ClinicalEvidence

# Sleep disorders in children

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## ABSTRACT

INTRODUCTION: Sleep disorders may affect between 20% and 30% of young children, and include problems getting to sleep (dyssomnias), or undesirable phenomena during sleep (parasomnias), such as sleep terrors and sleepwalking. Children with physical or learning disabilities are at increased risk of sleep disorders. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of treatments for dyssomnias in children? What are the effects of treatments for parasomnias in children? We searched: Medline, Embase, The Cochrane Library, and other important databases up to September 2009 (Clinical Evidence reviews are updated periodically, please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found 28 systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review we present information relating to the effectiveness and safety of the following interventions: antihistamines; behavioural therapy plus antihistamines, plus benzodiazepines, or plus chloral and derivatives; benzodiazepines alone; exercise; extinction and graduated extinction; 5-hydroxytryptophan; light therapy; melatonin; safety/protective interventions for parasomnias; scheduled waking (for parasomnias); sleep hygiene; and sleep restriction.


## QUESTIONS



## INTERVENTIONS



### Footnote

* Based on consensus; few RCT data

## Key points

- Sleep disorders may affect between 20% and 30% of young children, and include problems getting to sleep (dyssomnias) or undesirable phenomena during sleep (parasomnias), such as sleep terrors and sleepwalking.

  Children with physical or learning disabilities are at increased risk of sleep disorders. Other risk factors include the child being the first born, having a difficult temperament or having had colic, and increased maternal responsiveness.

- There is a paucity of evidence about effective treatments for sleep disorders in children, especially parasomnias, but behavioural interventions may be the best first-line approach.
- Extinction and graduated extinction in otherwise healthy children with dyssomnia may improve sleep quality and settling, and reduce the number of tantrums and wakenings compared with no treatment.

  Extinction and graduated extinction in children with physical disabilities, learning disabilities, epilepsy, or attention-deficit disorder with dyssomnia may be more effective at improving settling, reducing the frequency and duration of night wakings, and improving parental sleep compared with no treatment; however, we don't know whether it is more effective in improving sleep duration.

  Graduated extinction may be less distressing for parents, and therefore may have better compliance.
- Sleep hygiene for dyssomnia in otherwise healthy children may be more effective in reducing the number and duration of bedtime tantrums compared with placebo, but we don't know if it is more effective at reducing night wakenings, improving sleep latency, improving total sleep duration, or improving maternal mood.

  Sleep hygiene and graduated extinction seem to be equally effective at reducing bedtime tantrums in otherwise healthy children with dyssomnia.

  We don't know whether sleep hygiene for dyssomnia in children with physical disabilities, learning disabilities, epilepsy, or attention-deficit disorder is effective.
- Melatonin for dyssomnia in otherwise healthy children may be more effective at improving sleep-onset time, total sleep time, and general health compared with placebo.

  Evidence of improvements in dyssomnia with melatonin is slightly stronger in children with physical disabilities, learning disabilities, epilepsy, or attention-deficit disorder.
- Little is known about the long-term effects of melatonin, and the quality of the product purchased could be variable as melatonin is classified as a food supplement.
- Antihistamines for dyssomnia may be more effective than placebo at reducing night wakenings and decreasing sleep latency, but we don't know if they are more effective at increasing sleep duration. The evidence for antihistamines in dyssomnia comes from only one small, short-term study.
- We don't know whether behavioural therapy plus antihistamines, plus benzodiazepines, or plus chloral and derivatives, exercise, light therapy, or sleep restriction are effective in children with dyssomnia.
- We don't know whether antihistamines, behavioural therapy plus benzodiazepines or plus chloral and derivatives, benzodiazepines, 5-hydroxytryptophan, melatonin, safety/protective interventions, scheduled waking, sleep hygiene, or sleep restriction are effective in children with parasomnia.

## Clinical context

**DEFINITION**

The International Classification of Sleep Disorders-2 (ICSD-2) [1] defines more than 70 sleep disorders classified into eight major categories: insomnia, sleep-related breathing disorders, hypersomnias of central origin, circadian rhythm sleep disorders, parasomnias, sleep-related movement disorders, isolated symptoms and normal variants, and other sleep disorders. For the purpose of this review we defined **dyssomnia** including only paediatric insomnia or excessive daytime sleepiness; and **parasomnias**. **Dyssomnia** Paediatric insomnia may be defined as difficulty initiating or maintaining sleep that is viewed as a problem by the child or carer. In the ICSD-2, paediatric insomnia is included in the category of "Behavioral Insomnia of Childhood" divided in two types: sleep-onset association type and limit-setting type. Both types of insomnia are common and have an estimated prevalence of 10% to 30%. [2] Sleep-onset association type occurs when a child associates falling asleep with an action (being held or rocked), object (bottle), or setting (parents' bed), and is unable to fall asleep if separated from that association. Limit-setting type occurs when a child stalls and refuses to go to sleep in the absence of strictly enforced bedtime limits. **Parasomnias** are defined as "undesirable physical events or experiences that occur during entry into sleep, within sleep, or during arousals from sleep." Parasomnias in childhood are common, more often benign, self-limited, and typically resolving in adolescence. Following the ICSD-2, they are subdivided into three groups: disorders of arousal (from NREM sleep); parasomnias usually associated with REM sleep; and other parasomnias. **Children with physical disabilities, learning disabilities, epilepsy, or attention-deficit disorder:** Sleep problems tend to be greater in prevalence and severity in this population. For example, pain is related to sleep disturbance, and attention paid to helping the child sleep better is likely to improve recovery. Across a range of physical problems, there are reports in the literature of sleep disturbance associated with them. In most cases, research is limited and the mechanisms are unclear. Children with visual impairment are prone to circadian rhythm problems: their light perception is poor and the primary cue for sleep onset is therefore lost. Many medications are known to cause sleep problems, such as severe drowsiness with many antiepileptic drugs. Learning disabilities vary considerably in the range of conditions covered by this global term. However, some conditions such as Smith–Magenis, Prader–Willi, and Williams syndrome have sleep disturbance as cardinal features. Others, such as Down's syndrome and

mucopolysaccharidoses, are associated with sleep-related breathing problems. Treatment for these groups of children needs to be tailored to their particular problems, and may be problematic for anatomical and neurological reasons. Nevertheless, in large part, these sleep problems should be regarded as treatable, and careful investigation of these problems is required. [3] [4]

## INCIDENCE/ PREVALENCE

Sleep problems, primarily settling problems and frequent night wakings, are experienced by about 20% to 30% of children aged 1 to 5 years, but cultural differences would seem to play at least some role. [5] [6] [7] [8] These sleep disturbances often persist in later childhood: [9] 40% to 80% of children displaying sleep problems when aged 15 to 48 months were found to have persistent sleep disorders 2 to 3 years later. [10] In toddlers, settling and night-waking problems are dominant, with rates about 20% to 25%. [11] A second peak in sleep problems occurs in adolescence, where sleep-timing problems occur, including delayed sleep phase syndrome. Such children have difficulty getting off to sleep, and then problems getting up in the morning for school. Across the age range, sleep-related breathing problems occur at rates about 2%. [12] **Children with physical disabilities, learning disabilities, epilepsy, or attention-deficit disorder:** The prevalence of sleep disorders tends to be even greater in children with physical or learning disabilities: about 86% of children aged up to 6 years, 81% of children aged 6 to 11 years, and 77% of children aged 12 to 16 years with physical or learning disabilities suffer from severe sleep problems. [13] Disorders of initiating and maintaining sleep, prolonged sleep latency, high number of night awakenings, and reduced total sleep time are also found in children with Angelman's syndrome compared with age-matched controls. [14] Furthermore, children with autism are reported to have a shorter sleep duration, a longer sleep latency, and bed wetting compared with controls. [15]

## AETIOLOGY/ RISK FACTORS

Evidence of the aetiology of sleep disorders in children is generally limited. The vast majority of insomnia in infancy is behavioural insomnia, without a specific aetiology other than the altered interaction between parents and infants at bedtime. [16] Factors related to sleep disorders are: having had colic, [17] the child being the first born, [18] and the child having a difficult temperament (e.g., low sensory threshold, negative mood, decreased adaptability). [19] Other factors have been suggested, such as being born prematurely and low birth weight; however, evidence of such associations is contradictory. [16] Recently, iron deficiency has also been related to the presence of insomnia, nocturnal hyperactivity, or restless leg syndrome, [20] [21] [22] [23] and therefore this kind of treatment could be considered in some forms of resistant insomnia in infancy and childhood. The factors described here may influence the onset of a sleep disorder, but the factors influencing the maintenance of a sleep problem are likely to be different. Increased maternal responsiveness is associated with the maintenance of sleep disorders in children. [24] **Children with physical disabilities, learning disabilities, epilepsy, or attention-deficit disorder:** Children with physical disabilities, learning disabilities, epilepsy, or attention-deficit disorders may have other additional risk factors that include the influence of the specific cerebral lesions, the effect of medications (either antiepileptic drugs or stimulant drugs), the altered circadian phase, etc. Almost all children with brain diseases may be at risk for the development of sleep–wake rhythm disorders. The altered perception of "common zeitgeber" (light–dark cycle, food schedule, maternal inputs, etc.) could lead to the development of irregular sleep habits and even to a free-running rhythm, not related to the 24-hour cycle. Children with learning disabilities or with brain damage/impairments may also exhibit endogenous dysfunction in hormone release. Hormone release synchronises circadian rhythms with sleep/wake alternation and can therefore interfere with the development of a normal sleep–wake cycle. It can be hypothesised that the difficulties in the perception of external stimuli and in their elaboration may be the first step in the development of disrupted sleep–wake organisation. [25]

## PROGNOSIS

Children with excessive daytime sleepiness or night waking are likely to suffer from impaired daytime functioning without treatment, and their parents are likely to have increased stress. In addition to these effects, children with parasomnias are at serious risk of accidental injuries. Between 40% and 80% of children aged 15 to 48 months displaying sleep problems had persistent sleep problems 2 to 3 years later. [10] **Children with physical disabilities, learning disabilities, epilepsy, or attention-deficit disorder:** Children with learning disabilities and sleep disorders are more likely to have greater challenging behaviour than those without sleep problems. [26] This may affect the quality of life of the parents, frequently resulting in parental stress, parents displaying less affection for their children, and marital discord. [13] [27] For children with epilepsy, sleep disorders may exacerbate their condition: a persistent lack of sleep has been associated with an increased frequency of seizures. [28]

## AIMS OF INTERVENTION

To improve child and parental satisfaction with sleep; to prevent daytime sleepiness; and improve functional and cognitive ability during the daytime, with minimal adverse effects of treatment.

