Non-invasive techniques for stimulating urine production in non-toilet trained children: a systematic review

Mathew Chandy, Ann Dewey, Carole Fogg, Karen Pilkington

ABSTRACT

Background Urinary tract infection requires collection of a sterile urine specimen for diagnosis, which is difficult and time consuming in pre-continent children. This systematic review summarises evidence of the effectiveness of bladder stimulation techniques on urine collection in pre-continent children, compared with standard techniques.

Methods MEDLINE, PubMed, EMBASE and CINAHL were searched to May 2019. Selection, data extraction, risk of bias and quality assessment were undertaken by two independent reviewers. Inclusion: (1) all study designs; (2) pre-continent, age <3 years receiving bladder stimulation techniques; (3) outcomes including time to urine collection or contamination rates; (4) English-language articles. Exclusion: coexisting neurological disorders.

Results Three randomised controlled trials (RCTs) were identified using three techniques in 568 participants aged 1 day to 35 months. Two RCTs demonstrated an increased success in voiding within 5 min, one using a finger tapping and lumbar paravertebral massage technique and the other cold saline-soaked gauze rubbed over the suprapubic region, compared with no active intervention. A third RCT using a mechanical vibration device demonstrated no difference in time to voiding from advice alone. Non-randomised studies compared different techniques for the same intervention and tapping alone versus urine bags. Six uncontrolled studies tested the finger tapping and massage technique. Risk of bias was low for one RCT and unclear for two RCTs with the other studies rated fair to poor quality. Overall, the evidence on success rates was graded low for tapping plus massage and moderate for the gauze rubbing intervention. Adverse effects included crying and mild distress.

Discussion The results suggest a positive effect of stimulation techniques, lack of replication in rigorous RCTs, heterogeneity of techniques and outcomes assessed prevents conclusive recommendations being made. Further RCTs are required comparing non-invasive stimulation methods and assessing time to successful collection, contamination rates, adverse effects, caregiver and clinical staff acceptability.

INTRODUCTION

Urinary tract infection (UTI) in pre-continent children remains a challenging diagnostic dilemma. Prompt treatment of a UTI is required to reduce the risk of complications such as renal failure and scarring and is an important diagnosis to exclude in any child with a fever.1 Prevalence of UTI among infants between birth and 24 months of age presenting with a fever is estimated at 7%.2 Following National Institute for Health and Clinical Excellence guidance, “infants and children presenting with explained fever of 38°C or higher should have a urine sample tested within 24 hours”.3

Within the UK, clean catch methods are regarded as the gold standard for urine collection in children.4 These methods reduce the risk of contamination of samples and involve cleaning of the genital area and then waiting for spontaneous voiding into a sterile container. The American Academy of Pediatrics recommends collection by suprapubic aspiration (SPA) or catheterisation to establish a diagnosis of UTI in children between 2 and 24 months of age,5 but highlights that if a mid-stream clean catch sample is negative for both leucocytes and nitrites, further immediate invasive sampling can be avoided while the clinical course is monitored. Other methods (urine collection pads and bags) carry significant risks of contamination and invasive methods (catheter and SPA) carry a risk of pain or iatrogenic harm.6 Current UK national guidance concludes that “Limited available evidence showed that the urine collection methods that produce a most diagnostically accurate sample
for testing are clean catch and SPA. The results of a systematic review on the effectiveness of pre-analytic practices on contamination and diagnostic accuracy indicates that, for non-invasive approaches, midstream collection with cleansing of the genitals prior to voiding should be used in place of collection in sterile urine bags.

Clean catch methods can be difficult to carry out and are time consuming in pre-continent children. This is a particular problem in the ED when obtaining a rapid diagnosis is essential for guiding management. There are published studies exploring non-invasive methods of stimulating urine production but no published comprehensive, systematic assessment of the evidence on these techniques.

This systematic review evaluates the published evidence for non-invasive bladder stimulation techniques compared with standard techniques on urine sample collection, contamination and adverse effects for children who are not yet toilet trained.

METHODS
A systematic review was undertaken according to the prospectively published protocol on the international register of prospective systematic reviews (PROSPERO 2017 CRD42017056224).

