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ORIGINAL ARTICLE

Adherence to the Swedish paediatric guidelines for urinary tract infections

Magnus Lindén[1,2] | Therese Rosenblad[3,4] | Sverker Hansson[2,5] | Per Brandström[2,5]

[1]Department of Paediatrics, Halland Hospital, Halmstad, Sweden

[2]Department of Pediatrics, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

[3]Department of Paediatrics, Lund Children's Hospital, Lund, Sweden

[4]Division of Microbiology, Immunology and Glycobiology, Institute of Laboratory Medicine, Lund University, Lund, Sweden

[5]Pediatric Uro-Nephrology Centre, The Queen Silvia Children's Hospital, Gothenburg, Sweden

Correspondence
Magnus Lindén, Department of Pediatrics, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden.
Email: magnus.linden@gu.se

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Abstract

Aim: To audit adherence to the Swedish paediatric guidelines for urinary tract infections (UTIs) in infants. Secondary objectives were to compare findings on imaging performed according to the guidelines with imaging without guideline support and to identify predictors of non-adherence.

Methods: A prospective multicentre study of infants <1 year treated at paediatric hospitals for their first UTI. Adherence to recommendations was assessed for diagnosis, treatment, and imaging of the urinary tract with a follow-up period of 1 year. Vesicoureteral reflux on voiding cystourethrography and findings on renal scintigraphy according to recommendations were compared to imaging without recommendation.

Results: A total of 1357 infants were included. Adherence to recommended diagnostic procedures, antibiotic treatment, and imaging was 86.1%, 91.0% and 64.2%, respectively. Non-adherence to imaging recommendations was associated with inpatient management and smaller hospitals but was also more often due to excessive rather than refrained imaging.

Conclusion: High adherence rates to diagnostic and treatment recommendations indicate careful attention to infant UTI among paediatricians. Lower adherence to imaging recommendations raises concerns regarding the guideline algorithm; particularly, early DMSA scans seem to be challenging for smaller hospitals.

KEYWORDS
adherence, clinical guidelines, infant, urinary tract infection

1 | INTRODUCTION

Urinary tract infection (UTI) is a common bacterial infection in early childhood with a prevalence of 7% in febrile infants,[1] and a minimum incidence of 2% during the first year of life.[2] Failure to diagnose and promptly treat a UTI may result in kidney damage with potential long-term sequelae or a missed chance of identifying underlying congenital conditions predisposing for kidney-related morbidity and recurrent UTIs. Several clinical practice guidelines have been published to assist the management of UTI in children.[3–7] However, there are considerable

Abbreviations: AAP, American Academy of Paediatrics; APD, anteroposterior diameter; CI, confidence interval; CRP, C-reactive protein; DMSA, 99mTc-dimercaptosuccinic acid scintigraphy; IQR, interquartile range; MAG3, 99mTc-mercaptoacetyltriglycine renography; NICE, National Institute for Clinical Excellence; OR, odds ratio; RBUS, renal and bladder ultrasound; SD, standard deviation; SPA, suprapubic aspiration; U, Le urine leukocyte esterase; UTI, urinary tract infection; VCUG, voiding cystourethrography; VUR, vesicoureteral reflux.

discrepancies in recommendations between different guidelines, indicating a lingering knowledge gap regarding best practice for UTI in young children.[8] Furthermore, previous studies addressing adherence to paediatric UTI guidelines suggest that implementation into clinical practice is problematic and there are obvious shortcomings in the adherence to recommendations.[9,10] The guidelines of the American Academy of Paediatrics (AAP) and the National Institute for Clinical Excellence (NICE) both recommend that a urine specimen for urinalysis and culture be collected before antibiotic administration in children with suspected UTIs aged 2–24 months and 3–36 months, respectively.[3,4] Yet, a large American study found that 32% of children with an outpatient visit for UTI had neither urinalysis nor culture performed prior to antibiotic treatment.[11] Similarly, a retrospective study in the UK evaluating the implementation of the 2007 NICE guidelines found that, even in paediatric units, only half of the children <36 months evaluated for UTI had a urine sample tested.[12] By using structured implementation methods, however, it is possible to achieve high adherence rates to guidelines, at least within a limited geographic setting.[13]

The main benefits of clinical guidelines are to improve health outcomes for patients and make it more likely to get similar management regardless of where or by whom they are treated.[14] Implementation of clinical practice guidelines requires time, economic and educational resources, and an organisation ready to adapt to a change of practice.[15,16] The guidelines also need to be adjusted to the level of care they are intended to support and to the current health care system for the specific patient group. It is therefore important to evaluate current management of UTIs in children, health outcomes, and adherence to clinical guidelines after implementation.

In Sweden, national guidelines for UTI in children were launched by the Swedish Society of Paediatric Nephrology in 2013.[8] Apart from harmonising the management of UTIs across the country, the principal objective was to decrease the burden of investigations for the children without jeopardising the safety of patients at risk of future morbidity. The guidelines include recommendations for all children under the age of 18 years but focus on those under 2 years of age. In a recent article we presented an overview of current management of infants with UTIs in Sweden and the findings on performed imaging of the kidneys and urinary tract.[17] The same cohort has now been evaluated for adherence to the UTI guidelines with addition of 51 infants who were clinically diagnosed, treated and followed up as UTI but did not fulfil all diagnostic inclusion criteria in the aforementioned study. The primary objective was to determine adherence to key recommendations in the guidelines. Secondary objectives were to compare findings on imaging performed according to the guidelines with imaging without guideline support and to identify possible predictors of non-adherence.

