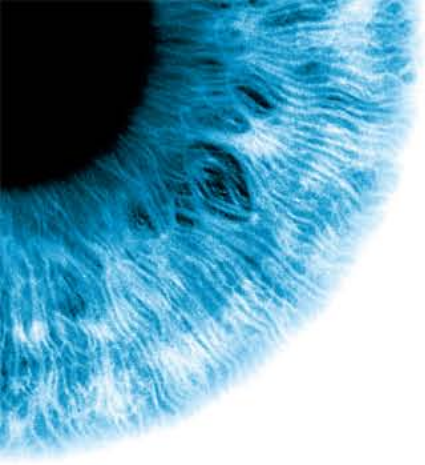

Nocturnal enuresis: Evidence Update July 2012

A summary of selected new evidence relevant to NICE clinical guideline 111 'The management of bedwetting in children and young people' (2010)

Evidence Update 21

Evidence Updates provide a summary of selected new evidence published since the literature search was last conducted for the accredited guidance they relate to. They reduce the need for individuals, managers and commissioners to search for new evidence and inform guidance developers of new evidence in their field. Evidence Updates highlight key points from the new evidence and provide a commentary describing its strengths and weaknesses. They also indicate whether the new evidence may have a potential impact on current guidance. For contextual information, this Evidence Update should be read in conjunction with the relevant guidance, available from the NHS Evidence topic page for nocturnal enuresis.

Evidence Updates do not replace current accredited guidance and do not provide formal practice recommendations.

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Contents

Introduction

This Evidence Update identifies new evidence that is relevant to and may have a potential impact on the following reference guidance:

 [1]**Nocturnal enuresis. NICE clinical guideline 111 (2010)**

A search was conducted for new evidence published between 13 November 2009 and 28 February 2012. A total of 241 pieces of evidence were identified and assessed, of which seven were selected for the Evidence Update (see Appendix A for details of the evidence search and selection process). An Evidence Update Advisory Group, comprised of subject experts, reviewed the prioritised evidence and provided a commentary.

Although the process of updating NICE guidance is distinct from the process of an Evidence Update, the relevant NICE guidance development centres have been made aware of the new evidence which will be considered when guidance is reviewed.

Other relevant information

The Evidence Update makes reference to standards used to indicate treatment response as set out by the International Children's Continence Society:

- Nevéus T, von Gontard A, Hoebeke P et al. (2006) The Standardization of Terminology of Lower Urinary Tract Function in Children and Adolescents: Report from the Standardisation Committee of the International Children's Continence Society. The Journal of Urology 176: 314–24

Feedback

If you have any comments you would like to make on this Evidence Update, please email contactus@evidence.nhs.uk

[1] NICE-accredited guidance is denoted by the Accreditation Mark 

Key points

The following table summarises what the Evidence Update Advisory Group (EUAG) decided were the key points for this Evidence Update. It also indicates the EUAG's opinion on whether the new evidence may have a potential impact on the current guidance listed in the introduction. For further details of the evidence behind these key points, please see the full commentaries.

The section headings used in the table below are taken from the guidance.

	Potential impact on guidance	
Key point	**Yes**	**No**
Initial treatment – alarms • Evidence suggests that desmopressin and enuresis alarms are equally effective initial interventions; however, compliance with alarm treatment may be more challenging.		✓
Lack of response to initial treatment options • Evidence suggests that desmopressin is an effective treatment following failure of initial treatment with an alarm. • Evidence suggests that an alarm may be a potentially effective treatment following failure of initial treatment with desmopressin but more research is needed.		✓ ✓
Anticholinergics • Evidence suggests oxybutynin[2] in combination with desmopressin is effective following partial or non-response to initial treatment with desmopressin.		✓
Children under 5 years with bedwetting • Limited evidence suggests that lifting[3] may offer a short-term solution for the management of bedwetting, and does not appear to adversely affect dryness in the longer term.		✓
Areas not currently covered by NICE guidance ***Complementary and alternative medicine*** • There is weak, insufficient, or a lack of evidence to support hypnosis, psychotherapy and counselling, acupuncture, chiropractic, diet or food restriction, faradisation[4], medicinal herbs, homeopathy and surgery for nocturnal enuresis. • Limited evidence suggests laser acupuncture may be effective in previously untreated primary monosymptomatic nocturnal enuresis but more research is needed.		✓ ✓