**OUTCOMES**

**Dyssomnia and parasomnias:** Sleep problems (e.g., difficulty falling asleep, frequent night-time awakenings, bed wetting, etc.); behaviours (e.g., snoring, talking in sleep, etc); quality of life of child measured by, for example, RAND-GHRI, Sleep Behavior Questionnaire; habits (e.g., bed/waking time, daytime naps, sleeping arrangements); quality of life of parent (notably parental sleep). **Dyssomnia:** Night wakings (frequency and duration); sleep-onset time; sleep-offset time; sleep duration; sleep latency; bedtime tantrums (number and frequency); settling; Composite Sleep Disturbance Score; Compostive Sleep Index Score. **Parasomnias:** severity of parasomnia; incidence of parasomnia; **Adverse effects of treatments**.

**METHODS**

*Clinical Evidence* search and appraisal September 2009. The following databases were used to identify studies for this systematic review: Medline 1966 to September 2009, Embase 1980 to September 2009, and The Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Clinical Trials 2009, Issue 3 (1966 to date of issue). An additional search within The Cochrane Library was carried out for the Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA). We also searched for retractions of studies included in the review. Abstracts of the studies retrieved from the initial search were assessed by an information specialist. Selected studies were then sent to the contributor for additional assessment, using pre-determined criteria to identify relevant studies. Study design criteria for inclusion in this review were: published systematic reviews of RCTs and RCTs in any language, at least single blinded, and containing more than 20 individuals of whom more than 80% were followed up. We included children aged between aged 2–16 years. There was no minimum length of follow-up required to include studies. We excluded all studies described as "open", "open label", or not blinded unless blinding was impossible. We included systematic reviews of RCTs and RCTs where harms of an included intervention were studied applying the same study design criteria for inclusion as we did for benefits. In addition, we use a regular surveillance protocol to capture harms alerts from organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA), which are added to the reviews as required. To aid readability of the numerical data in our reviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 22 ). The categorisation of the quality of the evidence (into high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the *Clinical Evidence* population and outcome of choice may represent only a small subset of the total outcomes reported, and population included, in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicalevidence.com).

## QUESTION What are the effects of treatments for dyssomnias in children?

## OPTION EXTINCTION AND GRADUATED EXTINCTION FOR DYSSOMNIA IN OTHERWISE HEALTHY CHILDREN

**Sleep onset, duration, and quality**

*Compared with no treatment* Extinction and graduated extinction may be more effective at improving sleep quality, improving settling, and reducing the number of weekly night wakes in otherwise healthy children who regularly wake up in the night (low-quality evidence).

**Bedtime tantrums**

*Compared with no treatment* Graduated extinction may be more effective in reducing the number and duration of bedtime tantrums in otherwise healthy children (very low-quality evidence).

*Compared with sleep hygiene* Graduated extinction may be no more effective in reducing the number and duration of bedtime tantrums compared with sleep hygiene in otherwise healthy children (very low-quality evidence).

**For GRADE evaluation of interventions for sleep disorders in children, see table, p 22 .**

**Benefits:**

**Extinction and graduated extinction versus no treatment in otherwise healthy children:** We found one systematic review (search date 2005, 5 RCTs, 303 children) comparing extinction or graduated extinction versus no treatment; the systematic review did not perform a meta-analysis. [29] Of the five RCTs included in the review, two RCTs did not meet *Clinical Evidence* reporting criteria; one RCT did not cover our population of interest (all children were <2 years of age), [30] and the other had a withdrawal rate of >20%. [31] The remaining RCTs are reported below.

The first RCT identified by the review (45 children aged 9–60 months who regularly woke in the night) found that both a sleep programme (behavioural advice booklet based on extinction plus support from staff) and the behavioural advice booklet alone significantly reduced the number of weekly night wakes (as recorded by the child's mother) compared with waiting list control at 4 weeks (6.9 with sleep programme *v* 4.9 with booklet only *v* 11.7 with waiting list control; P <0.05 for each treatment *v* control) (for details of the interventions see table 1, p 20 ). [32] The RCT found no significant difference in the number of weekly night wakes between the sleep programme compared with behavioural advice booklet alone (P value not reported).

The second RCT identified by the review (36 children aged 18–48 months who were having about 5 bedtime tantrums/week before treatment) compared three interventions: graduated extinction, sleep hygiene, and no treatment (for details of the interventions see table 1, p 20 ). It found that, compared with placebo, children receiving graduated extinction had significantly less-frequent and shorter bedtime tantrums during the 6 weeks of treatment (absolute results presented graphically; P <0.05), and at 3 and 6 weeks' follow-up, as reported by the parents (absolute results presented graphically; P <0.001). [33]

The third RCT identified by the review (49 children aged 16–48 months with at least 4 difficult bedtimes/week [taking at least 30 minutes to settle or not settling alone], 4 difficult night times/week [child waking in the night and not resettling without the parent, or sleeping in the parental bed], or both) (for details of the interventions see table 1, p 20 ) found that both extinction and graduated extinction significantly improved mean settling score ("good bedtimes" = number of bedtimes/week that the child settled in <10 minutes) and mean sleeping score ("good night times" = number of nights/week that the child slept through without sleeping with or waking up the parents) compared with waiting list control at 3 weeks (good bedtimes: 5.36 with extinction *v* 4.92 with graduated extinction *v* 0.62 with waiting list control; P = 0.0005 for each treatment *v* waiting list control; good night times: 3.43 with extinction *v* 4.91 with graduated extinction *v* 0.88 with waiting list control; P = 0.0005 for each treatment *v* waiting list control). [34] However, the difference between extinction and graduated extinction was not significant (P value not reported). The RCT also found that, compared with waiting list control, extinction significantly reduced verbal discipline (P = 0.001), decreased stress in parents (P = 0.02), and improved parent–child relationships (P = 0.002; all outcomes assessed on the Parenting Scale, absolute results tabulated). [34]

**Graduated extinction versus sleep hygiene in otherwise healthy children:**
See benefits of sleep hygiene in otherwise healthy children, p 6 .

**Harms:**

**Extinction and graduated extinction versus no treatment in otherwise healthy children:**
The systematic review found no adverse effects associated with behaviour programmes. [29]

**Graduated extinction versus sleep hygiene in otherwise healthy children:**
See harms of sleep hygiene in otherwise healthy children, p 6 .

**Comment:**

One RCT that found that a predictor of compliance and outcome with extinction treatment is stress about parenting and depression — mothers who were less depressed and stressed about parenting tended to have better outcomes with extinction. [34] No such predictor was found for graduated extinction. The RCT also achieved positive results with about 3 hours of therapist contact per person, suggesting that brief treatments can be effective.

The two RCTs that did not meet *Clinical Evidence* reporting criteria identified by the systematic review [29] also found that extinction and graduated extinction had beneficial effects. One RCT (156 mothers with infants aged 6–12 months with severe sleep problems) compared graduated extinction (parents responding to cries at increasing time intervals) versus no intervention. [30] It found that graduated extinction significantly reduced maternal reports of an infant sleep problem compared with no intervention at 2 months; however, there were no significant differences between groups at 4 months. Maternal depression was improved at 2 months with controlled crying compared with no intervention, but the difference was not significant.

The other RCT (50 children with sleep problems aged 6–54 months [mean 20 months]) compared extinction, scheduled awakenings, and no intervention. It found that extinction and scheduled awakenings decreased night waking and crying episodes compared with no intervention, but the extinction group showed the fastest improvement. The withdrawal rate for this RCT was high (17/50 [34%]). [31]

**Clinical guide:**
These findings are from short-term studies, and longer-term studies are required to assess the sustainability of the results of this treatment. We have not separated extinction and graduated extinction here, because combining them reflects practice: they are often used in combination, and

people often change from extinction to graduated extinction mid-treatment. Extinction can be upsetting to parents, and may not meet with consistent parental compliance, and this may lead to reinforcement of the negative behaviour. Graduated extinction may be less distressing for parents, and thus may be a more acceptable treatment option.

## OPTION EXTINCTION AND GRADUATED EXTINCTION FOR DYSSOMNIA IN CHILDREN WITH PHYSICAL DISABILITIES, LEARNING DISABILITIES, EPILEPSY, OR ATTENTION-DEFICIT DISORDER

**Sleep onset, duration, and quality**
*Compared with no treatment* Graduated extinction-based behavioural programmes supported with therapist's telephone calls may be more effective at improving settling and reducing the frequency and duration of night wakings; however, we don't know whether they are more effective in improving sleep duration after 3 months in children with severe learning disabilities and severe sleep problems (very low-quality evidence).

**Parental sleep**
*Compared with no treatment* Graduated extinction-based behavioural programmes supported with therapist's telephone calls may be more effective at improving parental sleep after 3 months in parents with children with severe learning disabilities and severe sleep problems (very low-quality evidence).

**For GRADE evaluation of interventions for sleep disorders in children,** **see table, p 22 .**

**Benefits:**

**Extinction and graduated extinction versus no treatment in children with physical disabilities, learning disabilities, epilepsy or attention-deficit disorder:**
We found one RCT (30 children, mean age 10 years, with any severe learning disability, and a severe sleep problem, and 1 form of a daytime challenging behaviour [for details of the interventions see table 1, p 20 ]) comparing an individually tailored graduated extinction-based behavioural programme supported with therapist telephone calls versus no treatment. [35] The RCT found that therapist treatment significantly improved mean Composite Sleep Index Score compared with no treatment post-treatment and at 3 months' follow-up (post-treatment: 6.62 with therapist treatment *v* 3.79 with no treatment; P = 0.001; 3 months: 6.29 with therapist treatment *v* 2.96 with no treatment; P = 0.001). The Composite Sleep Index Score covered the frequency and duration of settling and night wakings, could range from 0 (worst) to 12 (best), and was measured by parental questionnaire. The RCT also reported that treatment also significantly improved mothers' sleep periods compared with no treatment at 3 months' follow-up (+0.3 hours with therapist treatment *v* –0.4 hours with no treatment; P = 0.03), whereas there was no significant difference between the children's sleep periods (+0.2 hours with therapist treatment *v* +0.4 hours with control; P value not reported).