This review is reported according to the criteria set out in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist for systematic reviews.

Literature search and selection
The search strategy was developed by MC, KP and AD with assistance from a research librarian. The strategy for MEDLINE is presented in online supplementary appendix i.

MEDLINE, PubMed, EMBASE and CINAHL databases were accessed via the NHS Athens HDAS portal and searched from inception.

Initial database searches were undertaken in June 2017. Attempts were made to contact authors of relevant articles to identify further or ongoing studies. The searches were updated on the 27 May 2019; no further studies were found.

Searches were also undertaken using the Cochrane Library (including the Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects (DARE), TRIP database (www.tripdatabase.com) and BestBETS (www.bestbets.com).

Clinical trials registries (ClinicalTrials.gov and controlled-trials.com) and websites of professional bodies (Royal College of

Figure 1  Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram of studies.
Paediatrics and Child Health and Royal College of Emergency Medicine) were reviewed for unpublished or ongoing trials. Reference lists for included studies were checked for additional publications and relevant journals were hand searched for the past 5 years.

Search results were combined using EndNote software and duplicates removed. The records were imported into Abstrackr for review (Brown University, USA). Titles and abstracts were screened independently by two researchers (KP and MC) and records identified as relevant, maybe or irrelevant. Full texts were obtained for studies marked as ‘relevant’ or ‘maybe’ by either reviewer and consensus on inclusion/exclusion was reached by discussion. Had agreement not been reached, a further reviewer (AD) was available to provide consensus (but was not required).

Initial scoping revealed limited randomised controlled trial (RCT) evidence on the interventions being reviewed and so eligibility criteria were designed to be broad with all study designs considered.

Eligibility criteria
Patients/population: Pre- continent children (<3 years of age) who were not toilet trained and without neurological problems in whom a urine sample was required to aid diagnosis.

Interventions: Any non-invasive techniques intended or designed to stimulate urine production.

Comparison: All types of control or comparative interventions were considered.

Study design: Any clinical study reporting at least one of the outcomes was included; thus, cohort, before and after and retrospective studies in which there was no control/comparison as well as RCTs and non-randomised trials were eligible for inclusion.

Outcomes: Primary or secondary outcomes that included at least one of the following—(1) success in obtaining a urine sample within a stated period of time, (2) mean time to obtain urine sample and (3) contamination rates.

Language: Only studies published in English.

### Data extraction
Data extraction was undertaken independently by two reviewers (KP and MC) onto standardised forms developed for this review including information on study characteristics, interventions, participant characteristics and outcomes. Extracted data were compared for accuracy and reviewers met to reach consensus.

### Quality assessment
Quality assessment was undertaken independently by two reviewers (KP and MC). Cochrane Risk of Bias tool was used for RCTs. The Newcastle-Ottawa scale for non-randomised trials was to have been used, but this was replaced with the Downs and Black assessment tool as being more appropriate to the wide range of study designs identified. The Downs and Black tool can be used to assess both RCTs and non-RCTs providing a comparative score when mixed designs are included in a systematic review as in this case. It is a validated scale assessing 27 aspects and is considered an acceptable alternative to the Newcastle-Ottawa scale based on a comprehensive analysis of a wide range of such tools.

### Results

#### Literature search and inclusion

Database searches identified 1536 records. Two further relevant studies were found on review of reference lists of included studies, and one further study found by other sources. No studies were removed from the initial scoping.

### Table 1  Summary of RCTs included

<table>
<thead>
<tr>
<th>Study; country; year</th>
<th>Setting</th>
<th>Sample size</th>
<th>Participants (age/gender)</th>
<th>Intervention</th>
<th>Control or comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kaufman et al; Australia; 2017¹⁹</td>
<td>Tertiary paediatric ED</td>
<td>344</td>
<td>Mean age months: Intervention 5.4 (SD 3.2) Control 5.4 (SD 3.0) Gender: Intervention M:F (55%-45%) Control M:F (45%-55%)</td>
<td>Rubbed the suprapubic region of the child in a circular pattern with gauze soaked in cold saline held with forceps</td>
<td>Wait for child to void spontaneously. Both maximum 5 min</td>
</tr>
</tbody>
</table>

