorder (34%), social phobia (16%), hypochondriasis (3%), obsessive-compulsive disorder (3%), and major depression (3%). **Controls**: normal. **Associated Factors**: Significant **Psychiatric illness and psychological problems**: Perfectionism variables (CS vs CT, mean score ± SD): 1) Doubts about action: 10.38 ± 3.59 vs 7.46 ± 2.47, t = 3.52, p = 0.001; 2) Parental criticism: 9.44 ± 4.49 vs 6.50 ± 2.32, t = 3.21, p = 0.002; 3) Concern over mistake: 20.97 ± 7.29 vs 16.11 ± 5.38, t = 2.83, p = 0.007; 4) Socially prescribed: 49.82 ± 10.95 vs 42.23 ± 13.92, t = 2.35, p = 0.02. Non-significant 1) Personal standards: 21.94 ± 4.87 vs 20.42 ± 5.08, t = 1.16, p = 0.25; 2) Parental expectations: 12.31 ± 4.61 vs 11.46 ± 3.74, t = 0.76, p = 0.45. 3) Self-oriented; 64.24 ± 18.23 vs 58.38 ± 14.51;T = 1.34, P=0.36; 4) Other-oriented: 54.76 ± 9.52 vs 54.23 ± 13.08, t = 0.17, p = 0.86.
AUTHOR / YEAR QUALITY (score)	**STUDY DESIGN & POPULATION CHARACTERISTICS**		**CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS**
Wang, W / 2001 Moderate (4/9)	**Study Design**: **Age Group** mean ± SD: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 30.2 ± 7.0 yrs (CS) 27.2 ± 5.0 yrs (CT) 12 (CS), 19 (CT) 11 (CS), 9 (CT) NS 51 total 23 (CS), 28 (CT) 100%, 23/23 (CS) 89.2%, 25/28 (CT)	**Associated Factors**: Significant **Psychiatric illness and psychological problems**: (CS vs CT; mean ± SD): 1) Thrill and adventure seeking behaviour (Zuckerman's sensation seeking scales): 4.0 ± 2.4 vs 6.4 ± 2.5; p<0.05; 2) Impulsivity (Zuckerman-Kuhlman's personality questionnaire): 4.0 ± 1.9 vs 2.7 ± 1.6; p<0.05; 3) Neuroticism-anxiety (Zuckerman-Kuhlman's personality questionnaire: 11.7 ± 4.6 vs 7.3 ± 2.8; p<0.05). Non-significant **Psychiatric illness and psychological problems**: Zuckerman's sensation seeking scales (CS vs CT; mean ± SD): 1) Experience seeking: 3.1 ± 1.7 vs 4.0 ± 1.9; 2) Disinhibition: 2.9 ± 2.1 vs 2.8 ± 1.8; 3) Boredom susceptibility: 2.5 ± 1.7 vs 1.5 ± 1.5. 4) Impulsive sensation seeking (Zuckerman-Kuhlman's personality questionnaire): 8.8 ± 3.2 vs 8.2 ± 3.0; 5) General sensation seeking: 4.8 ± 2.3 vs 5.5 ± 2.1; 6) Aggression-hostility: 7.8 ± 3.7 vs 6.3 ± 2.7; 7) Activity 7.6 ± 3.4 vs 8.7 ± 2.7; 8) Sociability: 7.3 ± 3.8 vs 7.3 ± 2.4. All p=NS.
AUTHOR / YEAR QUALITY (score)	**STUDY DESIGN & POPULATION CHARACTERISTICS**		**CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS**
Yeo, BKL / 1996 Moderate (3/8)	**Study Design**: **Age Group**: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional 15-55 yrs 50%, 1209/2418 50%, 1209/2418 All Asian (Chinese and Malays) 2418 NR	**Prevalence**: **One-year prevalence**: 15.3% (370/2418) (95%CI: 13.8-16.73). **Male**: 12.9% (159/1209) (95%CI: 11.02-14.78). **Female**: 17.5% (211/1209) (95%CI: 15.36-19.64). **Associated Factors**: Significant **Gender**: 1) Female (OR: 1.39; 95%CI: 1.11- 1.74; p<0.01). **Race/ethnicity**: 1) Malay vs Chinese (OR: 1.37; 95%CI: 1.06-1.75; p<0.05). **Psychiatric illness and psychological problems**: 1) Moderate to severe stress (OR: 2.01; 95%CI: 1.56-2.58; p<0.001), 2) Phobic disorder (Insomnia vs Non insomnia; 20.5% vs 13.6%; p<0.001), 3) Major depression (19.7% vs 7.0%; p<0.001), 4) Anxiety disorder (6.5% vs 13.5%; p<0.001). Non-significant **Age**: % Insomniacs (15-29 vs 30-49 vs 50+) 40.8 vs 46.85 vs 12.4%, p=NS. **Psychiatric illness and psychological problems**: Source of stress – work and others (financial, travel etc) p=NS