[2] Oxybutynin is not recommended specifically by current guidance and at the time of publication of this Evidence Update, did not have UK marketing authorisation for nocturnal enuresis in children under 5 years.
[3] Defined in the study as waking the child 1.5–2 hours after falling asleep and taking them to the toilet.
[4] Defined by the authors as 'the application of faradic current to stimulate muscles and nerves'.

1 Commentary on new evidence

These commentaries analyse the new evidence identified specifically for the Evidence Update. The commentaries focus on the 'Key references' (those identified through the search process and prioritised by the EUAG for inclusion in the Evidence Update), which are identified in bold text. Supporting references provide context or additional information to the commentary. Section headings are taken from the guidance.

1.1 Principles of care

No new key evidence was found for this section.

1.2 Information for the child or young person and family

No new key evidence was found for this section.

1.3 Assessment and investigation

No new key evidence was found for this section.

1.4 Planning management

No new key evidence was found for this section.

1.5 Advice on fluid intake, diet and toileting patterns

No new key evidence was found for this section.

1.6 Lifting and waking

See section 1.16 for commentary on evidence for lifting and waking in children under 5 years with bedwetting.

1.7 Reward systems

No new key evidence was found for this section.

1.8 Initial treatment – alarms

Alarm versus desmopressin

NICE CG111 recommends offering an alarm as first-line treatment if bedwetting has not responded to advice on fluids, toileting or a reward system, unless it is undesirable or inappropriate. The guideline does not specify a minimum age for alarm treatment and notes that it should be considered for children under 7 years depending on ability, maturity, motivation and understanding. It also recommends informing about the potential challenges of using an alarm, and explaining that alarms are not suitable for all children and young people and their families. If an alarm is deemed inappropriate or undesirable, or if rapid-onset and/or short-term improvement in bedwetting is a priority, initial treatment with desmopressin is recommended (at an initial dose of 200 micrograms Desmotabs [120 micrograms DesmoMelt], increasing to 400 micrograms Desmotabs [240 micrograms DesmoMelt] in children not dry after 1–2 weeks).

An open-label, multicentre randomised controlled trial (RCT) by **Evans et al. (2011)** conducted in 29 UK enuresis clinics compared desmopressin (n = 192) with enuresis alarm (n = 59) in children aged 5–16 years (mean age 8.3 years) with severe primary monosymptomatic nocturnal enuresis (mean 5.5 wet nights per week in the desmopressin group, 5.6 in the alarm group) that was previously untreated, or treated over 1 year ago or for less than 4 weeks. Children in the desmopressin group received 0.2 mg desmopressin daily for a 2-week run-in period and then entered a 3-month treatment period (0.2 mg or 0.4 mg desmopressin daily for those with ≤ 1 and > 1 wet night during run-in respectively). There then followed a 2-week washout period of no treatment at which point children who had achieved 14 consecutive dry nights were given no further treatment, and those who were not dry entered another 3-month treatment phase (receiving the same desmopressin dose as previously assigned). In the alarm group, children were treated for up to 6 months until they were dry for 14 consecutive nights, or the investigator felt further treatment was not beneficial.

For the primary outcome (using the International Children's Continence Society [ICCS] definition of 'responders' as those with a ≥ 50% reduction in mean wet nights per week), there was no significant difference between response rate at the end of treatment with desmopressin and alarm (37.5% vs 32.2% respectively; between-group difference = 5.3% [95% CI -9.0 to 17.9%]).