| Altuntas et al; Turkey; 2015¹⁸ | Tertiary neonatal intensive care unit | 127 | Median age weeks: Intervention 7 (4–14) Control 8 (5–15) Gender: Intervention M:F (52%-48%) Control M:F (53%-47%) | Fed according to weight 25 min before stimulation (excluded if poor feeding/dehydration). One examiner held baby under the armpits with legs dangling in males and hip flexion in females. The second examiner stimulated the bladder by tapping and lumbar paravertebral massage as per Herreros fernández et al 2013²² | Held under the armpits with legs dangling until they urinate |

| Davies et al; UK, 2008¹⁷ | Paediatric ED | 110 (data for 97) | Mean age (range) months Intervention: 10.76 (1–31) Control: 10.72 (0.5–35) Gender: Intervention M:F (54%-46%) Control: M:F (42%-58%) | Queen Square bladder stimulator held on the patient for 1 min out of every 5 min | Written advice on methods of stimulating urine flow by massage and tapping the abdomen |

RCT, randomised controlled trial.

were excluded due to publication language. Following initial title and abstract screening, 24 studies were assessed as relevant or maybe relevant. Full-text versions of these publications were reviewed, and 11 studies were selected for inclusion. Reasons for exclusion of remaining publications are listed in figure 1. Three abstracts of studies were excluded because they did not report enough information to allow risk of bias and quality assessment to be performed.14–16

**Description of studies included**

Three RCTs,17–19 two non-randomised studies (a feasibility study which compared an intervention at two different temperatures and a comparison of tapping with collection in urine bags) 20 21 and six uncontrolled pre–post trials were identified22–27 (tables 1 and 2).

### Randomised controlled trials

**Risk of bias and quality assessments**

While none of the included studies were blinded, the objective nature of the outcomes (time to voiding) mitigated the risk of bias posed. The nature of the interventions would make blinding of participants and those delivering the intervention challenging. The trial using gauze soaked in cold saline was judged to be at low risk of bias,19 with the overall risk of bias in the remaining trials being unclear.17 18 (tables 3 and 4).

#### Table 1 Summary of non-RCTs included

<table>
<thead>
<tr>
<th>Study</th>
<th>Country; year</th>
<th>Setting</th>
<th>Sample size</th>
<th>Design</th>
<th>Participants (age/gender)</th>
<th>Downs and Black score*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kaufman et al, 2017</td>
<td>Australia</td>
<td>Tertiary paediatric ED</td>
<td>40</td>
<td>Prospective feasibility study</td>
<td>Mean age 7.5 months (range 2–15) room temperature group (RT) 5.7 months (range 1–16) cold temperature group (CT) M:F 30:10 (75%:25%)</td>
<td>11</td>
</tr>
<tr>
<td>Nepal et al, Nepal, 2016</td>
<td>Nepal</td>
<td>Neonatal intensive care unit and postnatal ward</td>
<td>100</td>
<td>Prospective feasibility study</td>
<td>Mean age 31.5 hours M:F 59:41 (59%:41%)</td>
<td>12</td>
</tr>
<tr>
<td>Labrosse et al, Canada, 2016</td>
<td>Canada</td>
<td>Tertiary-care paediatric ED</td>
<td>126</td>
<td>Prospective cohort study</td>
<td>Median age 55 days IQR 37–92 M:F 64:62 (51%:49%)*</td>
<td>17</td>
</tr>
<tr>
<td>Tran et al; France, 2016</td>
<td>France</td>
<td>Paediatric ED</td>
<td>142</td>
<td>Cross-sectional study</td>
<td>Mean age 4.7 months (±4.8) M:F 68:74 (48%:52%)*</td>
<td>11</td>
</tr>
<tr>
<td>Valleix-Leclerc et al; France; 2016</td>
<td>France</td>
<td>3 Paediatric EDs</td>
<td>48</td>
<td>Prospective non-controlled study</td>
<td>Median age 10 months IQR 3–17.25 M:F 21:27 (44%:56%)*</td>
<td>16</td>
</tr>
<tr>
<td>Herreros et al; Spain; 2015</td>
<td>Spain</td>
<td>ED</td>
<td>60</td>
<td>Cross-sectional study</td>
<td>Mean age 44 days Median age 40 days (range 2–90) M:F 42:18 (70%:30%)</td>
<td>11</td>
</tr>
<tr>
<td>Herreros Fernández et al; Spain; 2015</td>
<td>Spain</td>
<td>Neonatal unit</td>
<td>80</td>
<td>Prospective feasibility and safety study</td>
<td>Mean age Male 6.66 days Female 6.23 days M:F 31:49 (39%:61%)*</td>
<td>10</td>
</tr>
<tr>
<td>Taylor et al; Ireland; 1986 (short report)</td>
<td></td>
<td>Children’s hospital</td>
<td>154 samples (133 children)</td>
<td>Non-randomised controlled study (three arm) Age range 1 week to 12 months M:F 62:71 (47%:53%)*</td>
<td>8 (based on short report)</td>
<td></td>
</tr>
</tbody>
</table>
Table 4  Cochrane risk of bias assessment for RCTs