Evidence Table C-1: Prevalence, natural history, incidence and associated factors of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	STUDY DESIGN & POPULATION CHARACTERISTICS		CO-MORBIDITY / PREVALENCE / NATURAL HISTORY / INCIDENCE / ASSOCIATED FACTORS
Zammit, GK / 1999 Moderate (4/9)	**Study Design**: **Age Group** mean ± SD: **Gender** Female: Male: **Ethnicity**: **Sample Size**: **Response Rate**:	Cross-sectional case-control 44.1±14.04 yrs (CS) 37.1±12.7 yrs (CT) 157 (CS), 63 (CT) 104 (CS), 38 (CT) NR 362 total 261 (CS), 101 (CT) NR	**Associated Factors**: Significant **Psychiatric illness and psychological problems**: 1) Depression (Zung Depression Scale: 2.22 ± 0.03 vs 1.53 ± 0.03; p<0.0001), 2) Anxiety (Zung Anxiety Scale: 1.96 ± 0.02 vs 1.4 ± 0.04; p<0.0001). **Quality of life**: (CS vs CT): 1) Overall quality of life (SF-36 overall: No scores provided. F-21.73; p<0.001). 2) Quality of life domains (SF-36 subscales: Body pain: 84.46 vs 62.80 (p<0.0001), General health: 84.00 vs 61.05 (p<0.0001), Mental health: 80.27 vs 55.69 (p<0.0001), Role emotional: 85.98 vs 48.82 (p<0.0001), Role physical: 94.48 vs 56.28 (p<0.0001), Social functioning: 88.65 vs 60.59 (p<0.0001), Vitality: 71.65 vs 41.13 (p<0.0001), Physical functioning: 93.31vs 77.82 (p<0.0001), 3) Number of hours watching TV (Quality of Life Inventory: 3.26 ± 0.15 vs 2.46 ± 0.24; p<0.006), 4) Hours reading per day (1.91 ± 0.11 vs 2.36 ± 0.17; p<0.03), 5) Hours of recreation per day (1.54 ± 0.11 vs 2.3 ± 0.18; p<0.0001). **Memory and cognitive function**: (CS vs CT; mean ± SD): 1) Cognitive functions (Medical Outcomes Study Cognitive scale sum scores; 25.34 ± 0.34 vs 31.91 ± 0.58; p<0.0001). **Work variables**: (CS vs CT): 1) Levels of optimism regarding career and future employment (Work and Daily Activities Questionnaire: 3.17 ± 0.11 vs 3.90 ± 0.18; p<0.0001). 2) Average # days absent from work / mo. (1.32 ± 0.15 vs 0.13 ± 0.22; p<0.001). Non-significant **Memory and cognitive function**: (Medical Outcomes Study Cognitive scale) Report no specific area of cognitive function significantly impaired.

Evidence Table C-1: References

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Evidence Table C-2: Efficacy and safety of treatments used in the management of chronic insomnia in adults

Abbreviations: **CBT** = cognitive behavioural therapy; **CT** = control; **d** = day; **f** = flunitrazepam; **GOV** = government; **hr** = hour; **min.** = minute; **mg** = milligrams; **NA** = not applicable; **NS** = not specified; **Pl** = placebo; **q** = quazepam; **RCT** = randomized controlled trial; **RT** = relaxation therapy; **SD** = standard deviation; **Tr** = treatment (drug): **wk** = week: **wks** = weeks; **yr(s)** = year(s).

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Aden, GC Moderate (2/5)	Private (funds and materials)	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 47 (NS) 23 – 59 29 / 21	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	quazepam 30 1 x night / 5 nights 30 min. before bed NS
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Allain, H / 2001 Moderate (3/5)	Private	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 45.6 (9.6) - Tr 46.7 (11.5) - Pl 25 – 64 188 / 57	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 6.7 (8.0) – Tr 6.6 (7.3) – Pl NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zolpidem 10 nightly x 2 nights, 2 tablets for rest of wk, final 3 wks as few as possible / 4 wks bedtime oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Allain, H / 1998 High (4/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 54.3 (11.0) 32 – 84 67.9% / 32.1%	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 19.5% < 1 yr 80.5% > 1 yr NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	triazolam, zolpidem 0.125; 10 1 x night / 4 nights bedtime oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Ascher, LM / 1979 Low (1/5)	NS	RCT Not reported as double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 39 (NS) 24 – 67 15 / 10	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 8 (NS) NS	**Type/Description**: **Frequency / Duration**:	paradoxical intention (CBT), Pl, CT 1 x wk / 4 wks
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Asnis, GM / 1999 Moderate (3/5)	Private	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 41.6 (1.2) Tr 41.6 (1.0) Pl 18 – 66 150 / 40	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	secondary various psychiatric conditions NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zolpidem 10 1 x night / 4 wks bedtime NS

Evidence Table C-2: Efficacy and safety of treatments used in the management of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Beary, MD / 1984 Moderate (3/5)	NS	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 NS 23 – 35 6 / 0	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS 0.3 – 2	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	temazepam 20 NS / NS 2230 hr oral

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Botter PA / 1983 High (4/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	Part 1: 44.3 (8) Tr 1mg 40.6 (7.7) Pl Part 2: 46.1 (7.2) Tr 2mg 44.8 (7.1) Pl NS 25 / 15	**Type**: **Co-morbidity**: **Duration (months)** Mean (SD): Range:	secondary anxiety neuroses Part 1: 1.3 (0.2) Tr 1mg 1.3 (0.2) Pl Part 2: 1.1 (0.2) Tr 2mg 1.1 (0.1) Pl NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	loprazolam 1, 2 NS / 7 nights 15 min. before bed oral

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Bowen, AJ / 1978 Moderate (3/5)	NS	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 NS 18 – 60 13 / 5	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	triazolam 0.5 NS / 2 nights NS NS

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Brown, CC / 1979 High (4/5)	NS	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 NS NS 18 / 0	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	l-tryptophan 1, 3 6 tablets for each 10 nights / 3 months 20 min. before bed oral

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Campbell, RD / 1987 High (4/5)	NS	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 38 (2) NS 25 / 31	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	flurazepam; zopiclone 30; 7.5 1 x d / 3 wks each Tr daily oral

Evidence Table C-2: Efficacy and safety of treatments used in the management of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Carr-Kaffashan, L / 1979 Moderate (2/5)	NS	RCT Not reported as double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 40.1 (NS) 18 – 76 18 / 12	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 11.48 (NS) NS	**Type/Description**: **Frequency / Duration**:	progressive relax-meditation (RT); quasi-desensitization (PI) 1 x wk / 4 wks

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Chaudoir, PJ / 1983 Moderate (3/5)	Private (pre-packed drugs)	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 50 (NS) 35 – 65 18 / 7	**Type**: **Co-morbidity**: **Duration:** Mean (SD): Range:	primary NA 6 months – Tr1 9 months – Tr2 NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zopiclone 7.5 1 x night / 7 nights NS oral

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Choliz, M / 1995 Moderate (2/5)	NS	RCT Not reported as double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 NS NS NS / NS	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Frequency / Duration**:	breathing process training (RT); CT 6 sessions in total / NS

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Cohn, JB / 1991 Moderate (3/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 NS 18 – 65 NS / NS	**Type**: **Co-morbidity**: **Duration**: Mean (SD): Range:	primary NA 3 months or more NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	estazolam; flurazepam 1, 2; 30 1 x night / 7 nights 30 min. before bed oral

