The position during urine sample collection from young precontinent children through a bag does not limit contamination rates: Results from a randomized controlled trial: Does infant position influence quality of urine collection?

Claire Bahans, Aymeric Dallocchio, Antoine Tran, Francois Dubos, Bertrand Soto, G. Schoder, Philippe Blanc, Veronique Messager, Diane Demonchy, Anaïs Labrunie, et al.

Version of Record: https://www.sciencedirect.com/science/article/pii/S0929693X22001087
Manuscript_c65c11117120a5c4721dc9095375e39c

The position during urine sample collection from young precontinent children through a bag does not limit contamination rates: results from a randomized controlled trial

Short title: Does infant position influence quality of urine collection?

C. Bahans*[a], A. Dallocchio[a], A. Tran[b], F. Dubos[c], B. Soto[d], G. Schoder[e], P. Blanc[f], V. Messager[a], D. Demonchy[b], A. Labrunie[g], F. Garnier[h], V. Guigonis[a]

[a] Département de pédiatrie, CHU de Limoges, 8 avenue Dominique Larrey, 87000 Limoges, France

[b] Urgences pédiatriques, Hôpitaux pédiatriques de Nice CHU Lenval, 57 avenue de la Californie, 06200 Nice, France

[c] CHU Lille, Urgences pédiatriques et maladies infectieuses, 2 avenue Oscar Lambret, 59000 Lille, France

[d] Service de Pédiatrie, Centre hospitalier de Troyes, 101 avenue Anatole France, 10000 Troyes, France

[e] Service de pédiatrie, CHR Metz-Thionville, 1 allée du château, 57100 Metz, France

[f] Service de pédiatrie, CHI de Poissy Saint Germain en Laye, 20 rue Armagis, 78100 Saint Germain en Laye, France

[g] Centre d'épidémiologie, de biostatistique et de méthodologie de la recherche (CEBIMER), CHU de Limoges, 2 avenue Martin Luther King, 87000 Limoges, France

[h] Laboratoire de bactériologie-Virologie-Hygiène, CHU de Limoges, 2 avenue Martin Luther King, 87000 Limoges, France

***Corresponding author:** Claire Bahans, Pédiatrie, CHU de Limoges, Limoges, France

claire.bahans@chu-limoges.fr, +33 5 55 05 63 58

Conflicts of interest: none.

Abstract

Aim. Despite its limitation, bag collection is still widely used for a preliminary urine screening test in non-toilet-trained children suspected of febrile urinary tract infection. A previous study conducted by our group raised the hypothesis that the absence of direct contact between urine and the perinea during urine collection could limit urine contamination by perineal flora. The aim of this study was to evaluate the impact of the patient's position during urine collection (upright standing position versus free position) on the rate of contaminated urine samples in non-toilet-trained children with suspected febrile urinary tract infection.

Methods. This prospective, randomized, controlled study took place in seven pediatric emergency departments. Two groups were compared: the intervention group (infants held in an upright standing position during urination) and the control group (free position during urination).

Results. Among the 800 pediatric patients randomized to the study, 124 had a urine culture, 60 in the intervention group and 64 in the control group. Among the 124 urine cultures, 12 (9.7%) were contaminated: eight (13.3%) in the intervention group and four (6.3%) in the control group (p=0.1824).

Conclusion. The results show that the patient's position does not have a significant impact on the quality of urine samples collected by bag.

Keywords: Urinary tract infection, urine collection in infants, urine contamination

1. Introduction

Urinary tract infections (UTIs) are a common cause of acute illness in infants and children. Indeed, this diagnosis may account for 7% of children under 24 months of age consulting with fever without a source and 8% of children over the age of 2 years with possible urinary symptoms [1]. A challenging concern regarding UTI in infants remains the reliability of the diagnosis depending on the choice of the urine collection method. Recommendations for UTI in children under 3 years of age focus on three main techniques: urine clean catch collection (CC), suprapubic aspiration (SA), and urethral catheterization (UC) [2–6]. Clean catch is a noninvasive and potentially efficient method, particularly in the smallest infants [7,8]. Nevertheless, the reported success rates in these studies are not high enough to address all situations in daily practice. Concerning SA and UC, these methods may have immediate or delayed traumatic adverse events such as induced pain, bladder bleeding, and urethral lesions [9]. This possible morbidity leads to reluctance in their use as a first-line technique despite guidelines on UTI management [10].

