CRD summary
The aim of this review was to review the effectiveness of melatonin for the treatment of sleep disorders. The authors concluded that the short-term use of melatonin is generally not effective in treating primary or secondary sleep disorders, or the sleep disturbance aspect of jet lag and shift-work disorder. These conclusions were derived from a well-conducted review of relevant randomised studies.

Authors’ objectives
To review the effectiveness of melatonin for the treatment of sleep disorders. Other than effectiveness, other sections of the review dealt with safety, pharmacology and mechanisms of action of exogenous melatonin, and the link between endogenous melatonin and circadian rhythms. This abstract focuses on the question about the effects of exogenous melatonin on people with sleep disorders.

Searching
The review authors searched 13 electronic databases (up to June, July or August 2003), with periodical update searches of MEDLINE and EMBASE. This was supplemented by checking the reference lists of some retrieved reports and key documents, plus handsearches of the Associated Professional Sleep Society Abstracts (1999 to 2003). The searches were limited to studies reported in the English language, unless there was evidence of publication bias, in which case non-English language studies were sought. Full details of the search were given in the report.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs), including crossover trials, were included in the review of effectiveness.

Specific interventions included in the review
Studies evaluating the effects of any formulation, dosage, timing, frequency and duration of melatonin administration as the primary intervention were included. The doses of melatonin given in the included studies ranged from 0.1 to 80 mg, with a mode of 5 mg. The control groups received placebo.

Participants included in the review
Studies were included in the review if they involved human participants suffering from a sleep disorder and this condition was explicitly mentioned in the report.

Outcomes assessed in the review
Studies were included in the review if at least one of the following outcomes was assessed: sleep onset latency (SOL), sleep efficiency, sleep quality, wakefulness after sleep onset (WASO), total sleep time, or the percentage time in REM (rapid eye movement) sleep.

How were decisions on the relevance of primary studies made?
Only studies that met all the inclusion criteria for a given question of the review, as determined by two independent reviewers, were considered relevant to that question. Any disagreements were resolved by discussion and consensus.

Assessment of study quality
The components of randomisation, blinding and the reporting of drop-outs and withdrawals for each RCT were assessed using the Jadad validity scale. Two reviewers independently assessed study quality. Any disagreements were resolved by discussion and consensus.
Data extraction
One reviewer extracted the data and a second reviewer checked these data for accuracy and completeness. Any disagreements were resolved by discussion and consensus. Data were extracted on relevant aspects of the study population and sample size, study design, and intervention or controls. Relative risks were calculated for dichotomous data, while weighted mean differences (WMDs) or standardised mean differences (SMDs) were calculated for continuous data.

Methods of synthesis
How were the studies combined?
The data were synthesised using a random-effects model. Separate analyses were conducted for people suffering from primary sleep disorders, secondary sleep disorders, and sleep restriction. Publication bias was assessed by visual inspection of a funnel plot, the rank correlation test, a graphical test, and the trim-and-fill method.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the I-squared statistic. Subgroup analyses were carried out to investigate the effects of participant characteristics, dosage and duration of melatonin, concurrent medications, primary diagnosis, study design and quality, and method of measurement of sleep outcomes on the results.

Results of the review
Thirty RCTs (1,449 enrolled) were included in the effectiveness section of the review.

The studies were generally of a moderate-to-high quality.

Effectiveness of melatonin in people with a primary sleep disorder.
Melatonin decreased SOL in people with a primary sleep disorder (WMD -10.7 minutes, 95% confidence interval, CI: -17.6, -3.7), though studies were heterogeneous (I-squared 81.5%). SOL was decreased greatly in people with delayed sleep phase syndrome (WMD -38.8 minutes, 95% CI: -50.3, -27.3). SOL was decreased marginally in patients with insomnia, but the size of this effect appeared to be clinically insignificant (WMD -4.3 minutes, 95% CI: -8.4, -0.1). The effects of melatonin did not vary with the dose or duration of treatment. Combining studies using a fixed-effect model suggested that melatonin did not have any effect on SOL in people with primary insomnia.

Melatonin did not have an effect on sleep efficiency, sleep quality, WASO, total sleep time, or percentage time spent in REM sleep.

Effectiveness of melatonin in people with a secondary sleep disorder.
Melatonin did not have an effect on SOL in people with a secondary sleep disorder. The effect of melatonin did not vary with the dose or duration of treatment.

Melatonin increased sleep efficiency in people with a secondary sleep disorder (WMD 1.9%, 95% CI: 0.5, 3.3; I-squared 0%). The effect of melatonin did not vary by age, dose or the duration of treatment. The magnitude of this effect appeared to be clinically insignificant.

Melatonin did not have an effect on WASO or percentage time spent in REM sleep in people with a secondary sleep disorder, but it did increase total sleep time in this population (WMD 15.6 minutes, 95% CI: 7.2, 24.0; I-squared 0%).

Effectiveness of melatonin in people with sleep restriction.
Melatonin did not have an effect on SOL in people suffering from sleep restriction. The effect of melatonin did not vary by dose or type of sleep restriction disorder (i.e. shift-work or jet lag).

Melatonin did not have an effect on sleep efficiency in people suffering from sleep restriction. The effect of melatonin did not vary by dose.
Melatonin did not have an effect on sleep quality, WASO or percentage time spent in REM sleep in people suffering from sleep restriction, but it significantly increased total sleep time in this population (WMD 18.2 minutes, 95% CI: 8.1, 28.3; I-squared 0%).

**Authors' conclusions**
The evidence suggests that short-term use of melatonin is not effective for treating most primary sleep disorders, although there is some evidence to suggest that such usage is effective in treating delayed sleep phase syndrome, and that short-term use of melatonin is not effective in treating most secondary sleep disorders. There was no evidence to suggest that melatonin is effective in alleviating the sleep disturbance aspect of jet lag and shift-work disorder. There was evidence to suggest that melatonin is safe to use in the short term.

**CRD commentary**
This was a very wide-ranging review of the effects of melatonin that was broken down into a series of sub-questions. The sub-questions presented here, relating to the effects of melatonin in the treatment of sleep disorders, were supported by appropriate and clearly defined inclusion criteria. Comprehensive search strategies and characteristics of the included studies were presented in detail, study validity was taken into account, and attempts were made to minimise bias and error throughout the review process. Though the searches were initially limited to English language studies, investigations into publication bias suggest that this was not a major influence on the results presented here. There was some heterogeneity among the included studies, but the authors went on to investigate the effects of between-study differences fairly thoroughly. Based on the evidence presented in the review, the authors' conclusions appear appropriate.

**Implications of the review for practice and research**
Practice: The authors did not state any implications for practice.

Research: The authors stated that further research is required in various areas within the field of melatonin and sleep disorders research. Specifically, they stated 'it remains unclear how the effects of melatonin vary by age, gender, ethnicity, and co-morbid conditions of the population, as well as formulation, timing, and duration of melatonin administration'. The authors suggested that the following need to be determined: the long-term effects of melatonin on people with primary and secondary sleep disorders beyond 4 weeks; the short- and long-term effects of melatonin on people with sleep apnoea; the safety of melatonin in people of different ethnicities and with different timing of administration; and the effects of long-term use of melatonin. In addition, a systematic approach is needed to determine the effects of melatonin relative to other treatments for sleep disorders.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.