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Effective Health Care

Bulletin on the effectiveness of health service interventions for decision makers

This bulletin summarises the research evidence on the effects of interventions for the treatment of nocturnal enuresis in children

Treating nocturnal enuresis in children

- Nocturnal enuresis in children (bedwetting) affects many families. Although it has a high rate of spontaneous remission, bedwetting may bring social and emotional stigma, stress and inconvenience to both the child and their family.
- A variety of interventions are used to treat nocturnal enuresis. These include alarms, drugs such as desmopressin, simple behavioural methods such as star charts, as well as more complex multi-faceted interventions.
- Much of the available research evaluating the effects of interventions is of poor quality and there are few direct comparisons between different types of intervention.
- Simple behavioural interventions are widely used as standard first-line treatment, but they require a high level of parental involvement. Currently, there is insufficient evidence to support the use of any particular intervention.
- The use of alarms has been shown to reduce night-time bedwetting both during treatment and after treatment stops. Before embarking on alarm treatment, families need to be made aware of both the time and the high level of parental involvement necessary to attain success.
- Drug therapy such as desmopressin reduces the number of wet nights per week compared with placebo, but only for as long as the drug is used. Drugs could be used to reduce bedwetting for a specific purpose, such as nights away from home. Children and their families need to be warned about possible side effects of some of the drugs.

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CENTRE FOR REVIEWS AND DISSEMINATION

A. Background

Nocturnal enuresis (bedwetting) is the involuntary loss of urine at night, in the absence of physical disease, at an age when a child could reasonably be expected to be dry (by consensus, at a developmental age of five years).[1,2] Although bedwetting has a high rate of spontaneous remission, it may bring social and emotional stigma, stress and inconvenience to both the child with enuresis and their family.[3] Children who wet the bed may experience parental disapproval, sibling teasing and repeated treatment failure which may lower self esteem.[4,5]

Prevalence and causes

Nocturnal enuresis affects many families. Estimating the prevalence is difficult, however, because there are variations in methods of diagnosis and in definitions.[6,7] In the UK, the most recent estimates suggest that the prevalence of frequent bedwetting (more than once a week) is higher in boys and shows a steady decline with age.[8-10] Around one in six of five-year-olds regularly wet the bed compared to around one in twenty 11-year-olds.[8-10]

The causes of primary nocturnal enuresis, where a child has never been dry at night, are unclear. Genetic,[2,11-13] physiological[14,15] and psychological[16-19] factors, as well as delay in maturation of the mechanism for bladder control,[20,21] have been suggested. Other factors which may contribute to bedwetting include: constipation, sleep apnoea and upper airway obstructive symptoms[22] and diet or mild caffeine drinks with diuretic effects (e.g. cola).[8]

B. Management of enuresis

A wide variety of interventions are used to treat nocturnal enuresis. These include enuresis alarms, drugs such as desmopressin, simple behavioural methods such as star charts and more complex behavioural methods including dry bed training. Other less common interventions include psychotherapy, surgery, fluid deprivation and complementary therapies. Box 1 describes the most commonly used behavioural, alarm and pharmacological interventions.

Box 1 Interventions used to treat nocturnal enuresis

Behavioural interventions

- Lifting: involves taking the child to the toilet during the night usually before the time that bedwetting is expected, without necessarily waking the child.
- Waking: involves waking the child to allow them to get up and urinate.
- Reward systems (e.g. star charts): the child might receive a star for every dry night, and a reward after a preset number of stars have been earned.
- Retention control training: attempting to increase the functional bladder capacity by delaying urination for extended periods of time during the day.
- Stop-start training: teaching children to interrupt their stream of urine in order to strengthen their pelvic floor muscles
- Dry bed training: can include enuresis alarms, waking routines, positive practice, cleanliness training, bladder training, and rewards.

Enuresis alarms

- Enuresis alarms: wake the child in the night at the onset of wetting. When a child begins to urinate, a sensor (either a bed pad or one worn inside pyjamas) is moistened, and the alarm is triggered.
- Over-learning: may be initiated after successful alarm treatment (e.g. achievement of 14 consecutive dry nights). Extra drinks are given at bed-time to cause additional stress to the detrusor muscles in the bladder. Alarm treatment is then continued until 14 consecutive dry nights are once again achieved.

Pharmacological interventions

- Drugs: include desmopressin and, less commonly, tricyclic drugs such as imipramine, amitriptyline and nortriptyline.