**Harms:**

**Extinction and graduated extinction versus no treatment in children with physical disabilities, learning disabilities, epilepsy, or attention-deficit disorder:**
The RCT did not report adverse effects. [35]

**Comment:**

**Extinction and graduated extinction versus placebo in children with physical disabilities, learning disabilities, epilepsy, or attention-deficit disorder:**
The RCT included in its sample children with a mix of disabilities. [35] It might have been preferable to use a sample of children with the same specific form of disability, as opposed to a mixture, or to conduct a subgroup analysis to ascertain whether treatment is more or less effective in certain types of disability. Treatment for the children's sleep problem seems to have had more beneficial effects on the mothers' sleep patterns than on their children's. The disparity between the results of the objective and subjective sleep measures could be because the treatment may have affected the children's signalling of their awake state to the parents, rather than their sleep quality or quantity. This may account for the improvement in the mothers' sleep. Alternatively, the authors suggest that the discrepancy may be because the objective variables used were primarily concerned with restlessness.

**Graduated extinction plus sleep hygiene versus placebo in children with physical disabilities, learning disabilities, epilepsy, or attention-deficit disorder:**
The effective use of a booklet-based treatment suggests that therapist contact may not be necessary. [36]

## OPTION SLEEP HYGIENE FOR DYSSOMNIA IN OTHERWISE HEALTHY CHILDREN

**Sleep onset, duration, and quality**
*Compared with no treatment* We don't know whether a bedtime routine is more effective at reducing night wakenings, or at improving sleep latency and total sleep duration, as no direct comparisons were performed (very low-quality evidence).

**Quality of life of carer**
*Compared with no treatment* We don't know whether a bedtime routine is more effective at improving maternal mood, as no direct comparisons were performed, but it may be more effective at improving parent's marital satisfaction (very low-quality evidence).

**Bedtime tantrums**
*Compared with no treatment* Sleep hygiene may be more effective in reducing the number and duration of bedtime tantrums in otherwise healthy children at 6 weeks (very low-quality evidence).

*Compared with graduated extinction* Sleep hygiene may be no more effective in reducing the number and duration of bedtime tantrums in otherwise healthy children (very low-quality evidence).

**Note**
Sleep hygiene in children has been categorised as Likely to beneficial by consensus.

**For GRADE evaluation of interventions for sleep disorders in children, see table, p 22 .**

**Benefits:**

**Sleep hygiene versus no treatment in otherwise healthy children:**
We found one systematic review (search date 1999, 1 RCT, 36 children) [37] and one subsequent RCT [38] comparing sleep hygiene versus no treatment.

The RCT identified by the systematic review (36 children aged 18–48 months who were having about 5 bedtime tantrums/week before treatment) compared three interventions: graduated extinction, sleep hygiene, and placebo. It found that, compared with placebo, children receiving sleep-hygiene treatment had tantrums before bedtime and settling problems less frequently and for shorter periods during the 6 weeks of treatment (results presented graphically; P <0.05), and at 3 and 6 weeks' follow-up (results presented graphically; P <0.001) as reported by their parents (for details of the intervention see table 1, p 20 ). [33] The RCT also found that the parents' marital satisfaction (measured as the difference in the pre- and post-Dyadic Adjustment Scale) was significantly improved with sleep hygiene compared with placebo (data not reported; P <0.02).

The subsequent RCT (199 children aged 18–36 months with a sleep problem but who did not have a severe sleep disorder) compared instruction to mothers to follow a bedtime routine (133 mothers) versus instruction to continue usual routine (control; 67 mothers) (for details of the intervention see table 1, p 20 ). [38] The RCT did not perform direct statistical comparisons between the groups, but compared results at baseline, 2 weeks, and 3 weeks. With the bedtime routine, the RCT found significant differences between baseline, 2 weeks, and 3 weeks in the number of night wakings (number of night wakings assessed by the Brief Instant Sleep Questionnaire [BISQ]: 1.3 at baseline *v* 0.9 at 2 weeks *v* 0.6 at 3 weeks; P <0.001), but it found no significant differences in sleep latency and total night-time sleep (sleep latency assessed by BISQ: 20.3 minutes at baseline *v* 16.9 minutes at 2 weeks *v* 16.3 minutes at 3 weeks; P = 0.01; total night-time sleep: 9.9 hours at baseline *v* 9.9 hours at 2 weeks *v* 10.0 hours at week 3; P = 0.61). The RCT found no significant differences in any of these variables between baseline, 2 weeks, and 3 weeks in the control group (number of night wakenings: 1.1 at baseline *v* 1.2 at 2 weeks *v* 1.0 at 3 weeks; P = 0.71; sleep latency: 21.8 minutes at baseline *v* 21.1 minutes at 2 weeks *v* 21.6 minutes at 3 weeks; P = 0.9; total night-time sleep: 9.8 hours at baseline *v* 9.8 hours at 2 weeks *v* 10.0 hours at week 3; P = 0.69). The RCT also reported significant differences in maternal mood (as assessed by the Profile of Mood States; lower scores are better) between baseline, week 2, and week 3 in the bed time-routine group (overall score not reported; P <0.001), but it found no significant differences in mood between baseline, week 2, and week 3 in the control group (overall score not reported; reported as not significant, P value not reported).

**Sleep hygiene versus graduated extinction in otherwise healthy children:**
The RCT identified by the first systematic review found similar improvements in the frequency and duration of tantrums before bedtime with sleep hygiene and graduated extinction (results presented graphically; significance not reported). [33]

**Harms:**

**Sleep hygiene versus no treatment in otherwise healthy children:**
The systematic review and RCT gave no information on adverse effects. [37] [38]

**Sleep hygiene versus graduated extinction in otherwise healthy children:**
The RCT gave no information on adverse effects. [33]

**Comment:**

**Clinical guide:**
This simple non-invasive set of options for parents should be a front-line treatment for sleep problems in children, especially in view of the difficulties some parents have with extinction methods. Although

no between-group comparisons have been carried out, the initial reduction of awakenings and the positive effect on maternal mood are sufficient to strongly suggest this first-line treatment.

## OPTION SLEEP HYGIENE FOR DYSSOMNIA IN CHILDREN WITH PHYSICAL DISABILITIES, LEARNING DISABILITIES, EPILEPSY, OR ATTENTION-DEFICIT DISORDER

**Note**
**We found no direct results from RCTs about the effects of sleep hygiene alone in the treatment of children with physical or learning disabilities.**

**For GRADE evaluation of interventions for sleep disorders in children, see table, p 22 .**

**Benefits:** **Sleep hygiene versus no treatment or other treatments in children with physical disabilities, learning disabilities, epilepsy, or attention-deficit disorder:**
We found no systematic review or RCTs.

**Harms:** **Sleep hygiene versus no treatment or other treatments in children with physical disabilities, learning disabilities, epilepsy, or attention-deficit disorder:**
We found no RCTs.

**Comment:** **Clinical guide:**
This simple non-invasive set of options for parents should be a front-line treatment for sleep problems in children, especially in view of the difficulties some parents have with extinction methods. For children with behavioural or learning difficulties, sleep hygiene is often used in conjunction with other behavioural treatments.

## OPTION MELATONIN FOR DYSSOMNIA IN OTHERWISE HEALTHY CHILDREN

**Sleep onset, duration, and quality**
*Compared with placebo* Melatonin may be more effective at improving sleep-onset time and total sleep time in otherwise healthy children (very low-quality evidence).

**Quality of life of child**
*Compared with placebo* Melatonin may be more effective at improving general health in otherwise healthy children (very low-quality evidence).

**Note**
Little is known about the long-term effects of melatonin, and the quality of the product purchased could be variable as melatonin is classified as a food supplement.

**For GRADE evaluation of interventions for sleep disorders in children, see table, p 22 .**

**Benefits:** **Melatonin versus placebo in otherwise healthy children:**
We found two systematic reviews, which identified the same RCTs (search date 2003, 2 RCTs, 102 children aged 6–12 years with sleep-onset insomnia [sleep-onset insomnia was defined as sleep onset later than 8.30 pm in children aged 6 years, then 15 minutes later a year until 12 years old; time from lights off until sleep had to be >30 minutes; >4 nights/week for >1 year]). [39] [40]

The first review performed a meta-analysis for sleep-onset latency, and found a significant difference between melatonin and placebo; however, this result was not clinically important (2 RCTs, 102 children; point estimate –16.7 minutes, 95% CI –29.4 minutes to –4.0 minutes; heterogeneity = 0; P = 0.0008). [39]

The second review did not perform any meta-analyses. [40]

The first RCT (40 children aged 6–12 years with sleep-onset insomnia) identified by the reviews found that melatonin 5 mg significantly improved mean time of sleep onset and total sleep time compared with placebo at 4 weeks (mean time of sleep onset: 9.09 p.m. [–1 hour 9 minutes] with melatonin *v* 10.06 p.m. [+45 minutes] with placebo; P = 0.005; total sleep time: 9 hours 43 minutes with melatonin *v* 9 hours 14 minutes with placebo; P = 0.026). [41] However, it found no significant difference between melatonin and placebo for sleep latency and wake-up time (sleep latency: 34.5 minutes with melatonin *v* 48.8 minutes with placebo; P = 0.128; wake-up time: 7.22 a.m. [–24 minutes] with melatonin *v* 7.21 a.m. [–1 minutes] with placebo; P = 0.144). Lights-off time and wake-up time were recorded by the parents; sleep latency and total sleep time were estimated; sleep onset was measured by actigraphy.

The second RCT (62 children aged 6–12 years with sleep-onset insomnia) identified by the reviews found that melatonin 5 mg improved mean time of sleep onset, wake-up time, sleep latency, and general health compared with placebo at 4 weeks (mean time of sleep onset: 9.00 p.m. [–1 hour 7 minutes] with melatonin *v* 9.54 p.m. [–10 minutes] with placebo; wake-up time: 7.32 a.m. [–19 minutes] with melatonin *v* 7.43 a.m. [+7 minutes] with placebo; sleep latency: 27 minutes with melatonin *v* 41 minutes with placebo; general health RAND-GHRI [General Health Rating Index]: 25.3 with melatonin *v* 24.6 with placebo; P values of comparisons between groups not reported). [42] Sleep-onset time was monitored by the parents, and general health score was measured by questionnaire to the parents; however, methods of measurement of other outcomes were not clear. In this RCT, the proportions of children with attention-deficit hyperactivity disorder (ADHD), and those receiving methylphenidate, were not similar between groups (melatonin group: 8/27 [30%] had ADHD, 6/27 [22%] took methylphenidate; placebo group: 20/35 [57%] had ADHD, 19/35 [54%] took methylphenidate; significance not reported). The second systematic review reported that methylphenidate has been associated with insomnia (no further data reported). [40]

**Harms:**

**Melatonin versus placebo in otherwise healthy children:**
The first review found no significant difference between melatonin and placebo in rates of the most commonly reported adverse effects (reported as not significant, results tabulated in review). [39] The most common adverse effects were headache, dizziness, nausea, and drowsiness.