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Cohn, JB / 1984 Moderate (3/5)	Private	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 41.4 (10.2) 18 – 61 18 / 12	**Type**: **Co-morbidity**: **Duration:** Mean (SD): Range:	primary various medical and psychiatric conditions 6 months or more (all but 1 patient) NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	triazolam; lorazepam 0.5; 2 NS / 4 d each Tr NS NS

Evidence Table C-2: Efficacy and safety of treatments used in the management of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Cohn, JB / 1983 High (4/5)	NS	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 41.5 (NS) 18 – 60 38 / 15	**Type**: **Co-morbidity**: **Duration** Mean (SD): Range:	secondary depression 1 month or more (all but 1 subject) NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	triazolam 0.25 2 x night / 4 night each Tr nightly oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Coxeter, PD / 2003 High (5/5)	NS	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 54 (15) 22 – 75 12 / 10	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	valerian 225 2 x night / 3 wks 30 min. before bed oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Davies, R / 1986 Moderate (2/5)	GOV	RCT Not reported as double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 58.59 (10.98) 35 – 78 16 / 18	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Frequency / Duration**:	immediate Tr (CBT); delayed Tr (Pl) 1 x wk / 4 wks
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Dawson, D / 1998 Moderate (2/5)	Private (supported research)	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 65.67 (1.68) NS NS / NS	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	melatonin 0.5 4 x wk / 1 wk 1900 hr patch placed on gums
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Declerk, A / 1999 Moderate (3/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 54 (NS) NS 17 / 5	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zolpidem 10 1 x day / 1 wk NS oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Dominguez, RA / 1986 Moderate (3/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 46.6 (NS) 21 – 65 46% / 54%	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	estazolam; flurazepam 2; 30 1 x night / 7 nights 30 min. before bed oral

Evidence Table C-2: Efficacy and safety of treatments used in the management of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Dominguez, RA / 1985 Moderate (3/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 NS 20 – 60 NS / NS	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	brotizolam 0.25 to 0.5 1 x night / 21 nights (option to double dose after 1 wk) bedtime oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Donath, F / 2000 Moderate (2/5)	Private	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 49 (NS) 22 – 55 12 / 4	**Type**: **Co-morbidity**: **Duration:** Mean (SD): Range:	primary NA 3 months to several yrs NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	valerian (short- and long-term) NS 2 x night / 15 night 1 hr before bed oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Drake, CL / 2000 High (4/5)	Private	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 41.6 (9.5) study 1 38.1 (11.1) study 2 21-60 38 / 45	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 5.7 (7.2) study 1 9.9 (9.8) study 2 NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zaleplon; triazolam 10, 40; 0.25 study 1 20, 60; 0.25 study 2 1 x night / 2 nights each Tr 30 min. before bed oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Dujardin, K / 1998 Moderate (3/5)	Private	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 NS 40 – 62 0 / 12	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zolpidem; flunitrazepam 10; 1 3 Tr sequences 1 wk apart bedtime oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Edinger, JD / 2003 Moderate (2/5)	GOV	RCT Not reported as double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 51.0 (13.7) NS 2 / 18	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary various medical conditions NS NS	**Type/Description**: **Frequency / Duration**:	abbreviated CBT; generic sleep hygiene (PI) 1 x every 2 wks / 4 wks

Evidence Table C-2: Efficacy and safety of treatments used in the management of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Edinger, JD / 2001 High (4/5)	GOV	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 55.8 (12.1) CBT 54.5 (10.2) RT 55.7 (9.5) Pl 40-80 35 / 40	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 13.6 (NS) NS	**Type/Description**: **Frequency / Duration**:	CBT, RT, quasi-desensitization (Pl) 1 x wk / 6 wks
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Elie, R / 1999 Moderate (3/5)	Private	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 42.5 - 44.3 (12.0 - 12.9) Tr 42.1 (12.0) Pl 18–65 370 / 204	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zaleplon; zolpidem 5, 10, 20; 10 1 x night / 4 wks before bed oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Elie, R / 1990 Moderate (3/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 76 (1.3) 60 – 90 33 / 11	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 7 >= 1 yr 17 > 10 yrs NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zopiclone, triazolam 5, 7.5; 0.125, 0.25 NS / 3 wks 30 min. before bed oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Ellis, CM / 1996 High (4/5)	GOV	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 46 (11) 32 – 67 6 / 9	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 21.7 (13) 1-45	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	melatonin 5 1 x day / 7 d 20.00 hr oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Espie, CA / 1989 Moderate (2/5)	NS	RCT Not reported as double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 44.9 (15.3) NS 47 / 23	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 12.4 (12.2) NS	**Type/Description**: **Frequency / Duration**:	progressive relax (RT); stimulus control (CBT); paradoxical intention (CBT); imagery relief (Pl) NS / 8 wks

Evidence Table C-2: Efficacy and safety of treatments used in the management of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Farag NH / 2003 High (4/5)	Private	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 37 (13) 21 – 63 20 / 5	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	herbal supplement NS 2 x night / 4 nights 1 hr before bed oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Ferguson, JM / 1991 High (4/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 43.4 (10.9) 18 – 65 56% / 44%	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	secondary major depression NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	estazolam 2 1 x night / 7 nights nightly NS
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Fillingim, JM / 1982 High (5/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 81 (NS) NS 89% / 11%	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 1 yr or more NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	temazepam; flurazepam 30; 30 1 x night / 4 nights bedtime oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Fleming, J / 1995 Moderate (3/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 33 – 37 (NS) 21 – 60 48% / 52%	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 7 – 10 (NS) NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zolpidem; flurazepam 10, 20; 30 NS / 3 nights NS NS
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Fry, J / 2000 Moderate (3/5)	Private	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 40 - 43 (10 - 13) Tr 43 (12) Pl 18 – 65 342 / 244	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zaleplon; zolpidem 5, 10, 20; 10 1 x night / 28 nights immediately before bed oral

Evidence Table C-2: Efficacy and safety of treatments used in the management of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Garfinkel, D / 1997 High (4/5)	NS	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 79 (5.2) 68 – 93 8 / 13	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary exhibiting various medical conditions NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	melatonin (controlled-release) 2 NS / 3 wks 2 hr before bed oral

