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ORIGINAL ARTICLE

Nocturnal enuresis: Application of evidence-based medicine in community practice

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Aim: To report the outcomes and follow-up at 2 years of children with monosymptomatic nocturnal enuresis (MNE) managed in a private paediatric community practice utilising body-worn alarms and supportive programmes.

Methods: 522 consecutive children presenting with MNE were assessed and managed with a comprehensive supportive programme and body-worn alarm. Data were recorded prospectively and outcomes assessed at 6 and 24 months.

Results: 505 proceeded with management. A total of 79.0% achieved initial dryness within a median of 10 weeks. Of those achieving initial dryness 73.0% had remained dry at 6-month follow-up and 64% had remained dry at 24 months. A total of 99.2% follow-up was achieved. Nineteen per cent of children required more than 16 weeks management with 56% achieving dryness. More girls achieved dryness than boys and in a shorter time. There was no gender difference in relapse rates at 6 and 24 months. No difference in achieving initial success was found with respect to initial severity of wetting, nor age. Relapse rates were unrelated to gender, age, or initial severity.

Conclusion: MNE can be successfully managed using body-worn alarms achieving good initial and long-term complete dryness, without the need for expensive pharmacologic intervention. A strong supportive programme can make the management less arduous for child and family.

Key words: desmopressin; enuresis; evidence-based medicine; follow-up studies; private practice.

Nocturnal enuresis is a distressing, and treatable problem in childhood with a prevalence of almost 19% in 5- to 12-year-olds.[1] Clear evidence exists as to the effectiveness of enuresis alarm treatment for nocturnal enuresis, without frequent relapse, and with minor adverse events (Level of evidence level 1, grade of recommendation grade A).[2–6] Application of this evidence-based medicine within community practice will help children and adolescents who still wet at night, to achieve the desired goal of long-term night-time dryness. This has been shown to be associated with substantial gains in self-esteem.[7,8]

In routine clinical practice many children however, are not being offered alarm treatment, or receive it without the appropriate support strategies needed to obtain good long-term outcomes. Despite the evidence of high relapse rates, many children receive initial management with pharmaceutical agents such as desmopressin and tricyclics.[6,9] The percentage reduction in wet nights while on treatment is often reported in trials of pharmaceuticals, and in the definitions of 'complete' cure.[10] This is not as important to the child as knowing with certainty that they will wake up dry every morning. To forgo curing bedwetting for 'mere palliative treatment' with pharmaceuticals, and under-utilise the most effective treatment for bedwetting has brought to question health care systems and their funding.[11]

Delivery of advice on continence has been dispersed between health care providers and between public and private sectors. Published reports on enuresis management have mostly been from hospital-based clinics or from polyclinics in metropolitan locations. These children may not be representative of the wider population due to problems of sample size, mode of recruitment and strict inclusion or exclusion criteria.[12] Most reports have not provided information on long-term outcome. Such evaluations are of limited value when the objective is long-term cure. Reports that exclude those who drop out from treatment, which may be high,[13,14] from any analysis of outcomes, or that underestimate relapse may be seriously overestimating the success from the management strategy under consideration.[15]

Our aim in this study was to report on the application, in a community paediatric practice, of the evidence for management of monosymptomatic nocturnal enuresis (MNE), utilising primarily the body-worn enuresis alarm. The outcomes reported

Key Points

1. Monosymptomatic nocturnal enuresis can be successfully managed using body-worn alarms achieving good initial and long-term complete dryness, without the need for expensive pharmacologic intervention.
2. The mean time taken to achieve dryness was 10.4 weeks (median = 8.7 weeks) with a range from 3.1 to 35+ weeks
3. Boys took longer to achieve dryness than girls, although there were no differences in relapse rates at 6 and 24 months.

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are of 522 consecutive children with MNE attending a single physician private paediatric practice and enuresis clinic. Outcome information was obtained for initial success, and for those who maintained dryness at 6 months and 2 years.

Methods

A continence clinic was established within an existing paediatric practice in a suburban and semirural non-hospital location in 1997. A total of 849 children were referred with continence problems by their family practitioners in the initial 5 years. There was no specific recruitment process, other than advertising in local media and to family practitioners as to the clinic's establishment. The paediatrician (DAC) initially saw each child and parent assessing past and present history, including severity of wetting and day or bowel symptoms. A examination was also performed including external genitalia and urinalysis. Recording fluid and bladder volumes charts was initially conducted, however, this proved unreliable in this group. Five hundred and twenty-two children (aged 5 years or more) of these 849 met the criteria for MNE[10] and were offered treatment. No child had been on medications for treating enuresis. Twenty-two (4%) had previously received alarm management of enuresis from a paediatrician or continence clinic. No further investigations were done before alarm therapy was introduced.