The second review did not report adverse effects from the RCTs it identified. [40]

The first RCT identified by the reviews reported the development of mild generalised epilepsy in one child who took melatonin, during the course of the trial, after 4 months of melatonin. [41] Additionally, two children developed mild headaches during the first 2 days of treatment.

The second RCT identified by the reviews reported adverse effects including cold feelings, decrease of appetite, dizziness, and deterioration of mood after initial melatonin intake. [42] However, these effects ceased after 3 days of treatment.

**Comment:**

Little is known about the long-term effects of melatonin. To determine the effectiveness of this treatment on outcome measures other than sleep onset, more large-scale studies are needed. Additionally, the few studies we found (but excluded because of the small sample size [<20 people] or large attrition [>80%]) based results on a short treatment span. Such methodological weaknesses need to be addressed in future trials.

In the first RCT included in the reviews, at the 18-month follow-up, 13/38 (34%) children had ceased treatment because they no longer had a sleep problem, and only one child ceased treatment because of no improvement. [41] Although this may suggest long-term effectiveness, such results are based on only one trial. Furthermore, little is known about the adverse effects of long-term use of melatonin. One review reported that, because research on the effects of melatonin has been carried out mostly in children with physical or learning disabilities, subtle adverse effects of melatonin may have escaped observation. [40]

**Clinical guide:**
Data on melatonin dosages are scarce, particularly in children. However, there is some suggestion of receptor flooding at higher doses, and of efficacy at very low doses — although which children need the higher doses remains unclear. [43] [44] Since melatonin is classified as a food supplement rather than a drug, it is unlikely to be of "pharmaceutical grade" when purchased by consumers from the Internet or from health food shops.

## OPTION MELATONIN FOR DYSSOMNIA IN CHILDREN WITH ATTENTION-DEFICIT DISORDER, EPILEPSY, NEURODEVELOPMENTAL DISABILITIES, OR PHYSICAL DISABILITIES

**Sleep onset, duration, and quality**
*Compared with placebo in children with attention-deficit hyperactivity disorder, epilepsy, or neurodevelopmental disabilities* Melatonin may be more effective at improving sleep latency, sleep duration, and total sleep score in children with attention-deficit hyperactivity disorder, epilepsy, or neurodevelopmental disabilities (very low-quality evidence).

**Note**
Little is known about the long-term effects of melatonin, and the quality of the product purchased could be variable as melatonin is classified as a food supplement.

**For GRADE evaluation of interventions for sleep disorders in children, see table, p 22 .**

**Benefits:**

**Melatonin versus placebo in children with attention-deficit hyperactivity disorder (ADHD):**
We found one small RCT. [45] The RCT (crossover design: 10 days' treatment with 5-day washout period; 23 children aged 6–14 years with ADHD and initial insomnia >60 minutes; two-thirds taking concomitant methylphenidate, one third taking concomitant dextroamfetamine) found that melatonin 5 mg significantly reduced sleep-onset latency (SOL) compared with placebo over 10 days (measured using an actigraph; mean SOL: 46.4 minutes with melatonin *v* 62.1 minutes with placebo; P <0.01). Melatonin treatment also significantly increased total night-time sleep by 15 minutes compared with placebo (P <0.01). [45]

**Melatonin versus placebo in children with epilepsy:**
We found no systematic review, but found two small RCTs published by the same centre. [46] [47]

The first RCT (31 children aged 3–12 years with epilepsy who had been seizure free for the previous 6 months, all receiving sodium valproate for epilepsy) found that melatonin (6 mg for children aged <9 years who weighed <30 kg; 9 mg for children aged more >9 years who weighed >30 kg; dose of melatonin outside these weight ranges for the age group not clear) significantly decreased the total sleep score at 4 weeks compared with placebo (score range 26–130, lower score indicates fewer sleep problems: median percentage decrease: 24% with melatonin *v* 14% with placebo; P = 0.005). [46] The total sleep score was from the Sleep Behavior Questionnaire, which assessed the quantity and quality of sleep, usual bedtime and waking time, sleep latency, parental involvement at sleep onset, night waking, co-sleeping, night-time events, daytime drowsiness, and unrefreshing sleep; a decrease in score corresponds to fewer sleep problems. [46] However, there was no significant difference between groups in actual post-treatment total sleep score (median: 52.5 with melatonin *v* 55.0 with placebo; P = 0.76). [46]

The second RCT (31 children aged 3 to 12 years with epilepsy who had been seizure free for the previous 6 months; all taking carbamazepine; included on basis of epilepsy, not sleep disorder) [47] also found that melatonin (same dosing as RCT above [46] ) significantly improved sleep at 4 weeks compared with placebo (score range 26–130, lower score indicates fewer sleep problems: % decrease in median total sleep score: 8% with melatonin *v* 15% with placebo, P = 0.01; post-treatment median score: 54.5 with melatonin *v* 57.0 with placebo; P = 0.03). [47] There were significant differences at baseline between groups, with significantly worse baseline sleep problems in children receiving placebo (P = 0.001). This means that, although % decrease in sleep problems appears significantly higher in the placebo group, the post-treatment scores in fact favour melatonin; these results are therefore difficult to interpret and should be treated with caution. There were no significant differences between treatment and control groups on any of the other included measures — daytime drowsiness, parasomnias, or sleep fragmentation (absolute data tabulated; P >0.05 for all outcomes). [47]

**Melatonin versus placebo in children with neurodevelopmental disabilities:**
We found two systematic reviews (search dates 2002 [48] and 2006 [49] ) comparing melatonin versus placebo in children with neurodevelopmental disabilities, which both identified the same three RCTs. Neither review performed a meta-analysis so we report here only the single RCT that met *Clinical Evidence* reporting criteria. [50]

The RCT (51 children, 31 male, mean age 7.38 years with multiple neurodevelopmental disabilities and dyssomnia) compared controlled-release melatonin 5 mg daily versus placebo for 25 days. [50] The crossover trial protocol involved 10 days of melatonin or placebo (order of intervention randomised), followed by a placebo washout for 3–5 days, followed by 10 days of the alternate intervention (melatonin or placebo second). It is unclear whether the washout period was sufficient to exclude crossover effects. The RCT did not report pre-crossover results. Fifteen of the participants had been taking melatonin before the trial commenced and discontinued treatment 2 weeks prior to entry into the trial. The RCT found that melatonin modestly but significantly improved total night-time sleep compared with placebo (mean: 535 minutes with melatonin *v* 504 minutes with placebo; mean increase in sleep of 31 minutes with melatonin *v* placebo; P <0.01). Analysis of secondary outcome measures of sleep characteristics found that melatonin significantly reduced sleep latency compared with placebo (mean: 43 minutes with melatonin *v* 67 minutes with placebo; mean reduction of 24 minutes with melatonin *v* placebo; P <0.01).

**Harms:**

**Melatonin versus placebo in children with attention-deficit hyperactivity disorder (ADHD):**
All reported adverse effects in the RCT [45] were mild or moderate, with the exception of a migraine, which was rated as severe. No serious adverse events, clinically significant changes in vital signs, or abnormalities were apparent on physical examination. [45]

**Melatonin versus placebo in children with epilepsy:**
The two RCTs reported no adverse effects, and children remained seizure free during the 8 weeks. [46] [47] Reports have suggested that, because of the contraceptive properties of melatonin, such

treatment could affect the onset of puberty. [51] [52] However, there is conflicting evidence about melatonin's effect on seizures. One small cohort study found that seizure frequency increased in 4/6 (67%) of neurologically disabled children who took melatonin. [53] Seizure activity returned to pre-treatment levels when the children discontinued melatonin.

**Melatonin versus placebo in children with neurodevelopmental disabilities:**
The RCT reported that "no adverse effects" were associated with melatonin. [50]

**Comment:**

**Melatonin versus placebo in children with attention-deficit hyperactivity disorder (ADHD):**
We also found one long-term open-label follow-up of an RCT assessing melatonin in children with ADHD. [54] The initial RCT randomised 105 children (mean age 8.72 years) with ADHD to receive melatonin or placebo for 4 weeks. At the end of the RCT, all participants were offered melatonin treatment in the context of regular care. The follow-up study assessed 90% of participants at a median of 3.7 years. The follow-up study found that 65% of the children still used melatonin daily and 12% occasionally. Parents judged long-term melatonin treatment to be effective against sleep-onset problems in 88% of cases, at improving behaviour in 71% cases, and at improving mood in 61% cases. Temporary discontinuation of treatment (mostly during a holiday period) resulted in a delay of sleep onset in 92% of the children. The RCT reported no serious adverse events or treatment-related co-morbidities; however, 20% of children experienced adverse events that they or their parents attributed to melatonin treatment. In 53% of children with adverse events, the events were self-limiting. In 32% children with adverse events, the events persisted, and these included sleep-maintenance insomnia, excessive morning sedation, decreased mood and headache, profuse perspiration, and daytime laziness. No new cases of epilepsy were reported.

**Melatonin versus placebo in children with neurodevelopmental disabilities:**
We found one follow-up study [55] of the RCT reported above (51 children, 31 male, mean age 7.38 years with multiple neurodevelopmental disabilities and dyssomnia [50] ) conducted and published while the original RCT was still in press. At the end of the RCT, all participants continued in an open-label follow-up study of melatonin. The follow-up study assessed 82% participants for up to 3.8 years. It found that all carers reported a benefit to their child and to their families on specific parameters (sleep, overall health, development, education/learning, behaviour). The study reported no adverse effects attributed to treatment, no epileptic seizures activated by melatonin in the 19 children who had seizure disorders, and no new cases of seizures.