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Garfinkel, D / 1995 High (4/5)	NS	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 76 (8) 68 – 93 5 / 7	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	melatonin (controlled-release) 2 1 x night / 3 wks 2 hr before bed oral

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Gelinas, B / 1985 High (4/5)	Private	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 40.9 (2.19) 18 – 60 16 / 10	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zopiclone 7.5 NS / 3 wks bedtime NS

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Goethe, JW / 1982 Moderate (2/5)	Private (provided materials & funding)	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 NS 19 – 60 50 / 19	**Type**: **Co-morbidity**: **Duration:** Mean (SD): Range:	primary NA 6 months or more (all but 3 patients) NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	quazepam 15 1 x night / 5 nights NS oral

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Goldenberg, F / 1994 High (4/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 42.5 (8.6) Tr 43.3 (9.2) Pl 25 – 60 291 / 167	**Type**: **Co-morbidity**: **Duration (months)** Mean (SD): Range:	primary NA 1.6 (0.8) Tr 1.7 (1.1) Pl NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zopiclone 7.5 1 x night / 14 nights, then as needed for 4 wks nightly oral

Evidence Table C-2: Efficacy and safety of treatments used in the management of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Haffmans, PMJ High (4/5)	NS	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 44 (NS) NS 3 / 4	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	secondary previous severe major depression NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	trazodone 150 – 250 1 x night / 7 nights 2200 hr oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Haimov, I / 1995 High (4/5)	NS	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 73.1 (3.9) independent living 81.1 (8.9) institutionalized NS 16 / 10	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	melatonin (sustained- and fast-release) 2 NS / 1 wk fast; 8 wk sustained 2 hr before bed oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Hajak, G / 2000 Moderate (3/5)	Private (grant-supported)	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 47.6 (11.3) Tr 47.4 (16.8) Pl NS 36 / 11	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 11.2 (9.7) NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	doxepin 25-50 1 x night / 4 wks 1 hr before bed oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Hajak, G / 1996 Moderate (3/5)	NS	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 41.3 (9.5) NS 3 / 7	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 10.7 (7.9) NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	doxepin 25 1 x first wk (IV); daily for 5 wk (oral) / 5 wks 30 min. before bed (oral) first hours of sleep (IV) IV and oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Hajak, G / 1994 High (5/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 51 (11) NS 939 / 566	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**, **Dose:** **Frequency / Duration**: **Timing**: **Route of Delivery**:	zopiclone, 7.5 mg funitrazepam, 1.0 mg triazolam, 0.25 mg 1 x daily / 28 d before bed oral

Evidence Table C-2: Efficacy and safety of treatments used in the management of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Hartmann, E / 1983 Moderate (3/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 38 - 46 (NS) 39 (NS) Pl 18–71 48 / 48	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 13 (NS) NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	l-tryptophan; secobarbital; flurazepam 1000; 100; 30 NS / 7 nights 30 min. before bed and 2 hr after eating NS

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Harvey, AG / 2003 Low (1/5)	NS	RCT Not reported as double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 21.1 (3.7) CBT 18.6 (5.1) CT NS 15 / 11	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary various psychiatric conditions (n=13) 6.4 (3.9) CBT 6.2 (5.8) CT NS	**Type/Description**: **Frequency / Duration**:	suppression (CBT); non-suppression (CT) envelop with instructions to follow each morning and evening / NS

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Haynes, SN / 1977 Low (1/5)	NS	RCT Not reported as double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 29.3 (NS) NS 15 / 9	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 7.1 (NS) NS	**Type/Description**: **Frequency / Duration**:	EMG feedback (RT); relax instructions (RT); control (Pl) 2 x wk / 3 wks

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Haynes, SN / 1974 Low (1/5)	Academic	RCT Not reported as double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 NS 18–21 5 / 9	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 5.3 (NS) NS	**Type/Description**: **Frequency / Duration**:	relax training (RT); Pl 2 x wk / 3 wks

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Hedner, J / 2000 Moderate (3/5)	Private	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 72.5 (5.9 – 6.8) Tr 72.5 (6.8) Pl 59 – 91 Tr 63 – 95 Pl 285 / 137	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zaleplon 5, 10 1 x night / 2 wks NS oral

Evidence Table C-2: Efficacy and safety of treatments used in the management of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Heidrich, H / 1981 High (4/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 44.6 (2) Tr 46 (2) Pl 64 – 21 Tr 63 – 28 Pl 67% / 33%	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 2.5 (NS) NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	loremetazepam 2 1 x night / 2 wks shortly before bed oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Hernandez, RL / 1983 Moderate (3/5)	Private	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 NS 22 – 65 24 / 12	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	quazepam 15 1 x night / 5 nights nightly oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Herrmann, WM / 1993 Moderate (3/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 NS 25 – 65 9 / 12	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zolpidem 10 1 x night / 2 wks 15 min. before lights out NS
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Hughes, RC / 1978 Low (1/5)	NS	RCT Not reported as double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 34.2 (NS) NS 24 / 12	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Frequency / Duration**:	EMG biofeedback (RT); EMG pseudo-biofeedback (Pl); relax training (RT); stimulus control instructions (Pl) EMG: 8 sessions relax: 4 sessions stimulus: 2 sessions
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Jacobson, AF / 1986 Moderate (3/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 72 (NS) Tr 69 (NS) Pl 60 – 82 slightly more than half female NS / NS	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 16 (16.4) Tr 14.5 (11.9) Pl 1 – 65 Tr 1 – 40 Pl	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	brotizolam 0.125 1 x night / 4 nights 30 min. before bed oral