<table>
<thead>
<tr>
<th></th>
<th>Kaufman et al</th>
<th>Altuntas</th>
<th>Davies et al</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation</td>
<td>+</td>
<td>+</td>
<td>?</td>
</tr>
<tr>
<td>Allocation concealment</td>
<td>+</td>
<td>?</td>
<td>+</td>
</tr>
<tr>
<td>Blinding of participants and personnel (based on primary outcome measure)</td>
<td>+</td>
<td>?</td>
<td>+</td>
</tr>
<tr>
<td>Blinding of outcome assessment</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Incomplete outcome data</td>
<td>+</td>
<td>+</td>
<td>?</td>
</tr>
<tr>
<td>Selective reporting</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Other sources of bias</td>
<td>+</td>
<td>+</td>
<td>?</td>
</tr>
</tbody>
</table>

Key
- Low risk of bias
- High risk of bias
- Unclear risk of bias

RCT, randomised controlled trial.

Patient characteristics and settings

The three RCTs included a total of 568 male and female patients aged from 2 days to 35 months. Two were carried out in Paediatric Emergency Departments and one in a neonatal intensive care unit (NICU).

Intervention and comparators

Three types of non-invasive interventions were evaluated. One trial assessed the efficacy of rubbing the suprapubic region with saline-soaked gauze.19 One trial evaluated a technique involving tapping with the fingers over the suprapubic region (at a rate of 100/min for 30 s) followed by lumbar paravertebral massage (for 30 s).18 One further RCT used a vibrating bladder stimulator held over the suprapubic region.17 The control interventions involved the same position without stimulation and providing advice only.

Personnel required to deliver intervention

The number of personnel required varied depending on the intervention. The intervention involving saline-soaked gauze required two operators: one to perform the intervention and one to collect the urine sample.19 Finger tapping over the suprapubic area and lumbar paravertebral massage required three operators; one to perform the intervention and one to collect the urine sample.17 The vibrating bladder stimulator was applied by the parent and it is inferred that they would be responsible for collection of the urine sample.17

Outcomes measured

Voiding within 5 min and voiding plus successful urine catch was assessed in one RCT,19 while time to voiding was assessed in another.17 The third RCT measured both voiding within 5 min and overall time to voiding.18 Contamination rates were recorded in two RCTs17 18 and one investigated parental and clinician satisfaction with the technique.19

Effects of the interventions

Outcome: voiding with a pre-specified time/time to void

Tapping plus massage

This technique was assessed in one RCT in a NICU setting; the infants had a median age of 7–8 days and a significant difference was found between the intervention and holding the infant in the same position without stimulation (success in <5 min in 78% in the intervention group vs 33% in the control group (p<0.0001)).18 Gender was not found to be an independent variable of success.

Gauze soaked in cold saline

Only one RCT was found which included 344 infants with a mean age of 5.4 months in a Paediatric Emergency Department setting. A significant difference was seen between the effects of the intervention and the control (waiting for spontaneous voiding) with successful voiding at 5 min of 31% and 12%, respectively (p<0.001).19 Age and gender were not found to affect primary outcome results.

