CRD summary
This review assessed melatonin for the treatment of tardive dyskinesia (TD). The authors concluded that there was insufficient evidence to support the use of melatonin for TD. Since the methods used to conduct the review were not reported, the reliability of the authors' conclusions could not be verified.

Authors' objectives
To assess the effectiveness of melatonin in the treatment of tardive dyskinesia (TD).

Searching
MEDLINE and PsycINFO were searched from inception to September 2002. No further details were given.

Study selection
Specific designs of evaluations included in the review
Reviews, case reports and case series were eligible for inclusion.

Specific interventions included in the review
Studies of melatonin treatment were included. The included studies compared slow-release melatonin (2 mg/day for 4 weeks) or controlled-release melatonin (10 mg/day for 6 weeks) with placebo.

Participants included in the review
The authors stated that studies of animals and humans were eligible for the review, although only studies of humans were included. Studies of patients with TD were included. One study included patients meeting the American Psychiatric Association's DSM criteria (4th edition) for schizophrenia and narcoleptic-induced TD who were being treated with typical antipsychotics (mean dose 238 mg/day equivalent of chlorpromazine). The other study included patients being treated with typical antipsychotics (mean dose 202 mg/day equivalent of chlorpromazine). The mean age of the participants ranged from 64 to 74 years, and the mean duration of mental illness was 24.8 to 31.3 years.

Outcomes assessed in the review
The inclusion criteria were not explicitly defined in terms of outcomes. The included studies assessed outcomes using the Abnormal Involuntary Movement Scale (AIMS). In both included studies a single rater assessed outcomes. The studies also assessed adverse effects.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Validity was not formally assessed, but some aspects of validity were discussed in the text (e.g. sample size, study duration and outcomes measured).

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
How were the studies combined?
The studies were combined in a narrative.

How were differences between studies investigated?
Differences between the studies were discussed in the paper.

Results of the review
Two placebo-controlled crossover randomised controlled trials (RCTs) were included (n=19 and n=24, respectively).

The included studies exhibited several methodological limitations: small sample size, short duration of treatment, older age of study populations and the use of means to report AIMS scores.

One crossover RCT (19 patients) found no statistically significant difference between baseline and end-of-treatment AIMS scores (change of less than 1 point with each treatment), or between baseline and end of washout, for either melatonin or placebo.

The second crossover RCT (24 patients randomised, two withdrew before the start of treatment) found that 10 mg/day melatonin significantly decreased the AIMS score compared with placebo: decrease of 2.45 points with melatonin versus 0.77 points with placebo (P=0.001). Melatonin significantly increased the proportion of patients with a decrease in AIMS score of more than 3 points versus placebo (7 patients with melatonin versus 1 patient with placebo, P<0.001).

No adverse effects were reported in either RCT, and there were no withdrawals due to adverse effects.

Authors’ conclusions
There was insufficient evidence to support the use of melatonin for patients with TD.

CRD commentary
Inclusion criteria were not explicitly defined for the interventions or outcomes of interest. In addition, the inclusion criteria relating to participants did not appear to have been adhered to. The search strategy was not described in full (no details of the search terms or any language restrictions), therefore the likelihood of missing relevant studies could not be judged. The methods used to select the studies, assess validity and extract data were not described, so it is not known whether any efforts were made to reduce errors and bias. Validity was not formally assessed, but some methodological limitations of the studies were discussed in the text. However, neither the adequacy of randomisation method nor the level of blinding were assessed. The lack of reporting of methods used to conduct the review make it difficult to comment on the strength of the evidence underpinning the authors’ conclusions.

Implications of the review for practice and research
Practice: The authors stated that melatonin could not be recommended for the treatment of TD, based on the available evidence.

Research: The authors stated that there is a need for larger studies with a younger study population, shorter duration of TD, longer treatment duration and use of a standardised drug formulation. They also stated that trials to assess the effect of melatonin on dopamine release and the use of melatonin in preventing TD are required.

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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.