We found one systematic review (search date 2008) of adults and children with mental disability, Rett's syndrome, tuberous sclerosis, developmental disabilities, mental retardation/learning disability, autistic spectrum disorder, intellectual disability, or Angelman's syndrome comparing melatonin 0.5 to 9 mg daily versus placebo for sleep problems. [56] The review did not analyse results separately for adults and children, and so did not meet *Clinical Evidence* reporting criteria. It found that melatonin significantly decreased sleep latency and increased total sleep time at 30 to 70 days compared with placebo (sleep latency, 7 RCTs, 166 people: WMD –34 minutes, 95% CI –43 minutes to –25 minutes; P <0.001; total sleep time, 7 RCTs, 153 people; WMD 0.83 hours, 95% CI 0.57 hours to 1.08 hours; P <0.001; absolute numbers not reported). The authors of the systematic review also reported that melatonin significantly decreased the mean number of wakes per night at 30 to 70 days compared with placebo, although the reported confidence intervals crossed 0 (mean number of wakes per night, 8 RCTs, 167 people: WMD –0.16 wakes, 95% CI –0.30 wakes to +0.02 wakes; P = 0.024; absolute numbers not reported). The RCTs were clinically heterogeneous with respect to type of neurodevelopment disability, age, length of treatment, dose, type of melatonin, and time of administration, and thus it is unclear whether the results of the review are applicable to children.

**Dosing of melatonin:**
Data on melatonin dosages are scarce, particularly in children. However, there is some suggestion of receptor flooding at higher doses, and of efficacy at very low doses — although which children need the higher doses remains unclear. [43] [44]

In the systematic review in children with neurodevelopmental disabilities, [56] differences in timing of melatonin administration did not affect the results of the meta-analysis; outcomes of studies with fixed times of administration were similar to those of studies with varying times of administration. There was also no association between melatonin dose and the effect on sleep parameters in the studies included in the meta-analysis.

Since melatonin is classified as a food supplement rather than a drug, it is unlikely to be of "pharmaceutical grade" when purchased by consumers from the Internet or from health food shops.

**Clinical guide:**
Little is known about the long-term effects of melatonin in children, although longer-term follow-up studies are emerging. [54] [55] To determine the effects of this treatment on outcome measures other than sleep onset, more large-scale studies are needed. Additionally, the few studies we found (but excluded) because of the small sample size (<20 people) or large attrition (>80%) based results on a short treatment span. Such methodological weaknesses need to be addressed in future trials. Although melatonin can be prescribed safely in individuals with sleep problems and intellectual disability, prescribers should realise that its long-term treatment effects are still unclear.

## OPTION ANTIHISTAMINES FOR DYSSOMNIA

**Sleep onset, duration, and quality**
*Compared with placebo* Antihistamines may be more effective at reducing night wakenings and decreasing sleep latency in children with dyssomnia, but we don't know if they are more effective at increasing sleep duration (very low-quality evidence).

**For GRADE evaluation of interventions for sleep disorders in children, see table, p 22 .**

**Benefits:**

**Antihistamines versus placebo:**
We found one crossover RCT (50 children aged 2–12 years [mean 5.2 years] with sleep disorders [difficulty falling asleep, interrupted sleep, abbreviated sleep, restless sleep, recurrent nightmares/terrors, difficulty awakening]) comparing diphenhydramine 1.0 mg/kg once daily before bedtime versus placebo each for 1 week. [57] Outcomes were assessed by parents using sleep records. It found that diphenhydramine significantly reduced sleep latency and number of night awakenings at 1 week (sleep latency: P <0.05; night awakenings: P <0.01; absolute numbers not reported). It found no significant difference between groups in sleep duration at 1 week (sleep duration: P = 0.07; absolute numbers not reported). Only 41/50 (82%) children received the recommended dosage.

**Harms:**

**Antihistamines versus placebo:**
The RCT found that 1/50 (2%) children experienced daytime drowsiness with diphenhydramine, and 1/50 (2%) children had a mild rash. [57]

**Comment:**

The results from one RCT indicate that diphenhydramine is a safe, effective bedtime sleep aid for paediatric patients and more effective than placebo. [57]

The regulation of antihistamines is different in different countries, and commonly they are not recommended as hypnotics in children. For example, promethazine is the only antihistamine licensed for sedation in UK, and diphenhydramine is available as a component of a cough syrup, but is not recommended for children under 6 years of age. The use of antihistamines may therefore be determined by country-specific pharmaceutical regulation.

## OPTION BEHAVIOURAL THERAPY PLUS ANTIHISTAMINES FOR DYSSOMNIA New

**We found no direct information from RCTs about behavioural therapy plus antihistamines in the treatment of children with dyssomnia.**

**For GRADE evaluation of interventions for sleep disorders in children, see table, p 22 .**

**Benefits:** We found no systematic review or RCTs.

**Harms:** We found no RCTs.

**Comment:** As we found no specific trials on behavioural therapy plus antihistamines, we cannot draw conclusions about their combined efficacy. However, because antihistamines are likely to be beneficial, and as they are commonly used by paediatricians and general practitioners in different countries, the combination of behavioural therapy plus antihistamines is unlikely to be harmful, and could potentially be a reasonable intervention strategy.

## OPTION BEHAVIOURAL THERAPY PLUS BENZODIAZEPINES FOR DYSSOMNIA

**We found no direct information from RCTs about behavioural therapy plus benzodiazepines in the treatment of children with dyssomnia.**

**For GRADE evaluation of interventions for sleep disorders in children, see table, p 22 .**

**Benefits:** We found no systematic review or RCTs.

**Harms:** We found no RCTs.

**Comment:** None.

## OPTION BEHAVIOURAL THERAPY PLUS CHLORAL AND DERIVATIVES FOR DYSSOMNIA

**We found no direct information from RCTs about behavioural therapy plus chloral and derivatives (chloral hydrate, triclofos sodium) in the treatment of children with dyssomnia.**

**For GRADE evaluation of interventions for sleep disorders in children,** **see table, p 22 .**

**Benefits:** We found no systematic review or RCTs.

**Harms:** We found no RCTs.

**Comment:** None.

## OPTION EXERCISE FOR DYSSOMNIA

**We found no direct information from RCTs about exercise in the treatment of children with dyssomnias.**

**For GRADE evaluation of interventions for sleep disorders in children,** **see table, p 22 .**

**Benefits:** We found no systematic review or RCTs.

**Harms:** We found no RCTs.

**Comment:** **Clinical guide:**
Although, intuitively, exercise would seem helpful for insomnia, there is a lack of evidence to support this theory.

## OPTION LIGHT THERAPY FOR DYSSOMNIA

**We found no direct information from RCTs about light therapy in treating children with dyssomnia.**

**For GRADE evaluation of interventions for sleep disorders in children,** **see table, p 22 .**

**Benefits:** We found no systematic review or RCTs.

**Harms:** We found no RCTs.

**Comment:** None.

## OPTION SLEEP RESTRICTION FOR DYSSOMNIA

**We found no direct information from RCTs about sleep restriction in the treatment of children with dyssomnia.**

**For GRADE evaluation of interventions for sleep disorders in children,** **see table, p 22 .**

**Benefits:** We found no systematic review or RCTs.

**Harms:** We found no RCTs.

**Comment:** **Clinical guide:**
Although, intuitively, sleep restriction would seem helpful for dyssomnias, there is currently a lack of evidence to support this theory.

## QUESTION What are the effects of treatments for parasomnias in children?

## OPTION ANTIHISTAMINES FOR PARASOMNIAS

**We found no direct information from RCTs about antihistamines in treating children with parasomnias.**

**For GRADE evaluation of interventions for sleep disorders in children,** **see table, p 22 .**

**Benefits:** We found no systematic review or RCTs.

**Harms:** We found no RCTs.

**Comment:** None.

## OPTION BEHAVIOURAL THERAPY PLUS BENZODIAZEPINES FOR PARASOMNIAS

**We found no direct information from RCTs about behavioural therapy plus benzodiazepines in the treatment of children with parasomnias.**

**For GRADE evaluation of interventions for sleep disorders in children,** **see table, p 22 .**

**Benefits:** We found no systematic review or RCTs.

**Harms:** We found no RCTs.

**Comment:** None.

## OPTION BEHAVIOURAL THERAPY PLUS CHLORAL AND DERIVATIVES FOR PARASOMNIAS

**We found no direct information from RCTs about behavioural therapy plus chloral and derivatives (chloral hydrate, triclofos sodium) in the treatment of children with parasomnias.**

**For GRADE evaluation of interventions for sleep disorders in children,** **see table, p 22 .**

**Benefits:** We found no systematic review or RCTs.

**Harms:** We found no RCTs.

**Comment:** None.

## OPTION BENZODIAZEPINES FOR PARASOMNIAS New

**We found no direct information from RCTs about benzodiazepines in the treatment of children with parasomnias.**

**For GRADE evaluation of interventions for sleep disorders in children,** **see table, p 22 .**

**Benefits:** We found no systematic review or RCTs.

**Harms:** We found no RCTs.

**Comment:** In children with organic cerebral disorders, benzodiazepines (midazolam) might be effective in reducing the episodes of sleep terrors and other parasomnias. [58] However, benzodiazepines are rarely used in paediatric clinical practice, but could be used in severe cases of parasomnia if the child's safety is a concern.

## OPTION 5-HYDROXYTRYPTOPHAN FOR PARASOMNIAS New

**We found no direct information from RCTs about 5-hydroxytryptophan in the treatment of children with parasomnias.**

**For GRADE evaluation of interventions for sleep disorders in children,** **see table, p 22 .**

**Benefits:** **5-hydroxytryptophan (5-HTP) versus no treatment:**
We found no systematic review or RCTs that met our inclusion criteria.

**Harms:** **5-hydroxytryptophan (5-HTP) versus no treatment:**
We found no RCTs.

**Comment:** We found two RCTs assessing 5-HTP in children with sleep terrors, other parasomnias (somnambulism and somniloquy), and frequent awakening that did not meet our inclusion criteria owing to weak methods (lack of blinding [59] and high loss to follow-up [only 52% followed up in assessment of outcome of sleep disorders]). [60] The open-label RCT (45 children) compared 5-HTP (31 children) versus no treatment (14 children). The RCT did not assess the significance of the difference in outcomes between groups. It found that proportionately more children receiving 5-HTP than no treatment had >50% reduction of sleep terrors (proportion who responded: 29/31 [94%] with 5-HTP *v* 2/14 [14%] with no treatment; significance not assessed). [59] The disproportionate randomisation

may have contributed to the low event rate in the control group, so these results should be interpreted with caution. The second RCT (48 children, crossover design) assessed headache as a primary outcome and did not directly compare 5-HTP versus no treatment. [60] An assessment of outcomes after crossover found that, when taking 5-HTP, children had lower rates of frequent awakenings and of some parasomnias such as night terrors, somnambulism, and somniloquy (no further data reported). The RCTs reported no adverse effects associated with 5-HTP, but they are likely to have been underpowered to detect adverse effects.