The study used the same dose of desmopressin as NICE CG111. A limitation of the study was the number of withdrawals (58% of children in the alarm group and 41% in the desmopressin group; among those who withdrew not enough data were collected to calculate reduction in wet nights in 32% and 7% of children respectively). Compliance was also lower in the alarm group (only 50–75% of patients were using the alarm as instructed when assessed at various points during the study versus 80–91% compliance with desmopressin).

Within its limitations, the evidence indicates that treatment with desmopressin or alarm is equally effective in reducing the number of wet nights, consistent with recommendations in NICE CG111 to offer either of these interventions as initial treatment depending on the needs and circumstances of the family. The higher withdrawal in the alarm group suggests that families may face more difficulties adhering to this intervention, in support of the current recommendations to inform of the challenges involved with the management of bedwetting using an alarm before commencing treatment.

Key reference

Evans J, Malmsten B, Maddocks A et al. (2011) Randomized comparison of long-term desmopressin and alarm treatment for bedwetting. Journal of Pediatric Urology 7: 21–9

1.9 Lack of response to alarm treatment

No new key evidence was found for this section.

1.10 Initial treatment – desmopressin

No new key evidence was found for this section.

1.11 Children and young people experiencing recurrence of bedwetting

No new key evidence was found for this section.

1.12 Lack of response to initial treatment options

Alarm and desmopressin

NICE CG111 recommends initial treatment with either desmopressin (to be offered to children and young people over 7 years, and considered in children aged 5–7 years) or alarm. If first-line treatment with an alarm fails, desmopressin is recommended either alone or in combination with alarm. If first-line desmopressin fails, there is currently no explicit recommendation to reconsider an alarm, either alone or in combination with desmopressin.

Monotherapy

A crossover RCT by **Kwak et al. (2010)** in a Korean urology department investigated the efficacy of desmopressin and alarm monotherapy as first- and second-line treatment in children aged 6–15 years with monosymptomatic nocturnal enuresis not treated with desmopressin or alarm in the previous 3 months. Children were randomised to desmopressin (0.2 mg daily increased to 0.4 mg daily if a full response was not seen after 2 weeks) or alarm for 12 weeks (initial desmopressin group [n = 54]: mean age 8.1 years, mean wet nights per 4 weeks 21.7; initial alarm group [n = 50]: mean age 8.6 years, mean wet nights per 4 weeks 23.1). Response was then assessed according to ICCS standards. Full responders were withdrawn from the study in a 4-week withdrawal period (comprising tapered reduction in desmopressin dose or continuation of alarm treatment), whereas partial and non-responders (0–89% reduction in wet nights) were transferred to the alternative treatment for 12 weeks.

After the 12-week first-line treatment period, there was no significant difference between the response with desmopressin (20 full responders, 22 partial responders, 12 non-responders) and alarm treatment (25 full responders, 16 partial responders, 9 non-responders; p = 0.433 for between-group difference). There was also no significant difference between the mean reduction in wet nights with desmopressin (69.5%, range 5–100%) and alarm (78.4%, range 15–100%; p = 0.105 for between-group difference). The 45 full responders were then withdrawn (along with three children who withdrew consent in the alarm group and two in the desmopressin group, and one discontinuation in each group due to adverse events) and the remaining 52 children continued the study. After 12 weeks of crossover treatment, there was no significant difference in the mean reduction in wet nights with second-line desmopressin (84.7%, range 0–100%) and second-line alarm (78.6%, range 0–100%; p = 0.295 for between-group difference). There was also no significant difference in the rate of successful response between desmopressin as second line (15 full or partial responders [71.4%]) and alarm second line (21 full or partial responders [67.8%]; p = 0.961 for between-group difference). Of the children who were withdrawn from the study after full response to first-line treatment, 50% of those given desmopressin had relapsed 12 weeks after treatment stopped versus a 12% relapse rate after alarm treatment (p = 0.005).

The study used the same dose of desmopressin as NICE CG111. A limitation of the evidence was the relatively short follow up period used to evaluate relapse rate. The authors also postulated that the low rate of dropouts seen in both groups may be explained by the location of the study in a hospital ‘in an area where the interest in child education is the highest in (the) country’. The authors went on to discuss the ‘active follow up, reassurance and education’ they provided during the study along with ‘regular contact with patients and families throughout the study’. These factors may have implications for the external validity of the data to the UK.