After categorisation as MNE a general explanation and a review of management options were provided by the paediatrician (DAC), followed by a further explanation and education session of up to 1 h by a paediatric nurse (FMC). These discussions included a demonstration of the alarm under consideration – the Malem body-worn alarm (http://www.malem.com.uk). When a strategy for management with an alarm was agreed, detailed instructions were given. (http://www.cambridgekids.com.au/profesnl.htm). Body-worn alarms, introduced in 1980[16] were primarily used as initial management for the children reported here. They provide similar results to bedside alarms, are less expensive and are preferred by children and parents who have experienced both forms of alarm.[13]

All other management strategies (restricted drinking, lifting at random or by the clock) were ceased. Parents were encouraged to give maximum support, especially initially, and after alarm activation. A telephone follow-up was routinely provided after the first night of alarm use. An alternative alarm with multiple or different sounds or with vibration was substituted for the 'standard' alarm initially supplied if non-arousal was observed. Non-arousal was assessed by parental observation, persistent size of large wet patch or failure to wake to the alarm. No specific protocol was in place as to when to change the alarm, rather consultation with parents and child regarding progress of arousal. A louder bedside alarm with under-sheet wetness sensor (http://www.ramseycoote.com.au) was substituted if non-arousal continued to be reported. Alarms were rented from the clinic. Instructions were to use alarms nightly until there had been 14 consecutive dry nights.

In the 237 children provided with alarms up to December 2000 an additional 7-night period of alarm use with night-time fluid intake of 500 mL water was advised after achieving 14 dry nights – 'over-learning'. Due to lack of acceptability, poor compliance and inadequacy of the evidence for efficacy, this advice was not given after December 2000.

The children and their parents kept a record diary of wet and dry nights. Success was defined as 14 consecutive dry nights. Treatment was continued after 16 weeks when required, continuing until dryness, agreement to cease, or dropout occurred. Despite the common practice of ceasing treatment after 16 weeks,[17] in this study treatment was continued after 16 weeks when required. Agreement to cease followed discussion with parents, child and practitioners taking into account family circumstances, compliance and progress with the patient, rather than at a specified time after commencement of the programme. Failure was defined as not achieving 14 consecutive dry nights, including those self-terminating after 16 weeks. Relapse was defined as two or more wet nights within a 2-week period. For the patients who achieved dryness relapse was assessed at 6 and 24 months. Dropouts were those who had failed to attend, without notification, two or more appointments within 16 weeks of commencement of treatment (see Table 1 for definitions).

Children were followed at clinic visits, 2–3 weekly by the Clinic Nurse and Paediatrician in a combined session of $^{1}/_{2}$ hour. Substantial encouragement and support was given. Between clinic visits the Clinic Nurse maintained contact by telephone, letter and email, providing continued support and encouragement to child and family. The child's progress was reviewed and

Table 1 Definitions of terms

Mono-symptomatic nocturnal enuresis	The involuntary voiding of urine during sleep in children over the age of 5 years in the absence of congenital or acquired abnormalities of the urogenital system, where there has been no prolonged dryness for 6 months or more and no bladder or voiding problems associated with their wetting
Success	Achieving 14 consecutive dry nights
Failure	Not achieving 14 consecutive dry nights, including those self-terminating after 16 weeks treatment
Severity	Severe = 6 or 7 wet nights per week Less severe = 5 or less wet nights per week
Relapse	2 or more wet nights within a 2-week period after achieving initial success
Dropouts	Those who failed to attend, without notification, two or more appointments within 16 weeks of commencement of treatment

Definitions in the above are based on International Children's Continence Society definitions.