Therefore, bag collection (BC) is still widely used in France despite its limitations [11], at least for the first screening test on urine (dipstick) as suggested by some guidelines [6]. Contamination rates of bag collectors range from 30% to 60% depending on the study [12–15]. Therefore, if used and in case of positive dipstick results, a more reliable (but more invasive) method is required in order to confirm UTI diagnosis. Our group has already tested a specific bag collector requiring the child to be in a standing position for urine collection in order to limit urine contamination during the collection process [16]. This study did not confirm the utility of this device, but interestingly, the contamination rate in this study was 9.6%, similar to the rate we had obtained previously with more reliable collection methods [16]. The main hypothesis to explain this unexpected result was the absence of direct contact

between urine and the perinea, thus limiting urine contamination by perineal flora. Therefore, perineal germs could be a key factor in urine contamination when bag collection is used.

We hypothesized that a standing position for urine bag collection, in order to limit contact between urine and perinea, could lower the contamination rate close to those obtained with more reliable but more invasive methods.

The aim of this study was to evaluate the impact of the position during urine collection (upright standing position versus free position) on the rate of contaminated urine samples in non-toilet-trained children with suspected febrile UTI.

2. Materials and methods

2.1 Design

The present study was a prospective, randomized, controlled study carried out between November 2013 and April 2017 in the pediatric emergency departments of seven French hospitals.

2.2 Selection criteria

Inclusion criteria were precontinent children aged between 2 and 36 months, an indication for urine specimen collection for suspicion of UTI, and informed consent from the parents.

Non-inclusion criteria were current diarrhea, a current antibiotic treatment or an antibiotic therapy in the preceding 8 days, an anomaly of the external genital organs, a known allergic reaction to the bag or its adhesive, or parental refusal.

2.3 Study procedure

Precontinent children meeting the inclusion criteria were fitted with a sterile urine collection bag (Urinocol Pediatric, B. Braun Medical SAS, Saint-Cloud, France) as per local guidelines for the procedure, including careful perineal skin cleaning with soapy water.

Concurrently, the parents were provided with oral and written information on the study. When consent was given, the patient was randomized to one of the two following groups:

- The intervention group, where infants had to be held by their parents in an upright standing position from bag fitting to urine emission. **Figure 1** illustrates the possible upright standing positions. Parents were asked to watch their child constantly to ensure proper positioning.
- The control group, where no specific information was delivered to the parents concerning their child's position during urination.

Information was provided and patient randomization was performed by ED physicians or nurses at the seven centers, who were not blinded to the randomization group. Bag fitting and removal was done by ED nurses. Data collection was performed by a clinical research associate.

Once urine had been obtained, a dipstick was performed by nurses. If the dipstick was positive for leukocyte esterase and/or nitrite, the urine sample was sent locally to the microbiology laboratory for urinalysis and culture. The biologists were blinded to whether or not the patients belonged to the randomization group.

2.4 Main outcome

The main outcome was the proportion of contaminated urine samples in each group. A urine sample was considered contaminated if the culture had $\geq 10^5$ colony-forming units (CFUs) /mL *and* contained more than one bacterial species [2]. Urine cultures with $< 10^5$ CFUs were considered negative. Since no consensus exists on the interpretation of contaminated urine

samples collected by bag, the contaminated urine culture was defined in accordance with the definition already used in our previous studies [16, 17],

2.5 Randomization

The allocation sequence for randomization to the intervention or control group was generated with a 1:1 ratio, mixed block sizes, and stratification by center, using Nquery Advisor v7.0. A biostatistician independent of the biostatistician responsible for data analyses generated the allocation sequence. Randomization was performed in each center via the Internet and the CSOnline module of Clinsight®.