Evidence Table C-2: Efficacy and safety of treatments used in the management of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
James, SP / 1990 Moderate (2/5)	NS	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 33.4 (NS) 20 – 57 6 / 4	**Type**: **Co-morbidity**: **Duration:** Mean (SD): Range:	primary NA > 6 months NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	melatonin 1, 5 NS / 2 wks – 1 for each Tr 15 min before bed oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Krystal, AD / 2003 Moderate (3/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 44 (11) 21 – 69 498 / 290	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	eszopiclone 3 1 x night / 6 months bedtime NS
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Lacks, P / 1983 Moderate (2/5)	Private (supported research)	RCT Not reported as double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 40.6 (NS) NS 48 / 16	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 13.8 (NS) NS	**Type/Description**: **Frequency / Duration**:	progressive relax (RT); stimulus control (CBT); paradoxical intention (CBT) 1 x wk / 4 wks
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Lacks, P / 1983 Moderate (2/5)	GOV	RCT Not reported as double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 43.0 (NS) 31 – 59 9 / 6	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 11.7 (NS) NS	**Type/Description**: **Frequency / Duration**:	stimulus control (CBT); visualization (PI) 1 x wk / 4 wks
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Lahmeyer, H / 1997 High (4/5)	Private (grant-supported)	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 44.9 (NS) 19 – 61 81 / 64	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zolpidem 10, 15 1 x night / 31 nights 30 min. before bed NS
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Lamphere, JK / 1989 Moderate (2/5)	NS	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 36 (10) NS 3 / 9	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zopiclone 2.5, 5.0, 7.5, 10, 15 3 x wk / 6 wks 30 min. before bed NS

Evidence Table C-2: Efficacy and safety of treatments used in the management of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Leppik, IE / 1997 Moderate (3/5)	Private	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 69 (NS) 59 – 85 63% / 37%	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zolpidem; triazomam; temazepam 5; 0.125; 15 1 x night / 4 wks bedtime oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Lichstein, KL / 2001 Moderate (2/5)	GOV	RCT Not reported as double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 68.03 (7.04) 59 – 92 53 / 21	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 8.93 (11.54) 0.5-51	**Type/Description**: **Frequency / Duration**:	relax (RT); sleep compression (CBT); quasi-desensitization (PI) 1 x wk / 6 wks
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Mamelak, M / 1989 Moderate (2/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 NS 60 – 72 NS / NS	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	brotizolam; flurazepam 0.25; 15 NS / 14 nights bedtime NS
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Mamelak, M / 1987 High (4/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 50 (NS) 32 – 60 21 / 9	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	flurazepam; zopiclone 30; 7.5 1 x d / 12 d 2300 hr oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
McAlpine, CJ / 1984 High (4/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 NS 18 – 94 90 / 57	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 72 > 1 yr NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	loprazolam; nitrazepam 1.0; 5.0 NS / 7 nights NS oral

Evidence Table C-2: Efficacy and safety of treatments used in the management of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Melo de Paula, A / 1984 Moderate (3/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 28 – 31 (NS) 19 – 55 42 / 16	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 1.3 – 2.1 (NS) 0.2-10	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	lormetazepam; flurazepam 1, 2; 30 NS / 2 wks NS NS

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Mendels, J / 1983 Moderate (3/5)	Private	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 47 (NS) Tr 45 (NS) Pl 20 – 58 Tr 22 – 60 Pl 19 / 41	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 36 < 10 yrs 24 > 10 yrs NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	quazepam 15 1 x night / 5 nights NS oral

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Milby, JB / 1993 Low (1/5)	Private	RCT Not reported as double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 30.4 (5.68) women 35 (6.13) men NS 8 / 7	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	triazolam & CBT; triazolam & sleep related info (CT) 0.25 1 x night / 13 nights 2 x wk / 3 wks 30 min. before bed NS

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Minnekeer, RJ / 1988 High (4/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 53.2 (14.5) Tr (q) 55.4 (12.5) Tr (f) 54.9 (13.7) Pl NS 130 / 74	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 30% > 5 yrs Tr (q) 32% > 5 yrs Tr (f) 34% > 5 yrs Pl NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	quazepam; flunitrazepam 15; 2 1 x night / 4 wks nightly oral

Evidence Table C-2: Efficacy and safety of treatments used in the management of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Mitchell, KR / 1979 Low (1/5)	NS	RCT Not reported as double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 37.4 (NS) 28 – 51 9 / 15	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 6.3 (NS) 2.1 – 8.1	**Type/Description**: **Frequency / Duration**:	progressive muscle relax (RT); relax training & cognitive control (RT & CBT); information & environmental change (Pl) 4 / 2 wks (RT) 2 / 2 wks (RT & CBT) 8 / wks (Pl)
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Mitler, MM / 1984 Moderate (3/5)	Private (grant-supported)	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 37.7 – 45.4 (NS) 27 – 61 17 / 4	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary or secondary personality disorder or sleep-related myoclonus NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	flurazepam; traizolam 30; 0.5 1 x night / 37 nights 30 min. before bed oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Monchesky, TC / 1986 High (4/5)	NS	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 47.1 (1.7) Tr 46.6 (1.8) Pl NS 65 / 26	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary various medical conditions 7.0 (1.2) Tr 6.4 (0.8) Pl NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zopiclone 7.5 1 x night / 4 wks bedtime oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Montes, LGA / 2003 Moderate (3/5)	NS	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 50 (12.7) 30 – 72 4 / 6	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 12.8 (12.1) 0.5 – 32	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	melatonin 0.3, 1.0 daily / 7d 1 hr before bed oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Monti JM / 2000 Moderate (3/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 53.8 (1.8) Tr 50.0 (5.3) Pl 27 – 59 12 / 0	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 12.6 (4.9) Tr 17.7 (6.5) Pl NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zolpidem 10 1 x night / 15 nights before turning of light oral

Evidence Table C-2: Efficacy and safety of treatments used in the management of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Monti, JM / 1996 Moderate (3/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 41.2 (3.9) Tr 47.3 (5.7) Pl NS 10 / 2	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 9.5 (3.5) Tr 9.3 (4.7) Pl NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zolpidem 10 1 x night / 27 nights night oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Morin, CM / 1999 Moderate (2/5)	GOV	RCT Not reported as double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 65 (7) 55 or older 50 / 28	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 16.8 (16.9) NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	temazepam; temazepam & CBT; CBT; Pl 7.5 and increasing to 30 based on response 2-3 minimum 7 maximum x wk / – Tr 1 x wk / 8 wks - CBT 1 hr before bed oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Nair, NPV / 1990 Moderate (3/5)	Private (grant-supported)	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 46.9 (1.4) 18 – 65 28 / 32	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 9.8 (1.2) NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zopiclone; flurazepam 3.75, 7.5, 11.25, 15; 30 1 x d / 7 d 30 min. before bed oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Negri, L / 1997 Moderate (2/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 42.95 (13.22) 15 – 68 70 / 30	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	secondary anxiety alone + mild depressive symptoms NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	pivagabine 900 1 x d / 30 d NS NS
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Nicassio, P / 1974 Low (1/5)	GOV	RCT Not reported as double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 45.1 (14.57) 22 – 71 21 / 9	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Frequency / Duration**:	autogenic training (RT); progressive relax (RT); self-relax (Pl) 1 x wk with 1 post-Tr session / 4 wks