The evidence from the study is consistent with recommendations in NICE CG111 that alarm and desmopressin are equally effective in the first-line and should be offered based on family preferences (although the relapse rate with desmopressin is higher, as already noted in the guidance). The evidence also indicates that following failure of first-line alarm treatment, switching to treatment with desmopressin can be effective, which is also in line with current

guidance. The study may additionally suggest that an alarm as second-line treatment following failure of desmopressin could be a potentially effective therapy sequence; however more research about the use of an alarm after failure of desmopressin (before moving to alternative pharmacological therapy such as anticholinergics and tricyclics) is needed.

Key reference

Kwak KW, Lee Y-S, Park KH et al. (2010) Efficacy of desmopressin and enuresis alarm as first and second line treatment for primary monosymptomatic nocturnal enuresis: prospective randomized crossover study. Journal of Urology 184: 2521–6

1.13 Anticholinergics

Desmopressin plus oxybutynin

NICE CG111 recommends an anticholinergic combined with desmopressin for bedwetting that has not responded to an alarm and/or desmopressin (including partial response to desmopressin alone, or no response to desmopressin alone or in combination with an alarm). A minimum age for treatment with anticholinergics is not specified in the recommendations, nor is a particular anticholinergic; it should be noted that the anticholinergic oxybutynin used in the following study did not have UK marketing authorisation in children under 5 years at the time of publication of this Evidence Update.

A double-blind RCT by **Montaldo et al. (2012)** examined the efficacy of desmopressin plus the anticholinergic oxybutynin in children aged 6–13 years (mean age 10.6 years, n = 206) with monosymptomatic nocturnal enuresis (median 6.6 wet nights per week) in an Italian paediatric urology department. Children were randomised to one of two groups receiving either 120 or 240 micrograms desmopressin daily for 2 weeks. Any 'non-responders' (0–49% decrease in wet nights per week) or 'partial responders' (50–89% decrease in wet nights per week) in the 120 microgram group had their dose increased to 240 micrograms for a further 2 weeks. All remaining partial and non-responders from both groups were then randomised to desmopressin (dose not stated) plus oxybutynin 5 mg or desmopressin (dose not stated) plus placebo for 4 weeks. Assignment to these two arms was stratified based on response to the previous desmopressin monotherapy phase to balance partial and non-responders between treatment groups.

At the end of treatment, there were more full and partial responders with desmopressin plus oxybutynin versus desmopressin plus placebo (45% vs 17%, odds ratio = 0.24, 95% CI 0.10 to 0.56, $p < 0.01$). A limitation of the study was the lack of follow up after the treatment phase, preventing any conclusions about the long-term efficacy of anticholinergics.

This evidence is consistent with NICE CG111 which recommends the addition of an anticholinergic for partial and non-responders to initial desmopressin treatment. It should be noted that this study used shorter treatment regimens (desmopressin monotherapy for 4 weeks followed by combination therapy for 4 weeks) than those recommended by current guidance (which suggests longer-term continuation of treatment with desmopressin alone or in combination with an anticholinergic because bedwetting may continue to improve for up to 6 months after starting treatment).

Key reference

Montaldo P, Tafuro L, Rea M et al. (2012) Desmopressin and oxybutynin in monosymptomatic nocturnal enuresis: a randomized, double-blind, placebo-controlled trial and an assessment of predictive factors. BJU International (Epub ahead of print)

1.14 Tricyclics

No new key evidence was found for this section.

1.15 Training programmes for the management of bedwetting

No new key evidence was found for this section.

1.16 Children under 5 years with bedwetting

Behavioural interventions

Although NICE CG111 recommends that parents or carers of a child under 5 years with bedwetting should take the child to the toilet if he or she wakes at night, no direct interventions such as waking the child to take them to the toilet are currently recommended. In terms of rewards, current guidance suggests trying a reward system alone in young children who have some dry nights.