**Clinical guide:**
It has been reported that L-tryptophan (not 5-HTP) caused an epidemic of eosinophilia-myalgia syndrome (EMS) in the US in 1989. [61]

All the findings indicate that the illness was probably triggered by an impurity formed when the manufacturing conditions were modified. Since then, several reports have examined the methodology of the epidemiological studies of the association between L-tryptophan and EMS and contest the validity of the conclusions from these studies, and therefore 5-HTP, which had been removed from the market, was subsequently re-approved. In comparison with antidepressant and hypnotic drugs, 5-HTP is characterised by a particularly low level of adverse effects. [62]

## OPTION MELATONIN FOR PARASOMNIAS IN HEALTHY CHILDREN OR IN CHILDREN WITH ATTENTION-DEFICIT DISORDER, EPILEPSY, NEURODEVELOPMENTAL DISABILITIES, OR PHYSICAL DISABILITIES

**Parasomnia severity**
*Compared with placebo* We don't know whether melatonin is effective in decreasing parasomnia scores in children with epilepsy (very low-quality evidence).

**Note**
We found no direct information from RCTs about melatonin in the treatment of otherwise healthy children with parasomnias.

**Adverse effects**
Little is known about the long-term effects of melatonin, and the quality of the product purchased could be variable.

**For GRADE evaluation of interventions for sleep disorders in children,** **see table, p 22 .**

**Benefits:**

**Melatonin versus placebo in otherwise healthy children:**
We found no systematic review or RCTs examining the effect of melatonin on otherwise healthy children with parasomnia.

**Melatonin versus placebo in children with epilepsy:**
We found no systematic review but found two RCTs. [46] [47] The first RCT (31 children aged 3–12 years with epilepsy who were seizure free for the previous 6 months; all taking concomitant sodium valproate) found that melatonin (6 mg for children aged <9 years who weighed <30 kg; 9 mg for children aged >9 years who weighed >30 kg; dose of melatonin outside these weight ranges for an unspecified age group) significantly decreased the median parasomnia score (a decrease in parasomnia score reflects the median percentage decrease of the parasomnia part of the Sleep Behavior Questionnaire) at 4 weeks compared with placebo (60% decrease with melatonin *v* 36% decrease with placebo; P = 0.03). [46] The second RCT (31 children aged 3–12 years with epilepsy who had been seizure free for the previous 6 months; all taking concomitant carbamazepine) found that melatonin (same doses as RCT above [46] ) had no significant effect on parasomnia score at 4 weeks compared with placebo (7.5 with melatonin *v* 7.5 with placebo). [47] The children in both of these RCTs were included on the basis of their epilepsy, not any sleep disorder.

**Harms:**

**Melatonin versus placebo in otherwise healthy children:**
We found no RCTs.

**Melatonin versus placebo in children with epilepsy:**
No adverse effects were observed, and children remained seizure free during the 8 weeks of both RCTs. [47] [46] See also harms of melatonin for dyssomnias in children with attention-deficit disorder, epilepsy, or neurodevelopmental disabilities, p 9 .

**Comment:**

See also comment of melatonin for dyssomnias in children with attention-deficit disorder, epilepsy, or neurodevelopmental disabilities, p 9 .

## OPTION SAFETY/PROTECTIVE INTERVENTIONS FOR PARASOMNIAS

**We found no direct results from RCTs about safety/protective interventions in the treatment of children with parasomnias.**

**For GRADE evaluation of interventions for sleep disorders in children,** **see table, p 22 .**

**Benefits:** We found no systematic review or RCTs.

**Harms:** We found no RCTs.

**Comment:** None.

## OPTION SCHEDULED WAKING FOR PARASOMNIAS

**We found no direct information from RCTs about scheduled waking in the treatment of children with parasomnias.**

**For GRADE evaluation of interventions for sleep disorders in children,** **see table, p 22 .**

**Benefits:** We found no systematic review or RCTs.

**Harms:** We found no RCTs.

**Comment:** **Clinical guide:**
Intuitively, scheduled waking would seem to be a promising treatment; however, high-quality trials are lacking.

## OPTION SLEEP HYGIENE FOR PARASOMNIAS

**We found no direct information from RCTs about sleep hygiene in the treatment of children with parasomnias.**

**For GRADE evaluation of interventions for sleep disorders in children,** **see table, p 22 .**

**Benefits:** We found no systematic review or RCTs.

**Harms:** We found no RCTs.

**Comment:** None.

## OPTION SLEEP RESTRICTION FOR PARASOMNIAS

**We found no direct information from RCTs about sleep restriction in the treatment of children with parasomnias.**

**For GRADE evaluation of interventions for sleep disorders in children,** **see table, p 22 .**

**Benefits:** We found no systematic review or RCTs.

**Harms:** We found no RCTs.

**Comment:** None.

## GLOSSARY

**Actigraphy** An actigraph is a motion sensing device. It can be worn on the wrist overnight to provide data when a person falls asleep owing to change in the person's motion.

**Extinction** involves the removal of the positive reinforcement for the child's resistance to go to bed and awakenings by ignoring demands for attention. The child is placed in its bed and ignored pending sleep onset.

**Graded extinction** follows the same principle as extinction, but involves the gradual withdrawal of parental attention. It may be recommended that parents respond to the child's cries at lengthening intervals to teach the child to soothe itself to sleep. [44] For example, parents may initially respond to cries after 2 minutes, then on the next occasion after 4 minutes and so on to a maximum of 20 minutes. Alternatively, parents may gradually increase the physical distance between themselves and the child. [63] For example, the parent may start off sitting next to the child's bed, then on the second night move 30 cm away and so on until the parent is outside the child's room.

**Parasomnias** are undesirable phenomena (physical or behavioural events) that occur predominantly during sleep. They can include nightmares, sleep terror disorder, and sleepwalking.

**Scheduled waking** is based on the rationale that by systematically waking the child before they usually awake the likelihood of spontaneous awakenings is reduced. [64] The frequency of the scheduled wakes is gradually reduced and eventually discontinued.

**Sleep hygiene** , also referred to as positive routines, is an umbrella term for several modifications to the environment, and to behaviour that parents would perform in order to prepare their child for sleep in a more effective way. Examples include: removing caffeine from the child's diet, a short regular routine leading up to bed, ensuring the bedroom environment is conducive to sleep (dark, quiet, comfortable, no extreme temperatures), and avoiding boisterous play immediately before bedtime. [31]

**Sleep latency** is the time between going to bed and going to sleep.

**Sleep restriction** is intended to increase the sleep efficiency of the child (the ratio of total sleep time to time spent in bed). The child is only allowed in bed when sleeping and the time allowed in bed is gradually increased. This increases the association of being asleep and being in bed.

**Dyssomnias** are disorders that produce either excessive daytime sleepiness or difficulty initiating or maintaining sleep. They can be intrinsic, extrinsic, or circadian rhythm sleep disorders.

**Low-quality evidence** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

**Very low-quality evidence** Any estimate of effect is very uncertain.

## SUBSTANTIVE CHANGES

**Behavioural therapy plus antihistamines for dyssomnia** New option for which we found no systematic reviews or RCTs. Therefore categorised as Unknown effectiveness.

**Benzodiazepines for parasomnias** New option for which we found no systematic reviews or RCTs. Therefore categorised as Unknown effectiveness.

**5-hydroxytryptophan for parasomnias** New option for which we found no systematic review or RCTs of sufficient quality. Therefore categorised as Unknown effectiveness.

**Antihistamines for dyssomnia** One RCT added comparing diphenhydramine versus placebo in children with dyssomnia. [57] It found that diphenhydramine reduced sleep latency and number of night awakenings at 1 week; however, it found no significant difference in sleep duration at 1 week. The trial represents the only evidence we found assessing antihistamines and outcomes were assessed at only 1 week, therefore categorisation unchanged (Unknown effectiveness).

**Extinction and graduated extinction for dyssomnia in otherwise healthy children** One systematic review added (search date 2005), [29] which compared extinction and graduated extinction versus no treatment in children with dyssomnia. The review identified no additional RCTs to those already reported in this *Clinical Evidence* review. Therefore categorisation unchanged (Likely to be beneficial).

**Melatonin for dyssomnias in children with attention-deficit disorder, epilepsy, neurodevelopmental disabilities, or physical disabilities** One large RCT added, which found that melatonin modestly improved total night-time sleep and decreased sleep latency compared with placebo. [50] However, little is known about the long-term effects of melatonin. Categorisation changed from Unknown effectiveness to Trade off between benefits and harms.

**Sleep hygiene for dyssomnia in otherwise healthy children** One RCT added, [38] which assessed instruction to follow a bedtime routine and no intervention. However, the RCT performed no direct comparisons between groups, and it is therefore difficult to draw conclusions from this RCT. Categorisation unchanged (Likely to be beneficial by consensus).

## REFERENCES

1. American Academy of Sleep Medicine. *Diagnostic and coding manual: international classification of sleep disorders.* 2nd ed: American Academy of Sleep Medicine. Westchester, IL, USA: 2005.
2. Mindell JA, Emslie G, Blumer J, et al. Pharmacologic management of insomnia in children and adolescents: consensus statement. *Pediatrics* 2006;117:e1223–e1232.[PubMed]
3. Quine L. Sleep problems in children with mental handicap. *J Ment Defic Res* 1991;35:269–290.[PubMed]
4. Pahl J, Quine L. *Families with mentally handicapped children: a study of stress and of service response*. Report to the South East Thames Regional Health Authority, University of Kent at Canterbury, UK: 1984.
5. Mindell JA. Sleep disorders in children. *Health Psychol* 1993:12;151–162.[PubMed]
6. Tynjala J, Kannas L, Valimaa R. How young Europeans sleep. *Health Educ Res* 1993:8;69–80.[PubMed]
7. Dollinger SJ. On the varieties of childhood sleep disturbance. *J Clin Child Psychol* 1982;11:107–115.
8. Jenkins S, Bax M, Hart H. Behaviour problems in preschool children. *J Child Psychol Psychiatry* 1980;21:5–17.[PubMed]
9. Salzarulo P, Chevalier A. Sleep problems in children and their relationships with early disturbances of the waking-sleeping rhythms. *Sleep* 1983;6:47–51.[PubMed]
10. Kataria S, Swanson MS, Trevathon GE. Persistence of sleep disturbances in preschool children. *J Pediatr* 1987;110:642–646.[PubMed]
11. Richman N, Graham J. A behaviour screening questionnaire for use with three year old children. *J Child Psychol Psychiatry* 1971;12:5–33.
12. Carroll JL, McColley SA, Marcus CL, et al. Inability of clinical history to distinguish primary snoring from obstructive sleep apnea syndrome in children. *Chest* 1995;108:610–618.[PubMed]
13. Quine L. Severity of sleep problems in children with severe learning difficulties: description and correlates. *J Community Appl Soc Psychol* 1992;2:247–268.
14. Bruni O, Ferri R, D'Agostino G, et al. Sleep disturbances in Angelman syndrome: a questionnaire study. *Brain Dev* 2004;26:233–240.[PubMed]
15. Miano S, Bruni O, Elia M, et al. Sleep in children with autistic spectrum disorder: a questionnaire and polysomnographic study. *Sleep Med* 2007;9:64–70.[PubMed]