Treatment for children who wet the bed is often carried out by health professionals in general practice. Bedwetting may be discovered when a child is seen for a complaint other than enuresis. Having established that the child is at an age where one could reasonably expect a dry bed (i.e. at least five years old) and wants to become dry,[23] consensus is that a thorough assessment should be undertaken including a general physical examination, urinalysis and investigation of attitudes.[8] In keeping with the objectives of the National Service Framework for Children, any intervention should be centred on the needs of the child.[27] Although it is yet to be subjected to rigorous evaluation, the 'three systems approach'[24] is advocated as a way to understand, assess and select appropriate treatment for nocturnal enuresis.

The Enuresis Resource and Information Centre (ERIC) has produced guidelines on minimum standards of practice in the treatment of enuresis to assist

managers and practitioners in the planning, execution and evaluation of enuresis services.[25] ERIC also has details of over 600 enuresis clinics in the UK.[26] Some clinics are based in hospitals and others in health centres (often run by school nurses) Most but not all clinics are open to clients without the need for a professional referral.

C. Nature of the evidence

This issue of *Effective Health Care* summarises the research evidence from randomised controlled trials (RCTs) on the effects of interventions for the treatment of nocturnal enuresis in children. The bulletin is based upon a series of systematic reviews that have been carried out by the Cochrane Incontinence Group, and are available via the Cochrane Library. The Cochrane reviews are all based on a previous systematic review originally published in 1997 as part of the CRD Report series.[28] Further details of review methods are available in the Appendix.

Although over 100 RCTs have been identified across the Cochrane reviews, there are few direct comparisons between different types of intervention. The difficulty in comparing interventions is exacerbated by the lack of uniformity in outcome measures and the failure of some studies to adequately assess baseline levels of bedwetting. Many of the included RCTs have methodological problems such as small sample sizes and high rates of attrition (drop-outs), leading to low statistical power and potential bias. In addition, many are poorly reported. For example, many trial authors give insufficient detail about the method of randomisation or inadequately report follow-up data.

A number of the included RCTs have recruited children by advertising in the media, or from enuresis clinics. Participating families may have been especially motivated to tackle the bedwetting. In addition, strict inclusion/exclusion criteria were imposed in many of the trials. Consequently, the children involved are not necessarily representative of the wider population of those who wet the bed, either in the community or in institutions.

D. Effects of interventions

D1. Behavioural interventions other than alarms Simple behavioural interventions are widely used as standard first-line treatment. Twelve RCTs were included in a Cochrane review assessing the effects of simple behavioural interventions.[29] None of the RCTs were of good methodological quality.

The review found that star charts, whether with or without lifting or waking, were associated with fewer wet nights and lower failure rates while on treatment, and longer-term success after treatment. However, each finding was based on a single