An RCT by **van Dommelen et al. (2009)** assessed the effects of behavioural interventions for bedwetting in children aged 4–5 years (21% aged 4 years, 79% aged 5 years; n = 570) with monosymptomatic nocturnal enuresis for two or more nights per week during the last 3 months, and with no prior alarm or drug treatment. Children were recruited during a standard health visit or through the internet and magazines. Most participants were Dutch (93%) from a household with two parents (97%) and two children (61%).

Children were randomised to one of four groups: parents asked to wake up and take the child to the toilet 1.5–2 hours after falling asleep with a request for a password to check the child was awake ('lifting with password'); the same intervention without a password ('lifting without password'); parents asked to award stars on a chart for dry nights with a reward given after a preset number of dry nights; or a control group receiving no intervention. The study period lasted for 6 months, with parents instructed to end their participation in the study once 14 consecutive dry nights were achieved.

At the end of the 6-month intervention period, only the lifting without password group showed a significantly higher rate of dryness than controls (37% vs 21%, $p < 0.01$). Rates of dryness among the lifting with password (27%) and reward groups (32%) did not differ significantly from controls (p value not stated). At a further follow-up at a mean of 2.6 years (365 [64%] parents responded), there was no significant difference (p value not stated) in the rate of dryness between any of the groups (control = 69%, lifting with password = 78%, lifting without password = 78%, reward = 76%).

The study had a number of limitations. The initial criterion proposed by the investigators to indicate success was 14 consecutive dry nights with intervention followed by 14 consecutive dry nights without intervention. However, most parents chose to end participation in the study following 14 dry nights irrespective of using the intervention, which was then adopted as the definition of 'dry' (although it was not clear when this change in definition was made). The study appeared to use the percentage of children achieving 14 consecutive dry nights at any time during the 6-month intervention period to report the rate of dryness at 6 months (figures that may not reflect achievement of long-term dryness, and did not indicate the number of children still managed by the intervention at this time). Results may also have been affected by the rate of dropout during the study (ranging from 14% among controls to 36% in the lifting with password group; multivariate impution was used to attempt to overcome the possibility that those dropping out may have been a subgroup who had difficulties with the intervention). Finally, other interventions were occasionally used by some parents (for example, 40% of children in the reward group and 36% of controls received other intervention types, most

commonly lifting), which may have confounded results. It should also be noted that the reward method used in the study (rewarding dry nights) is different from the approach recommended in NICE CG111 (rewarding agreed positive behaviour such as helping to change sheets; although these recommendations are not specifically aimed at children under 5 years).

Due to the limitations discussed, the data at 6 months do not provide a robust assessment of the efficacy of these interventions in achieving long-term dryness, but there is some evidence that lifting without a password is more effective than no intervention in achieving dryness on 14 consecutive nights within a 6-month period, which may be a useful solution for some family circumstances.

Although this evidence is unlikely to affect NICE CG111, the results from the longer follow-up period indicate that lifting does not appear to affect the tendency of children to become naturally dry as they get older, which has been a concern with this type of intervention. The absence of long-term adverse outcomes with lifting is a potentially important finding given that lifting is frequently reported as a management strategy. A study in which parents of 7.5 year olds with nocturnal enuresis responded to a questionnaire found that among children wetting the bed twice or more a week (n = 213), over 70% of parents had used lifting strategies at some time in the past (Butler et al. 2005).

Key reference

van Dommelen P, Kamphuis M, van Leerdam FJM et al. (2009) The short- and long-term effects of simple behavioral interventions for nocturnal enuresis in young children: a randomized controlled trial. The Journal of Pediatrics 154: 662–6

Supporting reference

Butler RJ, Golding J, Heron J et al. (2005) Nocturnal enuresis: a survey of parental coping strategies at 7 1/2 years. Child: Care, Health & Development 31: 659–67

Areas not currently covered by NICE guidance

Complementary and alternative medicine

NICE CG111 does not currently include recommendations for the use of complementary and alternative medicine (CAM) in nocturnal enuresis; however, it contains a detailed research recommendation about the effectiveness of CAM when used independently or in conjunction with conventional treatments.