2.6 Sample size calculation

According to previous studies published by our group [16,17], the proportion of contaminated urine samples in the control group was expected to be about 30% in infants presenting with a clinical risk of UTI *and* a positive dipstick versus 10% in the intervention group. With an α-risk of 5% and a β-risk of 20%, we determined that each group of the present study would need 62 assessable precontinent children (i.e., a total recruitment of 124 children with a urine culture decided based on urine dipstick results; calculations done with Nquery Advisor v7.0, Stat Sols, Cork, Ireland).

2.7 Statistical analysis

All statistical analyses were performed using SAS v9.3 (SAS Institute, Cary, NC, USA). Statistical significance was set at $p<0.05$ for all analyses with the biostatistician blinded to the treatment groups. The analyses were performed and presented according to the revised CONSORT 2010 Statement.

For the descriptive analysis, quantitative variables were reported as means and standard deviation (means [SD]) and qualitative variables were reported as frequency and percentage (*n* [%]).

The rates of contaminated urine samples were compared using the Pearson chi-square test or the Fisher exact test.

A sensitivity analysis was performed comparing the rates of contaminated urine samples with a modified definition of contamination as "more than one bacterial species found in the urine sample irrespective of CFUs."

An additional post hoc analysis was performed on the subgroup of patients for whom urine analyses were prescribed in accordance with the American Association of Pediatrics guidelines [6]. Given that the risk of false-positive results of the urine culture could increase due to overly broad indications, this analysis was restricted to samples with a validated indication of urine collection in a context of UTI suspicion.

2.8 Ethics

The present study was approved by a French research ethics committee (CPP12-031/2012-A01486-37) and published in Clinical Trial NCT01862822.

3. Results

Between November 2013 and March 2017, a total of 800 patients were randomized into the study (**Figure 2**). The mean age was 13.1 months (SD, 7.9 months) and 50.3% were girls (sex ratio, 0.98).

Among these patients:

- 398 were randomized to the intervention group, 60 of them had a urine culture.
- 402 were randomized to the control group, 64 had a urine culture.

The clinical data of the 124 patients with a urinalysis are presented in **Table 1**. Out of these 124 patients (and their families), 99 complied with the randomized position throughout their participation in the study.

Among the 124 urine cultures, 12 (9.7%) were contaminated: eight (13.3%) in the intervention group and four (6.3%) in the control group (**Table 2,** p=0.1824).
In the per protocol analysis (exclusion of patients who did not comply with their randomized position or when the information was missing), among the 99 urine cultures, five (14.3 %) were contaminated in the intervention group and four (6.3%) in the control group (**Table 2**, p=0.27).

In the subgroup of patients for whom the AAP criteria were respected for indication of urine culture (n=69), three were contaminated: one (2.9%) in the intervention group versus two (5.7%) in the control group (p=1).

If the definition of a contaminated urine culture was modified to "more than one bacterial species found in the urine sample irrespective of CFUs," the results were similar: 25 (20.3%) urine cultures were contaminated, 15 (25.4%) in the intervention group versus 10 (15.6%) in the control group (p=0.1773).

Adverse effects were not reported by parents or ED nurses.

4. Discussion

The working hypothesis (reduction of urine contamination by avoiding contact between urine and the perinea) was not confirmed by the study. Therefore, the results of this study do not support the hypothesis of urine contamination through contact between urine and the perineum.

Since the results did not differ between the intention-to-treat and per protocol analyses, we assume that this negative result is not secondary to potential protocol deviations, such as compliance with positioning.

Nevertheless, it should be noted that the percentage of contaminated urine cultures obtained with bag collectors in this study (9.7%) appears to be rather low compared with other studies, which report contamination rates ranging from 30% to 60% [12–14]. The initial statistical hypothesis based on our previous studies (on which the sample size was calculated) was that 30% of infants presenting with a clinical risk of UTI and a positive dipstick could present contaminated urine samples in the control group, versus 10% in the intervention group. In the results reported here, only 6.3% of infants in the control group presented a contaminated urine culture, approximately one-fifth of the expected percentage. The choice of our statistical hypothesis was relevant based on the hypotheses used, but the actual figures were unexpectedly low in the study and impacted the statistical power (a posteriori calculated power, 26%).