Table 2 Characteristics and treatment outcome of total sample and relapse results for those achieving initial dryness

Characteristic	*n* (%)	*n* (%) achieving initial dryness	*n* (%) dry at 6-month	*n* (%) dry at 24-month
Gender				
Male	329 (65.1)	246 (74.8)	169 (72.8)	116 (67.4)
Female	176 (34)	153 (86.9)	101 (74.3)	55 (58.5)
Age (years)				
<6	105 (21)	83 (79)	56 (75.7)	31 (58.5)
6.1–7.0	118 (23)	96 (81.4)	73 (82)	44 (71
7.1–8.0	72 (14)	57 (79.2)	37 (69.8)	26 (65)
8.1–9.0	76 (15)	58 (76.3)	36 (65.5)	24 (54.5)
9.1–10.0	52 (10)	42 (80.8)	28 (73.7)	21 (75)
≥10.1	82 (16)	63 (76.8)	40 (67.7)	25 (64.1)
Severity				
More severe	428 (85)	341 (79.7)	225 (71.7)	141 (61.8)
Less severe	77 (15)	58 (75.3)	45 (83.3)	30 (78.9)

More severe = 6–7 nights wet/week; Less severe = 5 or less nights wet/week.

any problems addressed including non-arousal with alarm and non-compliance. Where necessary urinalysis was repeated and in most children with poor progress renal and post-micturition ultrasound was performed. Further details are available at http://www.cambridgekids.com.au/profesnl.

Children were discharged after reporting 14 days consecutive dry nights but with open access in the event of relapse. A questionnaire was sent by mail to all who had achieved initial dryness, at 6 months and 2 years after dryness, with telephone follow-up if this was not returned.

Statistical analyses

All statistical analyses reported in this study were conducted using SPSS version 11. Preliminary data screening procedures revealed the presence of a number of influential outliers on the variable assessing weeks taken to achieve dryness. Six cases recorded scores to achieve dryness above 35 weeks (ranging from 37 weeks to 61 weeks), far exceeding the time taken by all other patients. Consistent with procedures recommended by Tabachnick and Fidell[18] these outliers were adjusted so that all values above 35 (5 boys, 1 girl; ranging in age from 6.3 to 10.3 years) were recoded back to 35 to reduce the impact of these outliers on overall results. χ^2-test for independence (with Yates Correction for Continuity for 2 by 2 tables) was used to assess the association between categorical variables. Kaplan–Meier survival analysis, with the log-rank test was used to assess the impact of gender on overall success rates and time taken to achieve dryness.

Results

Five hundred and twenty-two of 849 children referred with incontinence problems within the period 1997–2002 (5 years) met the criteria for MNE.[10] Five hundred and five of the 522 (97%) proceeded to commence enuresis alarm management as their initial strategy of management. The outcomes from these 505 children are reported, the 17 of 522 (3%) declining alarm treatment have been excluded from the analysis. Three hundred and twenty-nine (65.1%) of the patients were male, 176 (34%) were female. At commencement of treatment 428 (85%) of the patients reported more severe wetting (6–7nights wet per week) while 77 (15%) reported less severe wetting (5 or less nights weekly) (see Table 2).

Outcome of treatment

A total of 79% (399/505) of the patients achieved dryness, with a further 13% experiencing a reduction in the number of wet nights. The mean time taken to achieve dryness was 10.4 weeks (median = 8.7 weeks) with a range from 3.1 to 35+ weeks (see Fig. 1). Figure 2 shows the cumulative percentage of patients achieving initial dryness at weekly intervals. Seven nights of over-learning was practised up to December 2000 (237 children), thereby extending time to dryness by 1 week for these children. Ninety-five patients (19%) were treated for more than 16 weeks. The 96 children who failed to achieve initial dryness were offered desmopressin or to retrial the programme in 12 months. Most chose not to trial medication.

During the period of this study 368 patients with an initial successful treatment outcome who had reached the required 6-month post-treatment time period were contacted, with 100% of these eligible patients providing details of their status. Seventy-three per cent of these patients were still dry, with 27% reporting a relapse (see Fig. 3). There was no significant difference in the relapse rates for patients who did and did not participate in over-learning ($\chi^2 = 0.37$, d.f. = 1, $P = 0.55$). For the 24-month follow-up 266 patients, who were dry at the completion of treatment, and who had reached the 24-month post-treatment time period, were contacted, with outcome data available for 264 patients (99%). Of these patients 171 (64%) reported continued dryness, while 95 (36%) had relapsed. Only two eligible patients (1%) were lost to follow-up.