Miscellaneous interventions

A Cochrane review by **Huang et al. (2011)** of 24 RCTs (n = 2334) investigated the effect of several complementary and other 'unconventional' interventions on nocturnal enuresis in children. The trials included in the review examined hypnosis, psychotherapy and counselling, acupuncture, chiropractic, diet or food restriction, medicinal herbs and faradisation (defined by the authors as 'the application of faradic current to stimulate muscles and nerves'). No trials were found for homeopathy or surgery.

The authors found some indication of an effect with hypnosis, psychotherapy, acupuncture, chiropractic and medicinal herbs but acknowledged that the findings were based on limited evidence from 'single small trials of dubious methodological rigour'. They concluded that current evidence does not support the use of these interventions and high quality RCTs are needed, consistent with the research recommendation in NICE CG111.

Key reference

Huang T, Shu X, Huang YS et al. (2011) Complementary and miscellaneous interventions for nocturnal enuresis in children. Cochrane Database of Systematic Reviews issue 12: CD005230

Laser acupuncture

Two RCTs published after the search dates for the Cochrane review by Huang et al. (2011) examined the efficacy of laser acupuncture in bedwetting.

A single-blind RCT by **Karaman et al. (2011)** examined laser acupuncture therapy in children aged 5–16 years (mean age 8.6 years, n = 91) with primary monosymptomatic nocturnal enuresis and no prior medical therapy in a Turkish urology outpatient clinic. Children were randomised to laser acupuncture, or placebo acupuncture with a nonlaser light source. Laser acupuncture comprised delivery of a red light with a wavelength between 635 and 670 nm to five acupuncture points on the torso and lower leg (as suggested by traditional Chinese medicine for bladder diseases) for 1 minute at each point for 4 weeks (three sessions per week). A sound signal was present in the laser device to assist with accurate location of the acupuncture points.

At 6-month follow-up after treatment, children experienced a reduction in mean number of weekly bed-wetting episodes from 4.3 (standard deviation [SD] 2.2) to 1.7 (SD 1.3) in the laser acupuncture group, and from 4.1 (SD 2.1) to 3.1 (SD 2.2) in the placebo group ($p = 0.001$ for between-group difference in reduction). The rate of complete improvement (defined as no bed-wetting episodes) at 6 months was significantly higher with laser versus placebo acupuncture (54.4% vs 11.5%, $p = 0.001$).

Children were asked to record their own wet and dry days on a calendar which may be a potential limitation of the evidence. The decision to exclude the eight children who failed to complete the study from the data analysis may also have introduced bias.

The results of this study suggest that laser acupuncture may be an effective intervention in children presenting with primary monosymptomatic nocturnal enuresis and no prior medical therapy. As this represents the largest proportion of the nocturnal enuresis population, further research into this modality may be warranted in larger studies, particularly versus standard interventions. The authors asserted that laser acupuncture is a painless, noninvasive and inexpensive treatment, but it should be noted that access to this therapy is likely to be limited and this evidence is unlikely to affect NICE CG111.

Laser acupuncture was also investigated in a single-blind RCT by **Radvanska et al. (2011)** in children from a secondary/tertiary referral centre (country not stated) aged 7–11.8 years (mean age 8.8 years, n = 31) with monosymptomatic nocturnal enuresis (mean 6.2 wet nights per week in the laser acupuncture group, 6.5 in placebo groups) and a maximal voided volume (MVV) less than 70% of normal. Children were randomised to one of three groups: laser acupuncture; placebo acupuncture without laser light but with skin contact; or placebo acupuncture without laser light and without skin contact. Laser acupuncture comprised delivery of laser light with a wavelength of 670 nm to 16 acupuncture points on the head, torso, back, lower arm and lower leg for 20 seconds at each point for 5 weeks (three sessions per week for 2 weeks, two sessions per week for the final 3 weeks).