16. France KG, Blampied NM. Infant sleep disturbance: description of a problem behaviour process. *Sleep Med Rev* 1999;3:265–280.
17. Weissbluth M, Davis AT, Poncher J. Night waking in 4- to 8-month-old-infants. *J Pediat* 1984;104:477–480.[PubMed]
18. Richman N. A community survey of characteristics of one-to-two-year-olds with sleep disruptions. *J Am Acad Child Psych* 1981;20:281–291.
19. Jimmerson KR. Maternal, environmental, and temperamental characteristics of toddlers with and toddlers without sleep problems. *J Pediatr Health Care* 1991;5:71–77.[PubMed]
20. Kordas K, Siegel EH , Olney DK , et al. The effects of iron and/or zinc supplementation on maternal reports of sleep in infants from Nepal and Zanzibar. *J Dev Behav Pediatr* 2009;30:131–139.[PubMed]
21. Kordas K, Siegel EH, Olney DK, et al. Maternal reports of sleep in 6-18 month-old infants from Nepal and Zanzibar: association with iron deficiency anemia and stunting. *Early Hum Dev* 2008;84:389–398.[PubMed]
22. Picchietti DL, Stevens HE. Early manifestations of restless legs syndrome in childhood and adolescence. *Sleep Med* 2008;9:770–781.[PubMed]
23. Mohri I, Kato-Nishimura K, Tachibana N, et al. Restless legs syndrome (RLS): an unrecognized cause for bedtime problems and insomnia in children. *Sleep Med* 2008;9:701–702.[PubMed]
24. Ungerer JA, Sigman M, Beckwith L, et al. Sleep behavior of preterm children at three years of age. *Dev Med Child Neurol* 1983;25:297–304.[PubMed]
25. Zucconi M, Bruni O. Sleep disorders in children with neurological diseases. *Semin Pediatr Neurol* 2001;8:258–275.
26. Wiggs L, Stores G. Severe sleep disturbance and daytime challenging behaviour in children with severe learning disabilities. *J Intellect Disabil Res* 1996;40:518–528.[PubMed]
27. Durand VM, Mindell JA. Behavioral treatment of multiple childhood sleep disorders. Effects on child and family. *Behav Modif* 1990;14:37–49.[PubMed]
28. Rajna P, Veres J. Correlation between night sleep duration and seizure frequency in temporal lobe epilepsy. *Epilepsia* 1993;34:574–579.[PubMed]
29. Mindell JA, Kuhn B, Lewin DS, et al. Behavioral treatment of bedtime problems and night wakings in infants and young children. An American Academy of Sleep Medicine review. *Sleep* 2006;29:1263–1276.[PubMed]
30. Hiscock H, Wake M. Randomised controlled trial of behavioural infant sleep intervention to improve infant sleep and maternal mood. *BMJ* 2002;324:1062–1065.[PubMed]
31. Rickert VI, Johnson CM. Reducing nocturnal awakenings and crying episodes in infants and young children: a comparison between scheduled awakenings and systematic ignoring. *Pediatrics* 1988;81:203–211.[PubMed]
32. Seymour FW, Brock P, During M, et al. Reducing sleep disruptions in young children: evaluation of therapist-guided and written information approaches: a brief report. *J Child Psychol Psychiatry* 1989;30:913–918.[PubMed]
33. Adams LA, Rickert VI. Reducing bedtime tantrums: comparison between positive routines and graduated extinction. *Pediatrics* 1989;84:756–759.[PubMed]
34. Reid MJ, Walter AL, O'Leary SG. Treatment of young children's bedtime refusal and nighttime wakings: a comparison of "standard" and graduated ignoring procedures. *J Abnorm Child Psychol* 1999;27:5–16.[PubMed]
35. Wiggs L, Stores G. Behavioural treatment for sleep problems in children with severe learning disabilities and challenging daytime behaviour: effect on sleep patterns of mother and child. *J Sleep Res* 1998;7:119–126.[PubMed]
36. Montgomery P, Stores G, Wiggs L. The relative efficacy of two brief treatments for sleep problems in young learning disabled (mentally retarded) children: a randomised controlled trial. *Arch Dis Child* 2004;89:125–130.[PubMed]
37. Mindell JA. Empirically supported treatments in pediatric psychology: bedtime refusal and night wakings in young children. *J Pediatr Psychol* 1999;24:465–481.[PubMed]
38. Mindell JA, Telofski LS, Wiegand B, et al. A nightly bedtime routine: impact on sleep in young children and maternal mood. *Sleep* 2009;32:599–606.[PubMed]
39. Buscemi N, Vandermeer B, Hooton N, et al. The efficacy and safety of exogenous melatonin for primary sleep disorders: a meta-analysis. *J Gen Intern Med* 2005;20:1151–1158.[PubMed]
40. Armour D, Paton C. Melatonin in the treatment of insomnia in children and adolescents. *Psychiatr Bull* 2004;28:222–224. Search date 2003.
41. Smits MG, Nagtegaal EE, van der Heijden J, et al. Melatonin for chronic sleep onset insomnia in children: a randomized placebo-controlled trial. *J Child Neurol* 2001;16:86–92.[PubMed]
42. Smits MG, van Stel HF, van der Heijden K, et al. Melatonin improves health status and sleep in children with idiopathic chronic sleep-onset insomnia: a randomized placebo-controlled trial. *J Am Acad Child Adolesc Psychiatry* 2003;42:1286–1293.[PubMed]
43. Brzezinski A, Vangel MG, Wurtman RJ, et al. Effects of exogenous melatonin on sleep: a meta-analysis. *Sleep Med Rev* 2005;9:41–50.[PubMed]
44. Jan JE, Freeman RD. Melatonin therapy for circadian rhythm sleep disorders in children with multiple disabilities: what have we learned in the past decade? *Dev Med Child Neurol* 2004;46:776–782.[PubMed]
45. Weiss MD, Wasdell MB, Bomben MM, et al. Sleep hygiene and melatonin treatment for children and adolescents with ADHD and initial insomnia. *J Am Acad Child Adolesc Psychiatry* 2006;45:512–519.[PubMed]
46. Gupta M, Aneja S, Kohli K. Add-on melatonin improves sleep behaviour in children with epilepsy: randomized, double-blind, placebo-controlled trial. *J Child Neurol* 2005;20:112–115.[PubMed]
47. Gupta M, Gupta YK, Aneja S, et al. Effects of add-on melatonin on sleep in epileptic children on carbamazepine monotherapy: a randomized placebo controlled trial. *Sleep Biol Rhythms* 2004;2:215–219.
48. Phillips L, Appleton RE. Systematic review of melatonin treatment in children with neurodevelopmental disabilities and sleep impairment. *Dev Med Child Neurol* 2004;46:771–775.[PubMed]
49. Sajith SG, Clarke D, Sajith SG, et al. Melatonin and sleep disorders associated with intellectual disability: a clinical review. *J Intellect Disabil Res* 2007;51:2–13.[PubMed]
50. Wasdell MB, Jan JE, Bomben MM, et al. A randomized, placebo-controlled trial of controlled release melatonin treatment of delayed sleep phase syndrome and impaired sleep maintenance in children with neurodevelopmental disabilities. *J Pineal Res* 2008;44:57–64.[PubMed]
51. Arendt J. Safety of melatonin in long-term use. *J Biol Rhythms* 1997;12:673–681.[PubMed]
52. Weaver DR. Reproductive safety of melatonin: a "wonder drug" to wonder about. *J Biol Rhythms* 1997;12:682–689.[PubMed]
53. Sheldon SH. Pro-convulsant effects of oral melatonin in neurologically disabled children. *Lancet* 1998;351:1254.[PubMed]
54. Hoebert M, Van Der Heijden KB, Van Geijlswijk I, et al. Long-term follow-up of melatonin treatment in children with ADHD and chronic sleep onset insomnia. *J Pineal Res* 2009;47:1–7.[PubMed]
55. Carr R, Wasdell MB, Hamilton D, et al. Long-term effectiveness outcome of melatonin therapy in children with treatment-resistant circadian rhythm sleep disorders. *J Pineal Res* 2007;43:351–359.[PubMed]
56. Braam W, Smits MG, Didden R, et al. Exogenous melatonin for sleep problems in individuals with intellectual disability: a meta-analysis. *Dev Med Child Neurol* 2009;51:340–349.[PubMed]
57. Russo RM, Gururaj VJ, Allen JE. The effectiveness of diphenhydramine HCl in pediatric sleep disorders. *J Clin Pharmacol* 1976;16:284–284.[PubMed]
58. Popoviciu L, Corfariu O, Popoviciu L, et al. Efficacy and safety of midazolam in the treatment of night terrors in children. *Br J Clin Pharmacol* 1983;16(Suppl 1):97S–102S.[PubMed]
59. Bruni O, Ferri R. L-5-Hydroxytryptophan treatment of sleep terrors in children. *Eur J Pediatr* 2004;163:402–407.[PubMed]
60. De Giorgis G, Miletto R. Headache in association with sleep disorder in children: A psychodiagnostic evaluation and controlled clinical study – L-5-HTP versus placebo. *Drugs Experim Clin Res* 1987;13:425–433.[PubMed]
61. Silver RM, Heyes MP, Maize JC, et al. Scleroderma, fasciitis, and eosinophilia associated with the ingestion of tryptophan. *N Engl J Med* 1990;322:874–881.[PubMed]
62. Meolie AL, Rosen C, Kristo D, et al. Oral nonprescription treatment for insomnia: an evaluation of products with limited evidence. *J Clin Sleep Med* 2005;1:173–187.[PubMed]
63. Lawton C, France KG, Blampied NM. Treatment of infant sleep disturbance by graduated extinction. *Child Family Behav Ther* 1991;13:39–56.
64. Minde K, Faucon A, Falkner S. Sleep problems in toddlers: effects of treatment on their daytime behavior. *J Am Acad Child Adolesc Psychiatry* 1994;33:1114–1121.[PubMed]