Bladder stimulator (mechanical/battery operated)

This method, using a vibrating bladder stimulator, was evaluated in one RCT in a Paediatric Emergency Department with 97 patients ranging in age from 0.5 to 35 months. No significant difference was observed between the effects of advice or a bladder stimulator on time to void (42% vs 53% waiting <1 hour; p=0.15).17 There were no significant differences in outcome found with age and gender.

Outcome: contamination rates

Two of the RCTs reviewed assessed contamination rates; however, they did not demonstrate a significant difference between intervention and control arms.18 19

Outcome: parent/carer and health professional/healthcare worker satisfaction

Satisfaction among carers and health professionals was found to be good with statistically significant differences in Likert scores of 2 (satisfied) versus 3 (neutral) in favour of the intervention using gauze soaked in saline.19

Outcome: adverse events

In the two RCTs that reported adverse events, one commented on crying in all participants (in both the control group and those receiving tapping and massage).18 The other found 5 of 49 children in the intervention group were more upset following use of the mechanical vibrating device and two had a transient red mark on the skin.17 In the third RCT, crying and mild distress were not regarded as adverse events as they commonly occur with routine clean catch urine and no other adverse events were observed.19

Non-randomised and observational/uncontrolled pre–post studies

Eight studies other than RCTs were identified and included a total of 729 patients.20–27 Age of participants varied with means ranging from 31.5 hours to 7.5 months (median of 10 months reported in one study). Techniques used in these studies included saline-soaked gauze rubbed over the suprapubic region,21 a finger tapping technique,20 while the majority of studies used the finger tapping and lumbar paravertebral massage technique described by Herrera Fernández et al (tables 2 and 5).22

Quality of the non-randomised and observational studies was assessed using the Downs and Black tool and was found to be poor with scores of less than 14 in six of the eight20–24 27 and fair in the remaining two.25 26