One may wonder whether this surprisingly low rate of contaminated urine samples could be the result of a temporary modification in the ED staff behavior. In a multicenter study that lasted 4 years, this hypothesis is very unlikely to explain this result; the participating centers did not modify the procedures that had already been used in other studies regarding skin antisepsis and laboratory urine analysis [17].

The results of this study seem to show that, in our group, the urine contamination rate during bag collection has been dramatically reduced over the last 10 years. No conclusive reason to explain this progress stands out, but it could be hypothesized that this result is a (good) clinical research side effect. We have been working on this issue for many years [15–18] and it could be possible that the more our team works on this topic, the better our everyday practices are, even with a device with as many limitations as the urine bag collector.

5. Conclusion

Even when taking into consideration that this study found a lower a posteriori power than expected, it does not contribute data to support the hypothesis that urine bag contamination could be significantly secondary to urine contact with the perineum. In addition, it is unlikely that a larger study could show different results. In accordance with the AAP and French guidelines, we consider that urine collected through urethral catheterization should always be preferred to bag-collected specimens to confirm the diagnosis of UTI, regardless of the infant position during micturition.

References

[1] Shaikh N, Morone NE, Bost JE, et al. Prevalence of urinary tract infection in childhood: a meta-analysis. Pediatr Infect Dis J 2008;27:302–8.

[2] Cohen R, Raymond J, Faye A, et al. Société française de pédiatrie, et al. [Management of urinary tract infections in children. Recommendations of the Pediatric Infectious Diseases Group of the French Pediatrics Society and the French-Language Infectious Diseases Society]. Arch Pediatr 2015;22:665–71.

[3] McTaggart S, Danchin M, Ditchfield M, et al. KHA-CARI guideline: Diagnosis and treatment of urinary tract infection in children. Nephrol Carlton Vic 2015;20:55–60.

[4] Mori R, Lakhanpaul M, Verrier-Jones K. Diagnosis and management of urinary tract infection in children: summary of NICE guidance. BMJ 2007;335:395–7.

[5] Robinson JL, Finlay JC, Lang ME, et al. Canadian Paediatric Society, Infectious Diseases and Immunization Committee, Community Paediatrics Committee. Urinary tract infections in infants and children: Diagnosis and management. Paediatr Child Health 2014;19:315–25.

[6] Subcommittee on Urinary Tract Infection, Steering Committee on Quality Improvement and Management, Roberts KB. Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. Pediatrics 2011;128:595–610.

[7] Kaufman J, Fitzpatrick P, Tosif S, et al. Faster clean catch urine collection (Quick-Wee method) from infants: randomised controlled trial. BMJ 2017;357:j1341.

[8] Tran A, Fortier C, Giovannini-Chami L, et al. Evaluation of the Bladder Stimulation Technique to Collect Midstream Urine in Infants in a Pediatric Emergency Department. PloS One 2016;11:e0152598.

[9] Ouellet-Pelletier J, Guimont C, Gauthier M, et al. Adverse Events Following Diagnostic Urethral Catheterization in the Pediatric Emergency Department. CJEM 2016;18:437–42.

[10] Hansson S, Bollgren I, Esbjörner E, et al. Urinary tract infections in children below two years of age: a quality assurance project in Sweden. The Swedish Pediatric Nephrology Association. Acta Paediatr Oslo Nor 1992 1999;88:270–4.

[11] Cousin E, Ryckewaert A, de Jorna Lecouvey C, et al. Urine collection methods used for non-toilet-trained children in pediatric emergency departments in France: A medical practice analysis. Arch Pédiatr 2019;26:16–20.

[12] Alam MT, Coulter JBS, Pacheco J, et al. Comparison of urine contamination rates using three different methods of collection: clean-catch, cotton wool pad and urine bag. Ann Trop Paediatr 2005;25:29–34.

[13] Al-Orifi F, McGillivray D, Tange S, et al. Urine culture from bag specimens in young children: are the risks too high? J Pediatr 2000;137:221–6.

[14] Bonadio WA. Urine culturing technique in febrile infants. Pediatr Emerg Care 1987;3:75–8.

[15] Ochoa Sangrador C, Pascual Terrazas A. [Systematic review of the validity of urine cultures collected by sterile perineal bags]. An Pediatr Barc Spain 2003 2016;84:97–105.