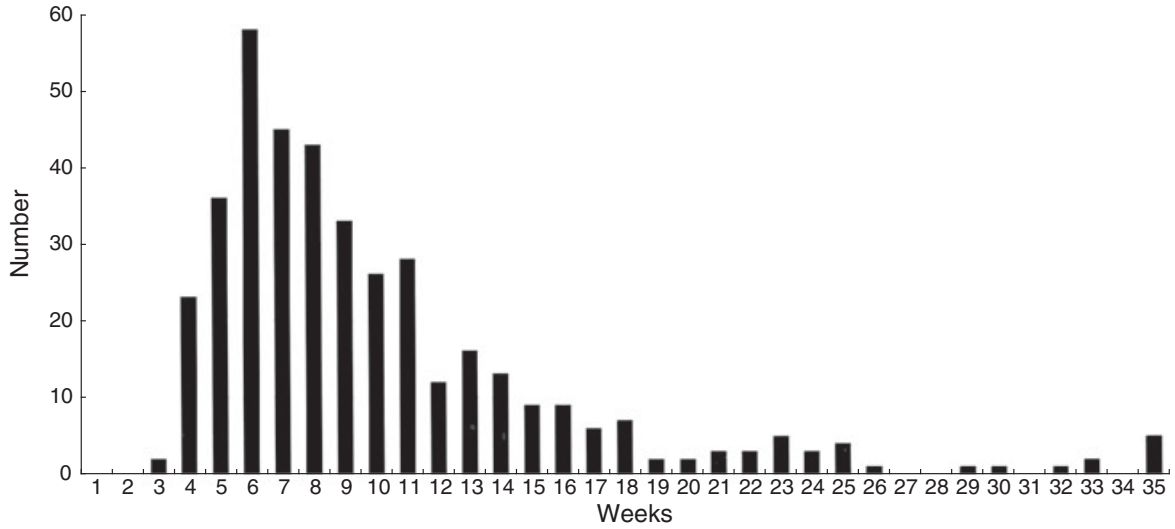

Fig. 1 Time in weeks taken to achieve dryness.