Six studies used the tapping plus lumbar paravertebral massage technique.22–27 Voiding within a pre-specified time was reported in five studies testing the tapping plus massage technique: three studies reported rates within 5 min of 27%, 49% and 86%, respectively.22 25 26 One study reported voiding within venues.
Table 5  Results: non-randomised trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>Control or comparison</th>
<th>Outcomes</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kaufman et al, 2017</td>
<td>10 s of standard peri-genital cleaning with room-temperature sterile water-</td>
<td>Saline-soaked gauze</td>
<td>Voided &lt;5 min, Satisfaction Adverse events</td>
<td>Room-temperature saline: 5/20 (25% CI 9 to 49); cold saline 7/20 (35% CI 15 to 59); all: 12/40 (30% CI 17 to 47)</td>
</tr>
<tr>
<td></td>
<td>soaked gauze at 2.8°C Suprapubic area rubbed in a circular motion with saline-</td>
<td>at room temperature</td>
<td></td>
<td>35/40 parents satisfied or very satisfied (87.5%, 95% CI 73 to 96) 36/40 clinicians satisfied or very satisfied (90%, 95% CI 76 to 97)</td>
</tr>
<tr>
<td></td>
<td>soaked gauze at room temperature for up to 5 min</td>
<td>for up to 5 min</td>
<td></td>
<td>No adverse events</td>
</tr>
<tr>
<td>Nepal et al, 2016</td>
<td>Fed according to weight 25 min prior to stimulation (excluded poor feeding/</td>
<td>None</td>
<td>Voided &lt;4 min, Time taken Adverse events</td>
<td>91/100 (91%) Mean 59.7 s (SD 46.4) No adverse events</td>
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<tr>
<td></td>
<td>dehydration). Baby held under the armpits with legs dangling. Examiner</td>
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<td></td>
<td>stimulated the bladder by tapping (100 taps/min for 60 s) and lumbar</td>
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<td></td>
<td>paravertebral massage (30 s) repeated for two cycles</td>
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</tr>
<tr>
<td>Labrosse et al, 2016</td>
<td>Opportunity to feed 20 min prior to intervention. Tapping and massage as</td>
<td>None</td>
<td>Voided &lt;5 min (all), Time taken, Voided &lt;5 min (&lt;30 days old) Contamination</td>
<td>62/126 49% (95% CI 40 to 58) Median 4 s (IQR 14–158) 14/23 61% (p=0.01) Contamination: 16% vs 6% (invasive)</td>
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<tr>
<td></td>
<td>per Herreros Fernández. Maximum 300 s or success</td>
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<td></td>
<td>Paired catheter or suprapubic aspirate urine sample after if urinalysis was</td>
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<td></td>
<td>positive or decision to prescribe antibiotics or unsuccessful urine</td>
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<td></td>
<td>collection</td>
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<tr>
<td>Tran et al, 2016</td>
<td>Tapping and massage as per Herreros Fernández et al 2013. Up to 3 min or</td>
<td>None</td>
<td>Voided &lt;3 min (all), Time taken, Voided &lt;3 min (&gt;1 year age)</td>
<td>55.6% (95% CI 47.5 to 63.8) Mean 63.6 s (±54.5) 28.6% (p=0.0001) Discomfort: 58.5% (95% CI 50.4 to 66.6)</td>
</tr>
<tr>
<td></td>
<td>success</td>
<td></td>
<td>Adverse events</td>
<td></td>
</tr>
<tr>
<td>Valleix-Leclerc et al, 2016</td>
<td>Received weight and age-appropriate drink. First operator held child under</td>
<td>None</td>
<td>Voided &lt;5 min, Time taken Adverse events</td>
<td>13/48 27% (95% CI 13 to 41) Mean 2 min Difficulties in maintaining child in correct position 22/48 (46%) Success rate according to weight &gt;9 kg—14.3%, &lt;9 kg—37%</td>
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<tr>
<td></td>
<td>the arms with legs dangling. Tapping and massage as per Herreros Fernández</td>
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<tr>
<td></td>
<td>et al 2013 repeated for up to 5 min or success</td>
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<td></td>
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</tr>
<tr>
<td>Herreros et al, 2015</td>
<td>Encourage oral intake based on age and weight (excluded infants with poor</td>
<td>None</td>
<td>Accuracy of diagnosis, Contamination</td>
<td>Sensitivity of 97% (95% CI 82% to 100%) Specificity of 89% (95% CI 65% to 98%) Contamination: 5% (bladder stimulation) vs 8% (invasive)</td>
</tr>
<tr>
<td></td>
<td>feeding), genital cleaning protocol and stimulation of voiding (suprapubic</td>
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<td></td>
<td>and lumbar paravertebral massage) Paired samples with urinary bladder</td>
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<tr>
<td></td>
<td>catheterisation within 1 hour</td>
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</tr>
<tr>
<td>Herreros Fernández et al,</td>
<td>Fed according to weight 25 min before stimulation performed (excluded poor</td>
<td>None</td>
<td>Voided &lt;5 min, Time taken Adverse events</td>
<td>69/80 86% Mean 57 s (SD 48.6) Controlled crying 100%</td>
</tr>
<tr>
<td>2013</td>
<td>feeding/dehydration). Tapping in the suprapubic area at 100 taps/min for</td>
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<tr>
<td></td>
<td>30 s Light circular massage of the lumbar paravertebral zone in the lower</td>
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<td></td>
<td>back for 30 s, repeat until success</td>
<td></td>
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</tr>
<tr>
<td>Taylor et al, 1988</td>
<td>Finger tapping just above the pubis with two fingers, 1 hour after a feed.</td>
<td>Urine bag (Hollister</td>
<td>Contamination, Time taken</td>
<td>Bag with washing: 25/49 (51% contaminated) Tap with washing: 4/52 (7.7%, p&lt;0.001) Tap, no washing: 7/53 (13.2%, p&lt;0.001) Mean 5.5 min (SD 6.0)</td>
</tr>
<tr>
<td></td>
<td>1 tap/s for 1 min followed by 1 min rest until urine sample obtained. With</td>
<td>U-bag) placed over the</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>or without genital washing prior to intervention</td>
<td>genitalia after</td>
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<tr>
<td></td>
<td></td>
<td>washing with sterile</td>
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<tr>
<td></td>
<td></td>
<td>water</td>
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<td></td>
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</table>