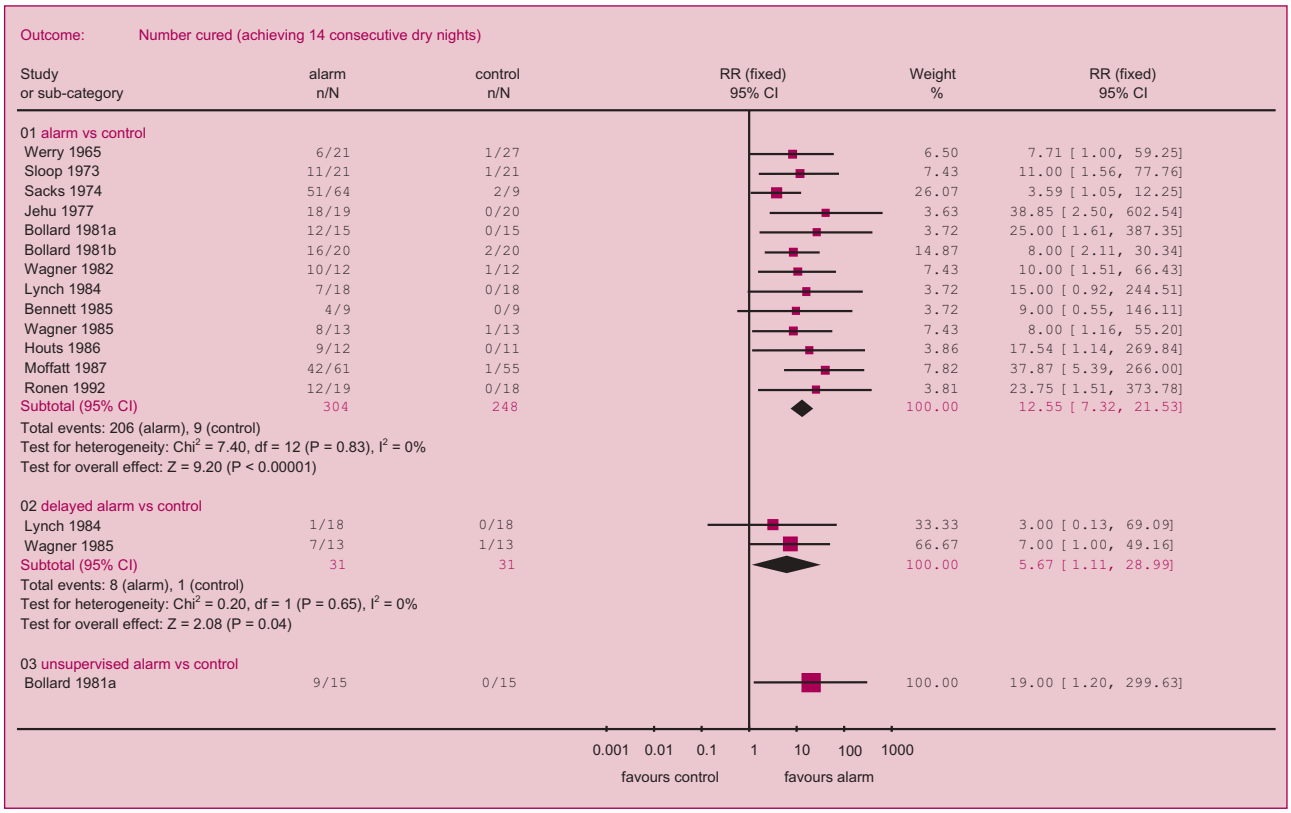

Figure 1 Comparison: alarm vs control – number cured during treatment

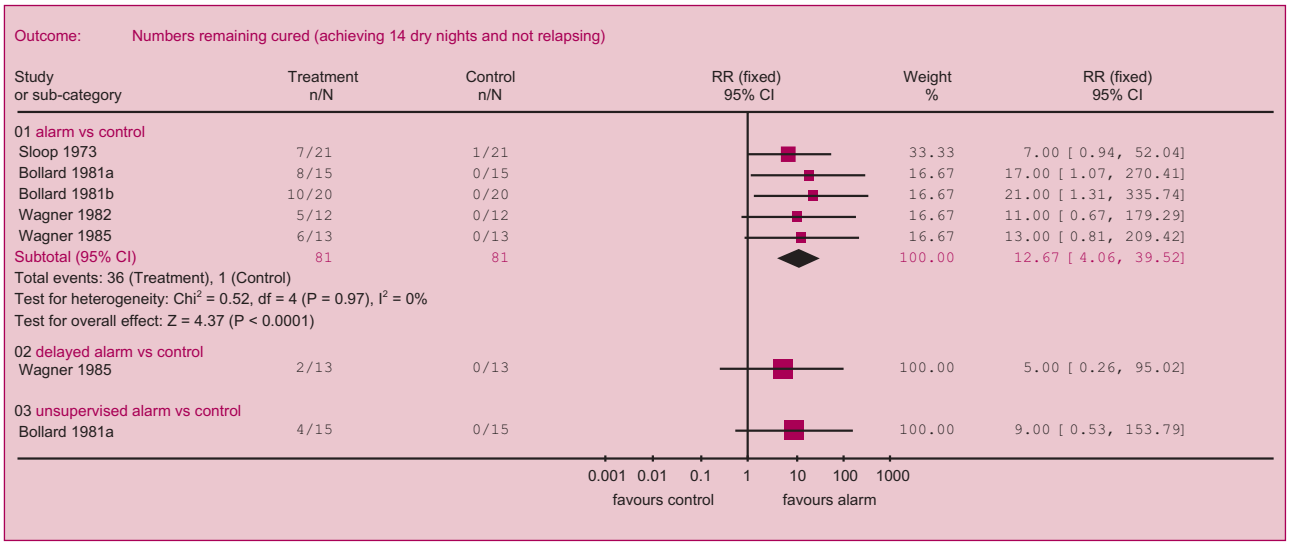

Figure 2 Comparison: alarm vs control – numbers remaining cured after treatment

small trial. Of the two trials addressing retention control training, one was too small to provide meaningful information, and the other had a very high (80%) drop-out rate. Another small trial showed that there might be some benefits associated with cognitive therapy compared with star charts, but these findings will need to be confirmed in larger trials.