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**TABLE 1** **Detailed descriptions of treatments in some included RCTs.** [32] [33] [34] [36] [35]

| Ref | Intervention/population | Description |
|---|---|---|
| [32] | Standardised sleep programme (based on extinction) | 8 page booklet — "Parent Guide" (that involved organised bedtime routines, procedures for settling the child, and for the handling of crying, calling out, and getting out of bed) plus a 1-hour interview<br>Telephone calls each day at first, then as needed<br>Total staff attention: 2 to 3 hours/family |
| | Written guide for parents | 8-page booklet — "Parent Guide" (that involved organised bedtime routines, procedures for settling the child, and for the handling of crying, calling out, and getting out of bed) plus any questions answered<br>Total staff attention: 5 to 10 minutes/family |
| [33] | Sleep hygiene | Therapist selects ideal bedtime for the child<br>Parents construct a "positive routine" of 4 to 7 quiet activities to last up to 20 minutes, with praise after each completed routine<br>Routine consists of, for example, teeth brushing, using the toilet, reading a short story, the parent helping the child into pyjamas, the parent gently scratching and massaging the child's back<br>Child told to go to sleep after routine<br>If the child left the bed or had tantrums after the routine is completed, the parent had to lift the child over the parent's back and tell the child firmly, "The routine is over; it is time for bed!"<br>Each week the routine began 5 to 10 minutes earlier, so that, by the fifth week, the routine finished at the time the parent(s) had originally attempted to establish bedtime |
| | Graduated extinction | Parents were told to maintain the child's established bedtime<br>Parents were told to ignore the child's tantrums for specific time intervals, depending on the child's age and the time the parents thought they could ignore the child<br>The parents were allowed to comfort their child for 15 seconds after each time interval, and then leave the room<br>If the child left the bed, it was told, "No, it is time for you to go to sleep"<br>The time intervals were increased weekly |
| | No treatment | Control group were told to continue what they already do when the child has a tantrum, and that some children "grow out" of bedtime tantrums |
| [34] | Extinction | Parents put the child to bed after pre-bedtime routines, said "good night", left the room, and did not return<br>Parents could check the child briefly in the night if they work, then leave and not return<br>If the child left the bedroom, they were given 1 warning each night<br>If the child left the bedroom a second time, they were kept in the room by the parents by closing the door or using a child gate. The door was kept closed until the child was asleep<br>Parents explained the routine to the child before treatment, and the child's successful behaviour was rewarded with praise and small rewards |
| | Graduated extinction | Parents put the child to bed after pre-bedtime routines, said "good night", and left the room<br>If the child cried or fussed, the parents could make a brief (30 seconds) check after 5 minutes, then left the room<br>Brief checks could be made after another 10 minutes, then at 15-minute intervals if the child was still crying<br>No checks were made after the child stopped crying<br>Checking intervals were lengthened by 5 minutes each night<br>If the child left the bedroom, he/she was given 1 warning each night<br>If the child left the bedroom a second time, the parent held the door closed for a short interval each time. The intervals were progressively lengthened until the child stayed in bed. Once the child stayed in bed, the door was left open<br>Parents explained the routine to the child before treatment, and the child's successful behaviour was rewarded with praise and small rewards |
| [35] | Sleep problem definition | Settling was severe if the child took at least 1 hour to settle and fall asleep, if the parents were disturbed in this time, and if the settling problems occurred at least 3 times/week<br>Night waking was severe if the child woke for more than a few minutes and disturbed the parents, or went into their room or bed, and if this happened at least 3 times/week<br>Early waking was severe if the child woke up before 5 a.m. at least 3 times/week |
| | Challenging behaviour definition | A child was included if they had any item on the Aberrant Behavior Checklist scored as quite serious or severe |

| Ref | Intervention/population | Description |
|---|---|---|
| | Treatment (extinction and gradual extinction) | The therapist discussed certain techniques with the parent:<br>Extinction and graduated extinction procedures such as checking and gradual withdrawal, and stimulus-control procedures and positive reinforcement |
| [36] | Severe sleep problem definition | Night waking at least 3 times/week for more than a few minutes with disturbing of the parents<br>Settling problems at least 3 times/week with the child taking at least 1 hour to settle, and disturbing the parents<br>Symptoms for at least 3 months, and not explicable by pain |
| | Brief treatment (booklet — gradual extinction and sleep hygiene) | Parents were given a simple booklet which dealt with:<br>outline of normal sleep<br>introduction of behavioural techniques<br>how to monitor the child's behaviour<br>good sleeping habits<br>specific techniques to change undesirable behaviour: ignoring the child during settling, and checking on the child only at increasing intervals, and decreasing the contact between the child and the parent during the undesirable behaviour; avoiding letting the child sleep in the parents' bed; and rewarding desirable behaviour |
| | Conventional treatment | Parents were given the same advice as in the booklet, but in a face-to-face interview |
| | Crossover control group | Parents were given no intervention for the first 6 weeks, then were re-randomised to a treatment group |
| [38] | Sleep problem definition | Sleep problem noted by their mother as "small" to "severe" [not further defined], but who did not have a significant sleep disorders (defined as >3 wakings per night, awake >60 minutes per night or total sleep duration <9 hours) |
| | Bedtime routine | The bedtime routine included one week of usual routine, followed by 2 weeks of a 3-step bedtime routine of bathing, applying lotion, and quiet activities such as cuddling with the lights out within 30 minutes of the end of the bath |
| | Control | Usual bedtime practices throughout the entire 3 weeks. This group was informed that the study was related to bedtime activities and sleep behaviours |

**TABLE** **GRADE evaluation of interventions for sleep disorders in children**

| Important outcomes | Sleep onset, duration and quality, parasomnia severity, bedtime tantrums, parental sleep, quality of life of child and carer, adverse effects | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Number of studies (participants)** | **Outcome** | **Comparison** | **Type of evidence** | **Quality** | **Consistency** | **Directness** | **Effect size** | **GRADE** | **Comment** |
| What are the effects of treatments for dyssomnias in children? | | | | | | | | | |
| 2 (94) [32] [34] | Sleep onset, duration, and quality | Extinction and graduated extinction *v* no treatment (in otherwise healthy children) | 4 | –2 | 0 | 0 | 0 | Low | Quality points deducted for sparse data and poor follow-up |
| 1 (36) [33] | Bedtime tantrums | Graduated extinction *v* no treatment (in otherwise healthy children) | 4 | –3 | 0 | 0 | 0 | Very low | Quality points deducted for sparse data, incomplete reporting of results, and poor follow-up |
| 1 (30) [35] | Sleep onset, duration, and quality | Extinction and graduated extinction *v* no treatment (in children physical disabilities, learning disabilities, epilepsy or attention-deficit disorder) | 4 | –3 | 0 | –1 | 0 | Very low | Quality points deducted for sparse data, incomplete reporting of results, and poor follow-up. Directness point deducted range of disabilities included |
| 1 (30) [35] | Parental sleep | Extinction and graduated extinction *v* no treatment (in children physical disabilities, learning disabilities, epilepsy or attention-deficit disorder) | 4 | –2 | 0 | –1 | 0 | Very low | Quality points deducted for sparse data and poor follow-up. Directness point deducted range of disabilities included |
| 1 (200) [38] | Sleep onset, duration, and quality | Sleep hygiene *v* no treatment (in otherwise healthy children) | 4 | –2 | 0 | –1 | 0 | Very low | Quality points deducted for no direct comparisons between groups and poor follow-up. Directness point deducted for recruitment of mothers only |
| 2 (236) [38] [33] | Quality of life of carer | Sleep hygiene *v* no treatment (in otherwise healthy children) | 4 | –3 | 0 | 0 | 0 | Very low | Quality points deducted for no direct comparisons between groups, incomplete reporting, and poor follow-up |
| 1 (36) [33] | Bedtime tantrums | Sleep hygiene *v* no treatment (in otherwise healthy children) | 4 | –3 | 0 | 0 | 0 | Very low | Quality points deducted for sparse data, incomplete reporting of results, and poor follow-up |
| 1 (36) [33] | Bedtime tantrums | Sleep hygiene *v* graduated extinction (in otherwise healthy children) | 4 | –3 | 0 | 0 | 0 | Very low | Quality points deducted for sparse data, incomplete reporting of results, and poor follow-up |
| 2 (102) [41] [42] | Sleep onset, duration, and quality | Melatonin *v* placebo (in otherwise healthy children) | 4 | –3 | 0 | –2 | 0 | Very low | Quality points deducted for sparse data, incomplete reporting of results, and poor follow-up. Directness points deducted for uncertainty of measurement of outcome and population differences |
| 1 (62) [42] | Quality of life of child | Melatonin *v* placebo (in otherwise healthy children) | 4 | –3 | 0 | –1 | 0 | Very low | Quality points deducted for sparse data, incomplete reporting of results, and poor follow-up. Directness point inclusion of children with co-morbidities and co-interventions |
| 4 (136) [45] [46] [47] [50] | Sleep onset, duration, and quality of sleep | Melatonin *v* placebo (in children with ADHD, epilepsy, or neurodevelopmental disorders) | 4 | –2 | 0 | –1 | 0 | Very low | Quality points deducted for sparse data and for different results with different measures of the same outcome in RCTs of epilepsy. Directness point deducted as clinical importance of difference in outcomes between groups unclear in all RCTs |

| Important outcomes | Sleep onset, duration and quality, parasomnia severity, bedtime tantrums, parental sleep, quality of life of child and carer, adverse effects | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Number of studies (participants)** | **Outcome** | **Comparison** | **Type of evidence** | **Quality** | **Consistency** | **Directness** | **Effect size** | **GRADE** | **Comment** |
| 1 (50) [57] | Sleep onset, duration, and quality | Antihistamines *v* placebo | 4 | –2 | 0 | –1 | 0 | Very low | Quality points deducted for sparse data and incomplete reporting of results. Directness point deducted for inclusion of non-recommended dose of antihistamine |
| What are the effects of treatments for parasomnias in children? | | | | | | | | | |
| 2 (62) [46] [47] | Parasomnia severity | Melatonin *v* placebo (in children with epilepsy) | 4 | –2 | 0 | –1 | 0 | Very low | Quality points deducted for sparse data and poor follow-up. Directness point deducted for broad inclusion criteria |

Type of evidence: 4 = RCT; 2 = Observational; 1 = Non-analytical/expert opinion.
Consistency: similarity of results across studies.
Directness: generalisability of population or outcomes.
Effect size: based on relative risk or odds ratio.