Evidence Table C-2: Efficacy and safety of treatments used in the management of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Pasche, E / 1996 Low (1/5)	Private	RCT Not reported as double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 39.0 (0.7) 21 – 55 59 / 47	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Frequency / Duration**:	low energy emission therapy 3 x wk / 4 wks
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Perlis, ML / 2004 Moderate (3/5)	Private (primary investigator-initiated project)	RCT Not reported as double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 41.3 (13.4) 25 – 60 70.4% / 29.6%	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	CBT; modafinil & CBT; modafinil & contact control (CT) 100 1 x wk / 8 wks (CBT) 1 x d / 4 wks (Tr) every morning oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Poyares, DR / 2002 Moderate (3/5)	Academic	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 43.3 (10.6) NS 15 / 4	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	valmane 100 3 x daily / 15 d NS NS
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Reeves, RL / 1977 High (4/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 68.6 (NS) Tr (t) 69.6 (NS) Tr (f) 70.4 (NS) Pl NS 27 / 14	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	triazolam; flurazepam 0.25; 15 1 x night / 28 nights bedtime oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Rickles, K / 1986 High (4/5)	Private (grant-supported)	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 46 (12) NS 63% / 37%	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 8.6 (9.2) NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	brotizolam 0.5 1 x night in wk 1 option of 2 x night in final 2 wks / 3 wks 30 min. before bed oral

Evidence Table C-2: Efficacy and safety of treatments used in the management of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Riemann, D / 2002 Moderate (3/5)	Private	RCT Double-blind Unclear	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 45.3 (10.3) Tr (l) 47.0 (10.8) Tr (t) 48.8 (11.6) Pl NS 23 / 32	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	lormetazepam; trimipramine 1; 25-200 NS / 28 d NS oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Rodenbeck, A Moderate (3/5)	NS	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 41.3 (9.5) NS 3 / 7	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 10.7 (7.9) NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	doxepin 25 1 x night / 1 night 30 min. before bed acute IV
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Roehrs, T / 1999 Low (1/5)	Unclear	RCT Not reported as double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 34.1 (8.8) 21 – 55 5 / 6	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	ethanol (alcohol) 0.5 g / kg random 4 nights, choice other 3 nights / 1 wk 1 hr before bed drink
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Roehrs, T / 1983 Moderate (3/5)	NS	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 33.3 (8.0) NS 8 / 4	**Type**: **Co-morbidity**: **Duration:** Mean (SD): Range:	primary NA > 6 months NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	brotizolam 0.25, 0.5 3 x wk / 1 wk each dose 30 min. before bed oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Roth, TG / 1997 Moderate (2/5	Private	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 65.9 (4.6) NS 15 / 15	**Type**: **Co-morbidity**: **Duration:** Mean (SD): Range:	primary NA > 3 months NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	quazepam 7.5, 15 1 x night / 7 nights 30 min. before bed NS

Evidence Table C-2: Efficacy and safety of treatments used in the management of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Roth, T / 1979 High (4/5)	Private (provided drugs and funding)	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 NS 18 – 65 0 / 16	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	unclear unclear NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	quazepam 25 NS / 1 night 30 min. before bed oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Saletu-Zyhlarz, G / 2003 Moderate (2/5)	Private (funded pharmacological part of study)	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 58 (5) 46 – 67 49 / 0	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary related to postmenopausal syndrome NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	climodien; estradiol valerate 3; 2 NS / 2 months NS NS
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Sanavio, E / 1990 Low (1/5)	NS	RCT Not reported as double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 39.6 (NS) 25 – 50 24 / 16	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 11.8 (NS) 5 - 25	**Type/Description**: **Frequency / Duration**:	EMG biofeedback (RT); cognitive therapy (CBT); stimulus control & relax (RT & CBT); waiting-list control (Pl) 3 x wk / 2 wks
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Sastre-y-Hernandez, M / 1988 High (4/5)	NS	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 NS 20 – 76 36 / 24	**Type**: **Co-morbidity**: **Duration:** Mean (SD): Range:	primary NA 53% > 1 yr 20% 3-12 months 27% < 3 months NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	lormetazepam 1 NS / 1 wk NS sublingual and oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Scharf, MB / 1994 Moderate (3/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 38 (NS) 22 – 60 48 / 27	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zolpidem 10, 15 NS / 5 wks 30 min. before bed oral

Evidence Table C-2: Efficacy and safety of treatments used in the management of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Scharf, MB / 1990 High (4/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 40.4 (13.5) Tr (e) 42.8 (13.9) Tr (f) 41.3 (13.0) Pl 21-65 NS / NS	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	estazolam; flurazepam 2; 30 1 x night / 7 nights 30 min. before bedtime oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Shaw, SH / 1992 Moderate (3/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 74.9 (1.0) Tr 10mg 72.9 (1.0) Tr 20mg 75.7 (0.8) Pl 65-85 81 / 38	**Type**: **Co-morbidity**: **Duration (months)** Mean (SD): Range:	secondary various psychiatric conditions 23 (4) Tr 10mg 2.9 (4.6) Tr 20mg 2.6 (4.9) Pl NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zolpidem 10, 20 1 x night / 21 days 30 min. before bed oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Shealy, RC / 1979 Low (1/5)	NS	RCT Not reported as double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 19.8 (NS) 17 – 30 70 / 0	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Frequency / Duration**:	group relax & stimulus control (RT & CBT); group relax (RT); group placebo (Pl) 2 x wk / 3 wks
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Stanton, HE / 1989 Low (1/5)	NS	RCT Not reported as double-blind Parallel (with option to crossover after Tr)	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 NS 23 – 67 26 / 19	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	unclear NS NS NS	**Type/Description**: **Frequency / Duration**:	hypnotic relax (RT); stimulus control (CBT); desensitization (Pl) 1 x wk / 4 wks
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Steens, RD / 1993 Moderate (3/5)	Private	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 58.2 (5.5) 35 – 69 9 / 15	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary mild to moderate chronic obstructive pulmonary disease 7.8 (6.9) 1 - 25	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zolpidem; triazolam 5, 10; 0.25 4 Tr sequences bedtime oral