A feature of the included RCTs was high dropout or non-adherence rates. Families reported that waking the child at night was disruptive and stressful, suggesting that some of these simple behavioural interventions are not suitable for all.

A number of RCTs have assessed the effects of complex behavioural treatment programmes such as dry bed training. In the 1997 systematic review undertaken by CRD,[28] complex behavioural treatment programmes such as dry bed training were not found to be more effective than alarm treatment. An update is nearing completion and will be available as a Cochrane review later this year.[30]

D2. Alarms Fifty-three RCTs were included in a Cochrane review assessing the effects of alarm interventions for nocturnal enuresis.[31] The methodological quality of many of the RCTs was poor. Many were too small to be likely to find statistically significant differences, even where some difference may exist, and often only one small trial compared alarms with another method. In these circumstances, no conclusions can be drawn.

Do alarms work? The review's main findings were that alarm treatment was more effective during treatment than control interventions (see Figure 1). In terms of success rates once treatment was completed (see Figure 2), about half the children remained dry after using alarms, compared with almost none of those who received no treatment or waiting list control.

Which type of alarm is best? Most of the alarms evaluated were of the type that woke the child immediately by means of a bell or buzzer. Insufficient evidence was found to draw conclusions about the relative effectiveness of different types of alarm. There was some limited evidence that an immediate alarm was better than a delayed alarm, and that one which woke the child rather than the parents had better results. Children were reported to prefer a body-worn alarm to a bed pad and alarm.

Are alarms better than other behavioural interventions? The Cochrane review included eight RCTs comparing alarms with a variety of simple behavioural interventions including star charts, rewards, wakening, lifting and stop-start training (pelvic floor muscle training).[31] Most of the trials comparing behavioural interventions with alarms tended to favour alarms. In one small trial, alarms were found to be better than stop-start training in terms of wet nights per week both during and after treatment. There were no statistically significant differences between alarms and methods such as lifting, wakening or rewards in four other small trials, although all trials favoured alarms in respect of a reduction in the mean number of wet nights. There was not enough evidence to conclude whether supplementing alarm treatment with behavioural interventions improved the effectiveness of the alarm.

Are alarms better than drugs? The Cochrane review included 18 RCTs that involved comparisons between alarms and drugs either alone or in combination.[31] Limited evidence suggested that alarms were better than drug treatment. Although desmopressin appeared to have a more immediate effect, alarms were more effective by the end of a course of treatment (RR 0.71, 95% CI 0.50 to 0.99) and after treatment stopped (RR 0.27, 95% CI 0.11 to 0.69). Alarms were also found to be better than tricyclics both during