4 min and a success rate of 91%, and another reported voiding within 3 min with a success rate of 56%. The lowest rate was reported in a study in France in 48 infants with a median age of 10 months; the highest rate was found in a study of 100 neonates less than 28 days old. No comparison with control was reported in these studies. Rates of 35% and 25% for voiding within 5 min were reported in a study comparing rubbing with gauze soaked with cold and room-temperature saline, respectively. One study reported time taken to voiding rather than success rates and the final study did not assess voiding time. Three studies assessed contamination as a primary outcome. A non-randomised trial compared finger tapping with sterile water-soaked gauze at 2.8°C Suprapubic area rubbed in a circular motion with saline-soaked gauze at room temperature for up to 5 min.
to urine collection bags and a statistically significant reduction in contaminated samples was demonstrated in the intervention arm of the study (7.7% vs 51%, p<0.001). A cross-sectional study using the finger tapping plus massage technique paired urine samples with a subsequent sample taken by catheter within 1 hour. This demonstrated that the technique was sensitive (97%) and specific (89%) with low contamination rates in both groups. A prospective cohort study found a non-statistically significant difference in paired urine samples with a contamination rate of 16% in the tapping plus massage samples compared with 6% in paired samples collected by either catheter or supra-pubic aspirate in a subgroup of the study population in the following situations (positive urinalysis, decision to prescribe antibiotics, unsuccessful non-invasive sampling).

Gender was not found to be an independent variable of success in any study. A number of studies demonstrated, in subgroup analysis or logistic regression, increased success in those of a younger age or lower weight. Challenges were noted in maintaining the child in the correct position in 22 out of 48 participants (48%) in one study using the tapping plus massage technique.

Satisfaction with use of the intervention was reported as 87.5% for parents and 90% for clinicians using gauze soaked in saline. Crying was the most common adverse event noted and incidence ranged from 77% to 100%. Local skin redness was reported in one study and discomfort in another.

### Overall grading of the evidence

The evidence was assessed for the primary outcome measure—voiding within a pre-specified period (<5 min)—for two interventions. For rubbing with saline-soaked gauze, the evidence from one RCT was not downgraded for risk of bias (low), indirectness or publication bias but was downgraded for imprecision due to sparse data (fewer than 300 events) being available. Thus, the evidence was rated as moderate. With only one RCT, consistency across RCTs could not be assessed. The non-RCT evidence (one study) reported similar success rates but was conducted by the same team and it is uncertain if similar effects would be achieved by other teams or in other settings. For the tapping plus massage technique, evidence from one RCT was not downgraded for indirectness or publication bias but was downgraded for risk of bias (unclear allocation concealment) and for imprecision due to sparse data. Thus, the evidence was rated low. Again, with only one RCT, consistency could not be assessed. More non-RCT evidence (five studies) was available for this intervention, but success rates varied and, in some cases, differed from those in the RCT. Similar grades were applied to contamination as an outcome. Grading of the evidence on crying/distress was precluded by differences in reporting; crying and mild distress rates up to 100% were observed in some studies but, in at least one study, were not regarded as adverse events and not recorded (see online supplementary appendix ii for table containing full grading assessment).

### DISCUSSION

This systematic review aimed to evaluate the evidence for non-invasive bladder stimulation techniques in non-toilet trained children. The 11 studies identified in this review included over 1200 patients with a wide age range performed within a variety of hospital settings.

A non-invasive bladder stimulation technique was initially described in 1985 but only three RCTs were located in this review and each of these assessed a different intervention. The most recent and rigorous of these indicated some success in stimulating voiding in less than 5 min with a non-invasive technique (rubbing with saline-soaked gauze), the evidence for this intervention being graded moderate. A second technique which involved tapping and massage and which has undergone the most frequent investigation in various preliminary studies and an RCT also appeared to be effective with the evidence for this intervention graded low.