Evidence Table C-2: Efficacy and safety of treatments used in the management of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Stip, E / 1999 High (4/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 42.6 (1.6) 20 – 64 21 / 29	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary or secondary mild non-psychotic disorders 10.1 (NS) Tr (z) 9.7 (NS) Tr (t) 12.4 (NS) Pl NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zopiclone; temazepam 7.5; 30 NS / 3 wks NS oral

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Tietz, EI / 1981 Moderate (3/5)	NS	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 41.2 (16.8) 18 – 60 0 / 15	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	quazepam 7.5, 15, 30, 45 1 x night / 5 non consecutive wks 30 min. before bed oral

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Tuk, B / 1997 Moderate (3/5)	NS	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 NS 18 – 78 15 / 6	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	temazepam 20 2 occasions just before usual bed oral

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Vallieres, A / 2004 Moderate (2/5)	GOV	RCT Not reported as double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 47.5 (7.92) 34 – 50 3 / 3	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 15.5 (9.2) NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zopiclone; CBT; zopiclone & CBT 3.75 – 7.5 NS / 5 wks 1 x wk / 5 wks – CBT 30 min. before bed NS

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Viukari, M / 1983 High (4/5)	NS	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 73.2 (2.9) group A 75.1 (1.5) group B NS 20 / 17	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary various medical and psychiatric conditions NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	flunitrazepam; nitrazepam 1; 5 1 x night / 2 wks 7:30 pm oral

Evidence Table C-2: Efficacy and safety of treatments used in the management of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Walsh, JK / 2002 Moderate (3/5)	NS	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 43.2 (1.2) Tr 45.0 (1.3) Pl NS 115 / 48	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zolpidem 10 as needed between 3-5 per wk / 4 wks nights oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Walsh, JK / 2000 Moderate (3/5)	Private (data analysis)	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 67.5 (NS) 60 – 79 17 / 31	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zaleplon 2, 5, 10 nightly / 2 nights 30 min. before lights out oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Walsh, JK / 2000 High (4/5)	Private (research design, selection of investigators, data analysis)	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 43.2 (1.2) Tr 45.0 (1.3) Pl 21 – 65 115 / 48	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zolpidem 10 10 capsules for each 2 wk period / 8 wks bedtime oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Walsh, JK / 1998 High (4/5)	Private	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 38.9 – 39.6 (10 – 11.7) Tr 43.1 (9.0) Pl 18 – 60 77 / 55	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA 7.4 – 11.8 (6.3 – 10.2) Tr 7.4 (7.3) Pl NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zaleplon; triazolam 5, 10; 0.25 1 x night / 14 nights 30 min. before bed NS
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Walsh, JK / 1998 Moderate (3/5)	Private	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 42 (NS) 21 – 65 193 / 85	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	zolpidem; trazodone 10; 50 1 x night / 14 nights before bed oral

Evidence Table C-2: Efficacy and safety of treatments used in the management of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Walsh, JK / 1984 Moderate (3/5)	Private	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 41.1 (NS) 19 – 65 52% / 48%	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	estazolam 1, 2 1 x night / 7 nights 30 min. before bed oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Wang, RIH / 1977 Moderate (3/5)	NS	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 NS NS NS / NS	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	penobarbitol; methyprylon; glutethimide 100; 300; 500 1 x every second night / over 5 nights 09:45 h oral
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Waters, WF / 2003 Low (1/5)	Foundation	RCT Not reported as double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 44.1 (NS) 18 – 59 37 / 16	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	flurazepam; sleep restriction & stimulus control (CBT); sleep hygiene (non-drug PI); sleep restrict & stimulus control & sleep hygiene (RT & CBT); aggressive muscle relax & cognitive distraction (RT & CBT) 15 NS / 2 wks bedtime NS
AUTHOR / YEAR QUALITY (score)	**FUNDING SOURCE**	**STUDY DESIGN**	**POPULATION CHARACTERISTICS**		**INSOMNIA CHARACTERISTICS**		**INTERVENTIONS**	
Winsauer, HJ / 1984 Moderate (3/5)	Private	RCT Double-blind Parallel	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	 NS 60 – 90 39 / 21	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	quazepam 15 NS / 5 nights NS NS

Evidence Table C-2: Efficacy and safety of treatments used in the management of chronic insomnia in adults (continued)

AUTHOR / YEAR QUALITY (score)	FUNDING SOURCE	STUDY DESIGN	POPULATION CHARACTERISTICS		INSOMNIA CHARACTERISTICS		INTERVENTIONS	
Zhdanova, IV / 2001 Moderate (2/5)	GOV	RCT Double-blind Crossover	**Age (years)** Mean (SD): Range: **Gender** Female / Male:	over 50 yrs NS NS NS / NS	**Type**: **Co-morbidity**: **Duration (years)** Mean (SD): Range:	primary NA NS NS	**Type/Description**: **Dose (mg)**: **Frequency / Duration**: **Timing**: **Route of Delivery**:	melatonin 0.1, 0.3, 3.0 1 x night / 4 wks 30 min. before fixed bedtime oral

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Appendix D: Technical Expert Panel

The Technical Experts for this review are outlined below. Some of their professional affiliations are briefly described. The panel was consulted for their opinion regarding the definition of chronic insomnia used in the review, the inclusion criteria for the review and data analysis. They were also asked to provide feedback on the draft report.

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Associate Director, Center for Sleep Medicine, Neurology, New York Presbyterian Hospital-Cornell, NY/Weill Medical College, Cornell University.