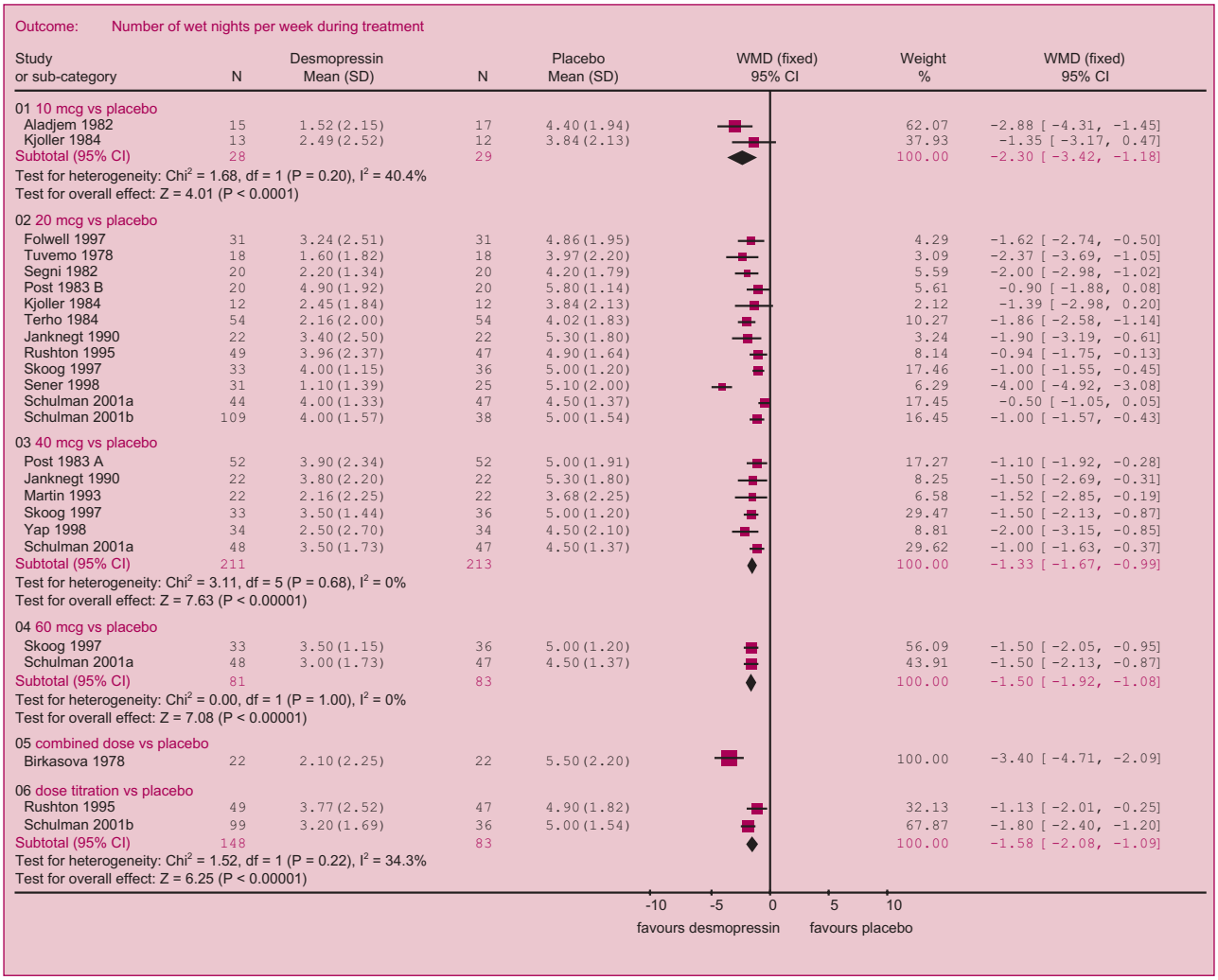

Figure 3 Comparison: Desmopressin vs placebo

(RR 0.73, 95% CI 0.61 to 0.88), and after treatment stopped (RR 0.58, 95% CI 0.36 to 0.94). Insufficient reliable evidence was found to support the practice of supplementing alarm treatment with drug interventions.

Acceptability of alarms Most alarms wake the child immediately using a bell or buzzer but then require nightwear, and perhaps bedding, to be changed. High dropout rates in some of the trials included in the Cochrane review suggest that there were problems with adherence, often reflecting the unacceptability of the intervention. Potential difficulties, such as the time needed to attain success and the disruption to the family, need to be discussed before embarking on alarm treatment. In two trials, non-adherence or dropout was attributed to the equipment being too difficult or complicated to use. A small number of RCTs included in the review involved alarms that delivered electric shocks to the children's skin. The use of these alarms was clearly unacceptable to parents and children, and they sometimes caused side effects such as skin burns and ulceration.

D3. Drugs Three Cochrane reviews have assessed the effects of drug therapy on nocturnal enuresis in children.[32-34] One of these reviews covers the less commonly used drugs and is currently being updated and will be available later this year.[34]

Forty-one RCTs were included in a Cochrane review assessing the effects of desmopressin.[32] The review found that there was clear evidence that desmopressin (in a variety of doses and forms) was better at reducing the number of wet nights per week during treatment compared to placebo (see Figure 3). However, after treatment stopped, the limited evidence available suggested that this improvement was not sustained.

Another Cochrane review of 54 RCTs found that treatment with tricyclic or related drugs (imipramine, amitriptyline, viloxazine, clomipramine and desipramine but not mianserin) was associated with a reduction of about one wet night per week while on treatment.[33] For example, imipramine was better at reducing the number of wet nights per week during treatment compared to placebo (WMD -1.19, 95% CI -1.56 to -0.82).

However, although about a fifth of the children became dry while on treatment (86/400 achieved 14 dry nights on imipramine compared to 22/413 on placebo), this effect was not sustained after treatment stopped (6/192 on imipramine compared to 7/209 on placebo).

Insufficient reliable evidence was found comparing desmopressin with tricyclics or other related drugs. Likewise, there was a lack of reliable evidence comparing desmopressin or tricyclics with simple and complex behavioural interventions.