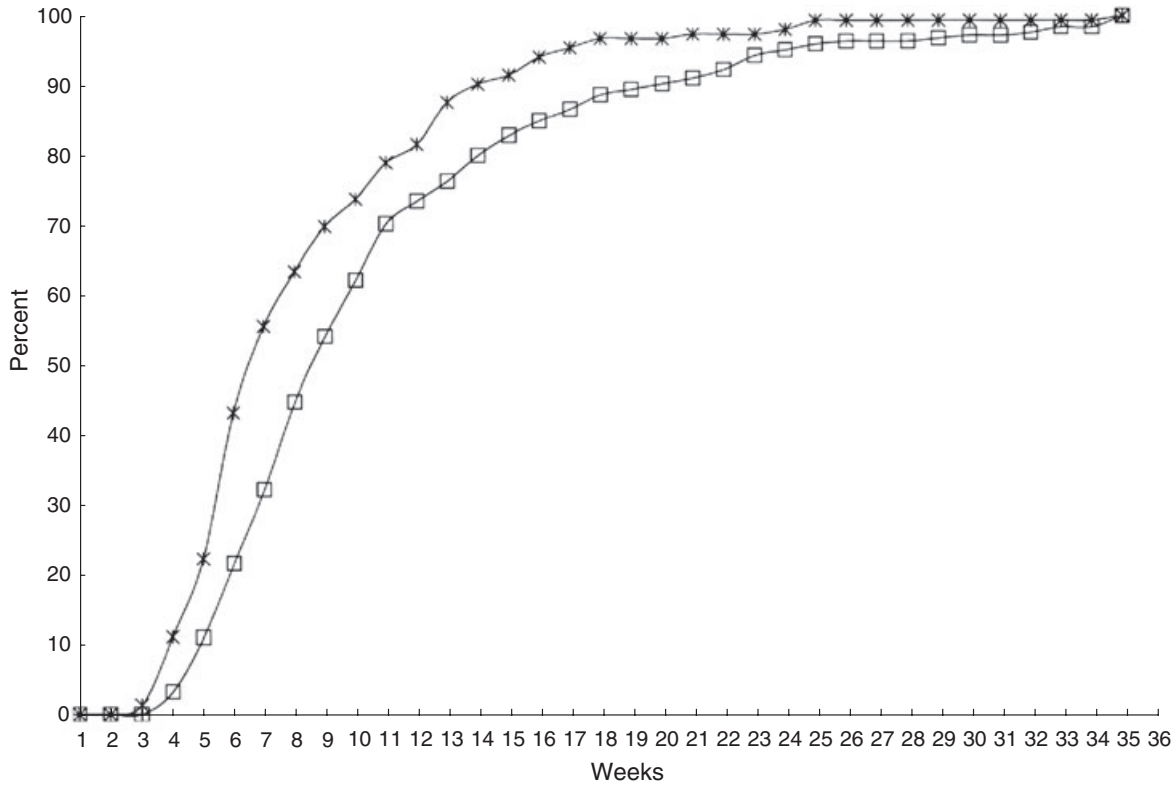

Fig. 2 Cumulative frequency showing percentage of patients achieving initial dryness. (–□–) Male ($n = 245$), (–✶–) female ($n = 153$).

Influence of gender, age and severity on outcomes

There was no gender difference in initial severity of wetting: 86.3% of boys and 81.8% of girls were classified as severe (6 or 7 wet nights per week) ($\chi^2 = 1.47$, d.f. = 1, $n = 505$, $P = 0.23$). There was a statistically significant gender difference in initial success rates (dry/not dry), with 74.8% of boys and 86.9% of girls achieving dryness ($\chi^2 = 9.5$, d.f. = 1, $n = 505$, $P = 0.002$) (see Table 2).

Gender differences in the success rate and the time taken to achieve dryness were explored using a Kaplan–Meier survival analysis. The log-rank test revealed a significant gender difference (log-rank = 30.63, d.f. = 1, $P < 0.0005$). The mean time taken to achieve dryness (adjusted for censored cases) in weeks

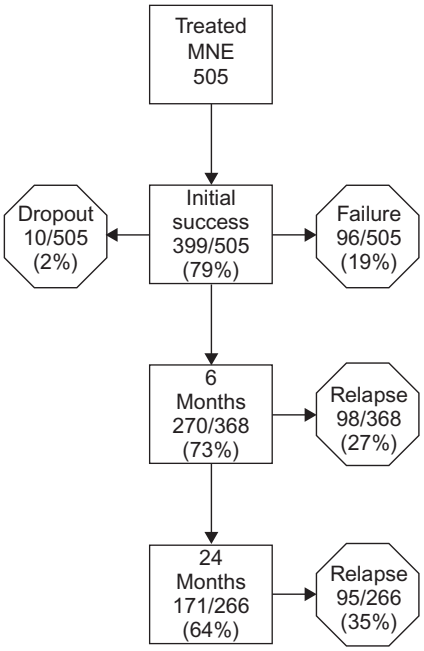

Fig. 3 Flowchart showing initial treatment outcome and 6-month and 24-month follow-up. MNE, monosymptomatic nocturnal enuresis.

for boys was 14.78 (standard error = 0.58, 95% CI 13.64, 15.93) with a median of 10.90 (standard error = 0.42, 95% CI 10.08, 11.72). For girls the average adjusted time in weeks was 10.35 (standard error = 0.57, 95% CI 9.24, 11.47) with a median of 7.70 (standard error = 0.61, 95% CI 6.51, 8.89).

There was no significant gender differences (see Table 2) in the relapse rates at 6 month follow-up for boys and girls ($\chi^2 = 0.031$, d.f. = 1, $n = 368$, $P = 0.86$) or in the relapse rate at 24 months ($\chi^2 = 1.74$, d.f. = 1, $n = 266$, $P = 0.19$).

To assess the impact of age group children were divided into categories according to their age (see Table 2). Comparison of pre-treatment severity for each age group revealed a significant result with the younger age groups recording higher percentages of severe cases (6, 7 wet nights per week) ($\chi^2 = 29.19$, d.f. = 5, $P < 0.001$). There was no statistically significant effect for age on treatment success rates (dry/not dry) ($\chi^2 = 1.05$, d.f. = 5, $P = 0.96$). There was no significant difference in relapse rates among the age groups ($\chi^2 = 7.16$, d.f. = 5, $P = 0.21$).