Appendix E: Excluded Studies

Four hundred and forty-nine studies were excluded for the questions on manifestations of chronic insomnia. The reasons for exclusion of studies potentially relevant to these questions are as follows: (1) the study was reported in a language other than English (n=9), (2) the report was a review (n=38), (3) the study was not relevant to the review topic (n=71), (4) the study was a case report (n=9), (5) the study did not have a control group (n=47), (6) the study did not examine an adult population (n=8), (7) the study population did not have chronic insomnia as defined in this report (208), (8) the study did not report on any of the outcomes of this review (n=58) and (9) data relevant to the study outcomes were not adequately reported (n=1).

Excluded - Non-English

The following studies were excluded because they were reported in a language other than English.

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Excluded - Review

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Excluded - Topic

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Excluded - Design (Case Report)

The following studies were excluded because they were case reports.

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Excluded - Population (Non-Adult)

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Excluded - Population (Not Chronic Insomnia)

The following studies were excluded because the participants did not suffer from chronic insomnia as defined in this report.

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58. Zorick FJ, Roth T, Hartze KM et al. Evaluation and diagnosis of persistent insomnia. Am J Psychiatry 1981; 138(6):769-73.

Excluded - Outcomes (Inadequate Reporting)

The following study was excluded because data relevant to the outcomes of interest were inadequately reported.

1. Winett CA. The mediating role of insomnia in the relation between life events and depression and mania. Miami (FL): University of Miami; 2001.

Five hundred and fifty six studies were excluded for the question on management of chronic insomnia. The reasons for exclusion of studies were as follows: (1) the study was reported in a language other than English (n=27), (2) the report was a review/commentary/practice parameter (n=32), (3) the study report was a duplicate publication (n=3) (4) the study did not examine an adult population (n=17), (5) the study population did not suffer from chronic insomnia as defined in this report (n=221), (6) the study was not a randomized controlled trial (n=160), (7) the study did not have a placebo arm (n=48), (8) the study was not double-blind (n=15), (9) the study did not report on any of the outcomes of this review (n=18) and (10) the study outcomes were not adequately reported (n=15).

Excluded - Non-English

The following studies were excluded because they were reported in a language other than English.

1. Altamura AC, Colacurcio F, Mauri MC et al. Controlled clinical study on the effect of quazepam versus triazolam in patients with sleep disorders [Ital]. Minerva Psichiatr 1989; 30(3):159-64.

2. Bourin M, Andre-David F. Triazolam 0.25 mg versus loprazolam 1 mg in common insomnia treated by general practitioners (double blind cross-over randomized study). [Fr]. Therapie 1989; 44(2):107-14.

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4. Carlini EA, Braz S, Troncone LR et al. [Hypnotic effect of homeopathic medication and placebo. Evaluation by double-blind and crossing technics]. [Portuguese]. Amb; Revista Da Associacao Medica Brasileira 33[5-6], 83-8. 1987 May-Jun.

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11. Herberg KW, Laux G, Fischer W. Analysis of the effects of a 14 days treatment with zopiclone 7.5mg/d on performance capability, actual well-being, and quality of sleep of patients with primary insomnia. [Germ]. Psychopharmakother 2002; 9(1):25-34.

12. Huang GG, Chen Q, Li L. Comparison between the effect of behavioral and drug therapy on the treatment of insomnia in patients with schizophrenia in rehabilitation period. [Chin]. Zhongguo Linchuang Kangfu 2004; 8(9):1628-9.

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16. Kurihara M, Jinbo M, Hirose T et al. A study of the clinical efficacy of triazolam on insomnia -Double-blind cross-over study among the smaller and larger doses of triazolam, and flurazepam. Rinsho Hyoka (Clin Eval) 1980; 8(1):79-110.

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Excluded - Review/Commentary/Practice Parameter

The following studies were excluded because they were reviews/commentaries/practice parameters.

1. Agargun MY, Kara H, Ozbek H et al. Restless legs syndrome induced by mirtazapine. J Clin Psychiatry 2002; 63(12):1179.

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Excluded - Duplicate Publication

The following studies were excluded because the report was a duplicate publication.

1. Demisch K, Bauer J, Georgi K et al. Treatment of severe chronic insomnia with L-tryptophan: Results of a double-blind cross-over study. Pharmacopsychiatry 1987; 20(6):242-4.

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Excluded - Population (Non-Adult)

The following studies were excluded because they did not examine an adult population.

1. Cartwright RD, Weiss MF. The effects of electrosleep on insomnia revisited. J Nerv Ment Dise 1975; 161(2):134-7.

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16. Weiss MF. The treatment of insomnia through the use of electrosleep: an EEG study. J Nerv Ment Dis 1973; 157(2):108-20.

17. Willis CS. Effects of problem-solving and relaxation treatments for insomnia on sleep-onset latency and cognitive arousal prior to sleep. Panama City (FL): Florida State University. 1991.

Excluded - Population (Not Chronic Insomnia)

The following studies were excluded because the participants did not suffer from chronic insomnia as defined in this report.

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Excluded - Design (Not Randomized Controlled Trial)

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Excluded - Design (No Placebo Arm)

The following studies were excluded because they did not have a placebo arm.

1. Agnoli A, Manna V, Martucci N. Double blind study on the hypnotic and anti-anxiety effects of zopiclone compared with nitrazepam in the treatment of insomnia. Int J Clin Pharmacol Res 1989; 9(4):277-81.

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Excluded - Design (Not Double-Blind)

The following studies were excluded because they were not double-blind.

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Excluded - Outcomes (Irrelevance)

The following studies were excluded because they did not report on any outcomes of this review.

1. Baillargeon L, Landreville P, Verreault R et al. Discontinuation of benzodiazepines among older insomniac adults treated with cognitive-behavioural therapy combined with gradual tapering: A randomized trial. Can Med Assoc J 2003; 169(10):1015-20.

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18. Scharf MB, Fletcher K, Graham JP. Comparative amnestic effects of benzodiazepine hyponotic agents. J Clin Psychiatry 1988; 49(4):134-7.

Excluded - Outcomes (Inadequate Reporting)

The following study was excluded because data relevant to the outcomes of interest were inadequately reported.

1. Chen D, Chernik DA, Ellinwood E et al. A multicenter study of sleep, performance, and plasma levels in chronic insomniacs during 14-day use of flurazepam and midazolam: executive summary. J Clin Psychopharmacol 1990; 10(4 Suppl):S3-4.

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