No significant differences were observed between the active treatment and the two placebo groups (which were analysed together as there was no statistical difference between the two placebo arms for any parameter) for maximal voided volume, voiding frequency, enuresis frequency or nocturnal urine production.

The lack of response in this trial compared with the positive effect observed by Karaman et al. (2011) may be explained by the difference in acupuncture technique (shorter duration of laser light across a greater number of acupuncture points), the smaller number of participants (which may not have been sufficient to demonstrate an effect), and particularly the population

characteristics (children in this study were selected for their reduced MVV, and were from a secondary/tertiary referral centre which the authors noted may bias the selection towards complex or treatment-resistant cases, whereas children in Karaman et al. [2011] were treatment naïve).

The small number of participants in the study by Radvanska et al. (2011) prevents any firm conclusions being made, but data potentially suggest that laser acupuncture may not be effective in patients with a smaller than normal MVV in a secondary/tertiary setting. The evidence is unlikely to affect NICE CG111.

Key references

Karaman MI, Koca O, Küçük EV et al. (2011) Laser acupuncture therapy for primary monosymptomatic nocturnal enuresis. Journal of Urology 185: 1852–6

Radvanska E, Kamperis K, Kleif A et al. (2011) Effect of laser acupuncture for monosymptomatic nocturnal enuresis on bladder reservoir function and nocturnal urine output. Journal of Urology 185: 1857–61

2 New evidence uncertainties

During the development of the Evidence Update, the following evidence uncertainties were identified that have not previously been listed on the NHS Evidence UK Database of Uncertainties about the Effects of Treatments (UK DUETs).

Lack of response to initial treatment options

- Enuresis alarm treatment for children and young people who are partial or non-responders to desmopressin

Complementary and alternative medicine

- Complementary and miscellaneous interventions for nocturnal enuresis in children

Further evidence uncertainties for nocturnal enuresis can be found in the UK DUETs database and in the NICE research recommendations database.

UK DUETs was established to publish uncertainties about the effects of treatments that cannot currently be answered by referring to reliable up-to-date systematic reviews of existing research evidence.

Appendix A: Methodology

Scope

The scope of this Evidence Update is taken from the scope of the reference guidance:

- Nocturnal enuresis. NICE clinical guideline 111 (2010)

Searches

The literature was searched to identify studies and reviews relevant to the scope. Searches were conducted of the following databases, covering the dates 13 November 2009 (15 December 2009 for MEDLINE; the end of the search period of NICE clinical guideline 111) to 28 February 2012:

- CDSR (Cochrane Database of Systematic Reviews)
- CENTRAL (Cochrane Central Register of Controlled Trials)
- CINAHL (Cumulative Index to Nursing and Allied Health Literature)
- EMBASE (Excerpta Medica database)
- MEDLINE (Medical Literature Analysis and Retrieval System Online)
- NHS EED (Economic Evaluation Database)
- PsycINFO

Table 1 provides details of the MEDLINE search strategy used, which was adapted to search the other databases listed above. The search strategy was used in conjunction with validated Scottish Intercollegiate Guidelines Network search filters for RCTs and systematic reviews.