[16] Verliat-Guinaud J, Blanc P, Garnier F, et al. A midstream urine collector is not a good alternative to a sterile collection method during the diagnosis of urinary tract infection. Acta Paediatr 2015;104:e395-400.

[17] Etoubleau C, Reveret M, Brouet D, et al. Moving from bag to catheter for urine collection in non-toilet-trained children suspected of having urinary tract infection: a paired comparison of urine cultures. J Pediatr 2009;154:803–6.

[18] Valleix-Leclerc M, Bahans C, Tahir A et al. Prospective evaluation of a cutaneous stimulation technique to induce on-demand urination in non-toilet-trained infants. Arch Pediatr 2016;23:815–9.

Table 1. Clinical data at study inclusion

	All patients	Intervention group *n* (%)	Control group *n* (%)	*p*
F/M ratio	1.88	3	1.22	0.019*
Fever ≥ 38.5°C	100 (87.0)	45 (84.9)	55 (88.7)	0.54*
Poorly tolerated fever, hemodynamic disorders	38 (33.0)	18 (34.0)	20 (32.3)	0.84*
No clinical cause of fever	77 (67.0)	36 (67.9)	41 (66.1)	0.83*
Age ≤ 12 months	71 (61.7)	35 (66.0)	36 (58.1)	0.38*
Fever ≥ 48 h	67 (58.3)	30 (56.6)	37 (59.7)	0.73*
History of UTI	10 (8.7)	5 (9.4)	5 (8.1)	1.00**
Circumcision	1 (2.4)	1 (6.7)	0 (0.0)	0.36**
Respected criteria of AAP recommendations for urine collection indication	69 (60.0)	34 (64.2)	35 (56.5)	0.40*

*Chi-square test; **Fisher test.

UTI, urinary tract infection; AAP, American Association of Pediatrics.

Table 2. Contaminated urine in intention-to-treat and per protocol analysis

	Intervention group *n* (%)	Control group *n* (%)	*p*
Intention-to-treat analysis (*N*=124)	*n*=60	*n*=64	
Polybacterial urine culture (*n*=12)	8 (13.3)	4 (6.3)	0.18*
Non-polybacterial urine culture (*n*=112)	52 (86.7)	60 (93.8)	
Positive (*n*=68)	37 (71.2)	31 (51.7)	0.035*
Negative (*n*=44)	15 (28.8)	29 (48.3)	
Per protocol analysis (*N*=99)⁺	n=35	*n*=64	
Polybacterial urine culture (*n*=9)	5 (14.3)	4 (6.3)	
Non-polybacterial urine culture (*n*=90)	30 (85.7)	60 (93.8)	0.27**

*Chi-square test; **Fisher test.

Polybacterial urine culture: ≥ 10^5 UFC (colony-forming units)/mL and more than one bacterial species.

Positive urine culture: one bacterial species ≥ 10^5 UFC/mL.

⁺ were excluded from this group patients who did not comply with their randomized position or when information was missing.

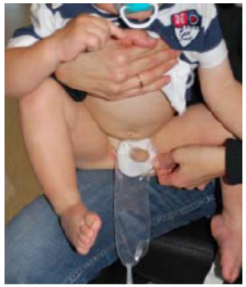
Figures:

Figure 1: Illustration of the possible upright standing positions

Figure 2: Flow diagram illustrating the inclusion or exclusion of patients in the study