Thus, this review indicates that although the evidence base is limited, bladder stimulation techniques appear to moderately improve the success of non-invasive urine collection in non-toilet trained children. This would be clinically significant if it could be replicated in clinical environments and further confirmation of findings is required. There was a lack of evidence to support the reduction in contamination rates using bladder stimulation techniques compared with other techniques. As this is a clinically important outcome, further investigation would be important to support the acceptance of these techniques within clinical settings.

Choice of technique is likely to be affected by the minimum number of personnel required in emergency and acute care settings. Interventions requiring more than two operators are likely to reduce the generalisability and applicability irrespective of their clinical effectiveness owing to the resource and time implications of using multiple members of staff. It is possible that some of these issues could be mitigated by teaching parents and caregivers to deliver the interventions using videos and written resources. Nevertheless, interventions requiring a child to be held suspended would be technically challenging with increasing age and weight of the child, as was demonstrated by Valleix-Leclerc et al. This would significantly limit their use in the older and heavier population.

The techniques appear to be safe but are likely to cause mild distress to children while being performed. Thus, further exploration of acceptability to parents and caregivers is also important, particularly if they will be actively involved in delivery of interventions. Caregiver and clinician satisfaction was high in the technique involving rubbing the suprapubic region with saline-soaked gauze method but was not assessed for other methods. In the majority of studies, children were held by members of the research team and bladder stimulation was delivered by trained personnel. It is unclear whether involvement of caregivers may affect the success and acceptability of the procedure, and it was not possible to ascertain caregiver or clinician preference for the different stimulation methods reviewed.

While the non-RCT evidence cannot be considered rigorous evidence, analysis of these studies has provided further information as to feasibility of these techniques. They also indicate that the proportion of infants voiding within 5 min is highly variable. The reasons for this are not completely clear but are likely to relate to age and weight of participants, with greater success in those of a younger age and lower weight in whom triggering of newborn voiding reflexes is more effective. Exclusion of participants with poor oral intake and co-interventions that include feeding prior to attempt stimulation method will also have increased success rates in some studies. These factors would, however, limit the generalisability in the ED setting when vomiting and decreased oral fluid intake are frequently seen. Reasons for urine specimen collection were also highly variable with exclusion of UTIs being the main reason in those studies conducted in the emergency setting and hyperbilirubinaemia being the predominant reason for those studies conducted on NICUs. These factors significantly limit the ability to apply the findings of these studies outside of the care environments or patient groups in which they were carried out.

Based on our review, we are not able to conclude which technique was superior as a randomised superiority trial has
not been undertaken. Six relevant studies were identified through the ClinicalTrials.gov website. Three of these are currently recruiting, one is not yet recruiting and two have been completed but not published. Two further studies were located only as conference abstracts. The results of ongoing trials should add to the evidence base.

Further exploration of the acceptability and feasibility of the techniques available should be followed by an adequately powered, multicentred RCT. This would focus on investigating the success of voiding (within 5 min to allow for standardised comparison to existing studies), contamination rates, adverse events and acceptability of the techniques compared with standard clinical practice to provide recommendations on which method is most effective and in which patient group.

Limitations of the review
It is possible that, owing to the variability with which the interventions of interest are described, relevant studies may have been missed. It is therefore possible that other published data may affect the conclusions drawn from this review.

The small number of studies found and the heterogeneity in the interventions and the outcomes measured mean that it is extremely difficult to provide definitive conclusions on the evidence found.

CONCLUSION
The bladder stimulation techniques evaluated appear to offer some hope in the long-standing challenge of obtaining urine samples for clinical evaluation in non-toilet trained children. Based on the studies included in this review, it is not possible to offer a definitive recommendation of any of the techniques evaluated. The highest quality evidence currently is provided by the study by Kaufman et al. (‘Quick-Wee’ method) but is based on a single-centre study and has not been further validated making generalisability difficult to assess.

There remains the need for a multicentre RCT to evaluate the variety of techniques available which should assess reduction in time to successful voiding, cost-effectiveness and contamination rates. Planned a priori subgroup analysis should include whether gender, age of participants and personnel involved in delivering the intervention (caregivers or healthcare practitioners) affect success. An investigation of the acceptability of these various techniques to parents and caregivers is also crucial, and a qualitative study is being undertaken by the authors to investigate this aspect.

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