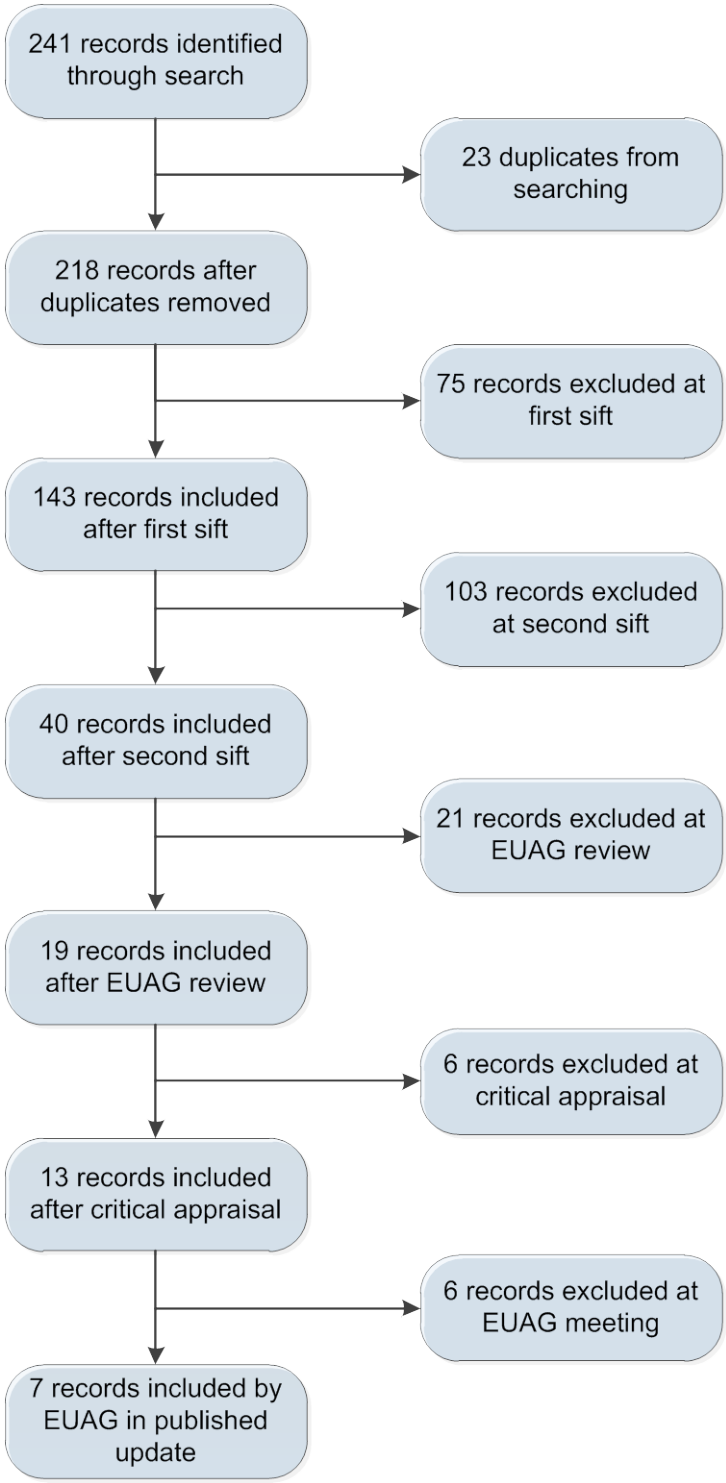
Figure 1 provides details of the evidence selection process. The long list of evidence excluded after review by the Chair of the EUAG, and the full search strategies, are available on request from contactus@evidence.nhs.uk

Table 1 MEDLINE search strategy (adapted for individual databases)

1	Nocturnal Enuresis/
2	(bedwett$ or (bed adj2 wett$)).ti,ab.
3	(enuresis adj nocturna$).ti,ab.
4	(nocturna$ adj2 (enuresis or enuretic$ or incontinence)).ti,ab.
5	(night$ adj2 (enuresis or enuretic$ or incontinence)).ti,ab.
6	(sleep adj2 (enuresis or enuretic$ or incontinence)).ti,ab.
7	(child$ adj enuresis).ti,ab.
8	or/1-7

9	Enuresis/
10	exp child/
11	pediatrics/
12	adolescent/
13	(child$ or pediatric$ or paediatric$ or boy$ or girl$ or juvenile$ or teen$ or adolescen$ or youth$).ti,ab.
14	or/10-13
15	9 and 14
16	8 or 15

Figure 1 Flow chart of the evidence selection process



EUAG – Evidence Update Advisory Group

Appendix B: The Evidence Update Advisory Group and Evidence Update project team

Evidence Update Advisory Group

The Evidence Update Advisory Group is a group of subject experts who review the prioritised evidence obtained from the literature search and provide the commentary for the Evidence Update.

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