The impact of initial severity on success of treatment was assessed. There was no significant difference in outcome (dry/not dry) for patients classified as more severe (6, 7 wet nights per week) or less severe (5 or less nights per week) ($\chi^2 = 0.505$, d.f. = 1, $P = 0.48$) (see Table 2). There was no significant difference between the more severe and less severe group in the number of weeks taken to achieve dryness. The average time taken to achieve dryness (adjusted for censored cases) in weeks for the more severe group was 13.2 weeks with a median of 9.9. For the less severe group the average adjusted time in weeks was 13.5 with a median of 9.6. There was no significant difference in relapse rates at 6 or 24 months for the initially more severe and less severe groups (6 months: $\chi^2 = 0.54$, d.f. = 1, $P = 0.46$; 24 months: $\chi^2 = 1.03$, d.f. = 1, $P = 0.31$).

Discussion

Our aim was to demonstrate that the use of the enuresis alarm and supportive programmes is effective in achieving high initial success rates and long-term cure for nocturnal enuresis. These results provide the evidence that the programmes are very effective. Three hundred and ninety-nine children of 505 treated achieved initial dryness, representing a 79% success rate. This is higher than results reported in the literature and reflects the intense and supportive programme. Meta-analysis of alarm conditioning studies has shown an initial success rate of 66%.[5] Mean time to dryness in the current study was 10 weeks after initiating alarm treatment. Relapse rates reported in the literature vary from 29% to 69% after successful treatment[2] although many have not had the complete and long-term follow-up of the current study. Our results showing 27% relapse rate at 6 months and 36% at 24 months compare very favourable with previous studies.

A substantial number of children ($n = 95$, 19%) required more than 16 weeks of alarm use and five children (1%) more than 35 weeks to achieve dryness. These children had shown slow but definite progress with the parents reluctant to cease management. By limiting alarm usage to 16 weeks or less, as some controlled trials report, or by definition,[17] the benefit of prolonged dryness may be denied for some children.

There was a significant gender difference in time to achieve dryness. Boys took longer to achieve initial dryness (boys 14.8 weeks, girls 10.9 weeks). However, there was no significant difference in relapse rates at 6 months or 24 months. Although younger groups had a significantly higher percentage of wet nights, there was no statistically significant effect for age on treatment success rates. The age and sex of the child has not been shown to affect the treatment outcome in previously reported studies.[19–23] Jensen[22] found a minor influence in success for girls related more to their higher initial rate of frequency of wetting compared with boys.

In the current study there were only 2% classified as drop-outs. The low rate reflected the acceptability of the treatment and high level of support given to the children and their families. One hundred per cent follow-up of eligible patients was achieved at 6 months and 99.2% follow-up at 2 years. Such complete follow-up has not been reported before. The relapse rate compares favourably with previous reports.[20,24] Reports of relapse in previous studies that are based only on those that do not default from follow-up enquiry will almost certainly underestimate the relapse rate.

Previous studies suggest that pharmacologic management with desmopressin or tricyclics can result in an increased likelihood of becoming dry, when compared with a placebo,[2,25,26] although studies vary in the definition of success, with some accepting a 90% reduction rather than complete dryness. Relapse rates on cessation of drug treatment, however, are high with the mean number of wet nights no different from placebo.[6] Pharmaceuticals can be very costly, and have the potential for serious complications of water toxicity or cardiac arrhythmias.[11,12]

The current study is the one of the largest studies reported on MNE, the largest utilising one type of enuresis alarm and management plan. The results compare very favourably with

others obtained with the enuresis alarm, a supportive programme for the family, and without the use of expensive pharmaceuticals or investigations. Not only can long-term dryness be achieved, but children can wake up knowing with certainty that they will be dry.

The outcomes reported in this study may be influenced to some extent by the type of clinic and patient group. The study was conducted in a private clinic, in a non-metropolitian area of Melbourne, Australia. The patient population may be biased towards slightly higher socio-economic groups. Given that they were required to fund a significant portion of the treatment programme, this might have resulted in greater motivation to complete the programme. In Australia the expense of treatment with pharmaceuticals is subsided by the government, whereas equipment rental or purchase of alarms is not.

Despite this potential sample bias the outcomes reported from this study are relevant to many families with children who have untreated or inappropriately managed MNE, as the methods used can be readily introduced into any hospital-based clinic, community clinic, or integrated into a general or specialist practice.

Conclusion

Nocturnal enuresis is a common childhood problem, with many significant reasons to treat and to achieve a lasting cure. MNE can be successfully managed using body-worn alarms, achieving good initial and long-term complete dryness, without the need for expensive pharmacologic intervention. Available health funding may be better utilised for community-based supportive programmes for enuresis, using simple alarm management.

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