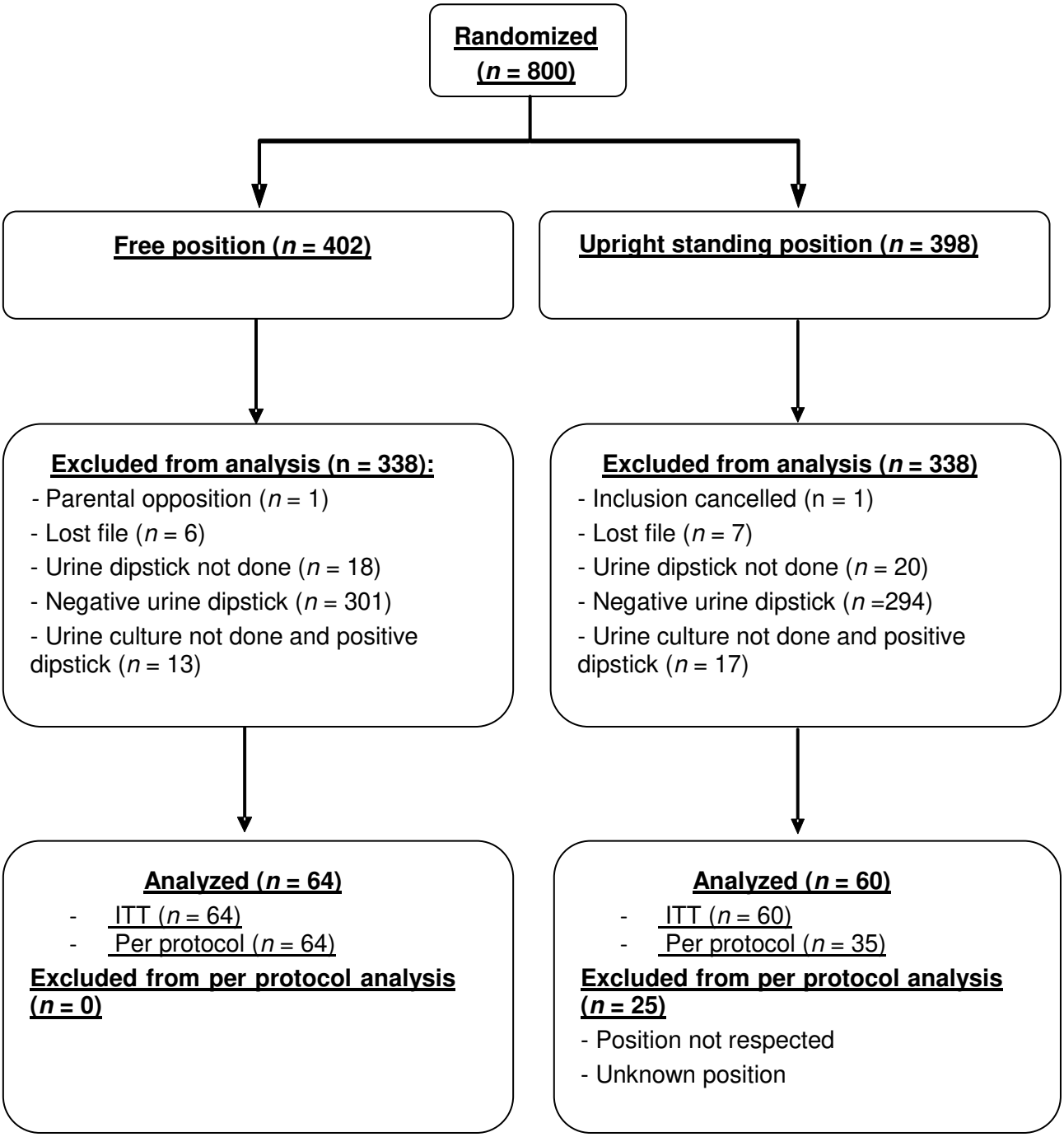
ITT, intention-to-treat

In a parent's arms



On a parent's lap

Standing (at a table)


Randomized
(n = 800)
Free position (n = 402)
Upright standing position (n = 398)
Excluded from analysis (n = 338):
- Parental opposition (n = 1)
- Lost file (n = 6)
- Urine dipstick not done (n = 18)
- Negative urine dipstick (n = 301)
- Urine culture not done and positive dipstick (n = 13)
Excluded from analysis (n = 338)
- Inclusion cancelled (n = 1)
- Lost file (n = 7)
- Urine dipstick not done (n = 20)
- Negative urine dipstick (n =294)
- Urine culture not done and positive dipstick (n = 17)
Analyzed (n = 64)
- ITT (n = 64)
- Per protocol (n = 64)
Excluded from per protocol analysis (n = 0)
Analyzed (n = 60)
- ITT (n = 60)
- Per protocol (n = 35)
Excluded from per protocol analysis (n = 25)
- Position not respected
- Unknown position