Acceptability of drugs The British National Formulary (BNF) currently suggests that drug therapy is not usually appropriate for children under seven years of age and is reserved for when alternative measures have failed.[35] Fluid overload is potentially the most serious complication with desmopressin. It is associated with over-drinking at bedtime and its symptoms include headache, nausea, hyponatraemia, cerebral oedema and convulsions. Tricyclics have significant adverse effects, including cardiotoxic and hepatotoxic effects in overdose. Minor side effects related to their anticholinergic actions include postural hypotension, dry mouth, constipation, perspiration, tachycardia, nausea, lethargy and insomnia. The BNF recommends that the possible side effects of the various drugs should be considered and that any prescription should not be continued for longer than three months without stopping for a full re-assessment.[35]

E. Implications

- Much of the available research on the effects of interventions used to treat nocturnal enuresis in children is of poor quality and there are few direct comparisons between different types of intervention.
- Simple behavioural interventions are widely used as standard first line treatment, but they require a high level of parental involvement. Currently, there is insufficient evidence to support the use of any particular intervention.
- The use of an alarm intervention has been shown to reduce night-time bedwetting in a majority of children both during treatment and after treatment stops. Over-learning (giving children extra fluids at bedtime after successfully becoming dry using an alarm) may reduce the relapse rate. Before embarking on alarm treatment, families need to be made aware of both the time and the high level of parental involvement necessary to attain success.
- Drug therapy such as desmopressin reduces the number of wet nights per week compared with placebo, but only for as long as the drug is used. However, drugs could be used as a way to reduce the frequency of wetting for a specific purpose such as nights away from home (e.g. for holidays or staying with friends). Children and their families need to be informed about possible side effects of some of the drugs.
- Future research must be of higher methodological quality, involve comparisons between those interventions used most commonly in practice, be undertaken in appropriate settings and include follow-up periods of longer duration.

Appendix on methods

The bulletin is based upon a series of systematic reviews that have been carried out by the Cochrane Incontinence Group. Full details of review methods are available on the Cochrane Library.

Relevant trials were identified from the Group's specialised register of controlled trials which is described under the Incontinence Group's details in The Cochrane Library. The register contains trials identified from MEDLINE, CINAHL, the Cochrane Central Register of Controlled Trials (CENTRAL) and handsearching of journals and relevant conference proceedings. In addition, the cited references from the included trials were searched. No language or other restrictions were imposed on any of these searches and non-English language papers were translated where necessary.

Studies were assessed using the methods of the Cochrane Collaboration.[36] All randomised or quasi-randomised trials of interventions for the treatment of non-organic nocturnal enuresis in children were included (as defined by the trialists, usually up to age 16). Two reviewers screened the studies independently for eligibility. Where the trials have been published in more than one publication, only the primary source has been referenced.

Two reviewers independently assessed the quality of the eligible trials, and extracted data using a standard form. Primary outcomes of interest were: the number of wet nights per week during treatment and at follow up; the number of children who were cured during treatment (defined as achieving 14 consecutive dry nights) or who relapsed at follow up; and any adverse events.

A fixed effect model was used to calculate the pooled estimates and the 95% confidence intervals.[37]

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Vol. 3

1. Preventing and reducing the adverse effects of unintended teenage pregnancies
2. The prevention and treatment of obesity
3. Mental health promotion in high risk groups
4. Compression therapy for venous leg ulcers
5. Management of stable angina
6. The management of colorectal cancer

Vol. 4

1. Cholesterol and CHD: screening and treatment
2. Pre-school hearing, speech, language and vision screening
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4. Cardiac rehabilitation
5. Antimicrobial prophylaxis in colorectal surgery
6. Deliberate self-harm

Vol. 5

1. Getting evidence into practice
2. Dental restoration: what type of filling?
3. Management of gynaecological cancers
4. Complications of diabetes I
5. Preventing the uptake of smoking in young people
6. Drug treatment for schizophrenia.

Vol. 6

1. Complications of diabetes II
2. Promoting the initiation of breast feeding
3. Psychosocial interventions for schizophrenia
4. Management of upper gastro-intestinal cancer
5. Acute and chronic low back pain
6. Informing, communicating and sharing decisions with people who have cancer

Vol. 7

1. Effectiveness of laxatives in adults
2. Acupuncture
3. Homeopathy
4. Interventions for the management of CFS/ME
5. Improving the recognition and management of depression in primary care
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