Key note

- Adherence to urinary tract infection (UTI) guideline recommendations on diagnosis and treatment is satisfactory, while there are shortcomings in adherence to imaging recommendations, more often due to excessive imaging.
- The recommendation to perform an early scintigraphy to detect kidney involvement of the first UTI is challenging, particularly in smaller hospitals.
- The results from the study will be a valuable basis for future revisions of the guidelines.

2 | PATIENTS AND METHODS

This was a nationwide, prospective, observational, multicentre study on infants with their first UTI. Paediatric departments at 29 out of 33 invited hospitals throughout Sweden participated in patient recruitment between March 2017 and September 2019. The infants were managed at county hospitals as well as larger university hospitals serving as primary caretakers for infants within their catchment area. Infants under the age of 1 year were eligible for inclusion when antibiotic treatment was started for suspected first-time UTI. Exclusion criteria were previous UTI, ongoing bladder catheterisation, myelomeningocele and overt urogenital malformations. The UTI diagnosis and following management were performed according to routines at the local centre, based on the Swedish national UTI guidelines. If the initial suspicion of UTI was abandoned, the case was excluded.

At inclusion, a clinical report form was used to record patient characteristics and clinical data, including age, gender, maximum temperature, urine collection method, urine dipstick tests for leukocyte esterase (U-Le) and nitrite, bacterial species in urine culture, maximum plasma C-reactive protein concentration (CRP), plasma creatinine, initial empiric antimicrobial treatment, and administration mode. In addition, this report included timepoints and findings on any imaging by renal and bladder ultrasound (RBUS), 99mTc-dimercaptosuccinic acid scintigraphy (DMSA), 99mTc-mercaptoacetyltriglycine renography (MAG3) and voiding cystourethrography (VCUG) conducted as part of an initial work-up. One year after inclusion, a second report was registered, including information on recurrent febrile UTIs (≥38.0°C), use of antimicrobial prophylaxis, and results from any new imaging of the urinary tract performed after the initial investigations. The reports were compiled by a coordinating paediatrician at each centre, pseudonymised at the participating hospital, and sent to the coordinating centre in Gothenburg for registration in a database.

Adherence to the national UTI guidelines was studied in three domains: diagnostic evaluation, treatment, and imaging. Recommendations in the guidelines were assigned a criterion number referring to one of these domains (Table 1). The activities reported in the clinical report forms were assessed according to the criteria and defined as adherent or non-adherent.

TABLE 1 Criteria corresponding to guideline recommendations used for evaluation of adherence in three domains.

Domain	Criteria
1 Diagnostic evaluation	1a Temperature recorded
	1b Correct urine sampling method (SPA, catheter, or clean catch)
	1c Urine dipstick test performed for U-Le and U-nitrite
	1d Urine culture performed
	1e Plasma or serum CRP performed
	1f Plasma creatinine performed
2 Treatment	2a Use of recommended antibiotics for initial empiric treatment[a]
	2b Any antimicrobial prophylaxis prescribed was in accordance with guideline recommendations[b]
3 Imaging	3a VCUG and scintigraphy performed if RBUS showed dilatation
	3b Scintigraphy performed within 1 month from the first UTI if no RBUS dilatation was seen but a risk factor[c] was present
	3c Scintigraphy performed if no RBUS dilatation was seen, no risk factors were present, but a recurrent febrile UTI occurred
	3d No further imaging performed if no RBUS dilatation was seen, no risk factors present and no recurrent febrile UTI occurred
	3e[d] VCUG performed if initial scintigraphy was abnormal with a relative function <45%
	3f[d] No VCUG performed if no dilatation on RBUS and relative function ≥45% on initial scintigraphy

Abbreviations: CRP, C-reactive protein; RBUS, renal and bladder ultrasound; SPA, suprapubic aspiration; UTI, urinary tract infection; U-Le, urine leukocyte esterase test; VCUG, voiding cystourethrography; VUR, vesicoureteral reflux.

[a]Cefotaxime (severely ill children or unable to tolerate oral fluids). Third-generation oral cephalosporin (not severely ill and able to retain oral fluids).

[b]VUR grade 3–5, recurrent febrile UTIs, and to be considered in infants with dilatation on RBUS while awaiting VCUG.

[c]Non-*E. coli*, maximum CRP ≥70 mg/L or creatinine >30 μmol/L.

[d]Not included in the overall adherence analysis in the imaging domain.

2.1 | Diagnostic evaluation

Guideline recommendations on diagnostic evaluation included recording of body temperature and the use of suprapubic aspiration (SPA), catheter, or clean catch as urine sampling methods for bacterial culture. Recommendations for laboratory work-up were urine dipstick tests for U-Le and nitrite, urine culture, and analysis of plasma CRP and creatinine.

2.2 | Treatment

As empiric antibiotic treatment before the urine culture report was available, the guidelines recommended intravenous cefotaxime in severely ill children and those unable to tolerate oral fluids. A third-generation oral cephalosporin was recommended for children not severely ill and able to retain oral fluids. The guidelines recommended a total treatment of 10 days. Indications for antibiotic prophylaxis were vesicoureteral reflux (VUR) grade 3–5, recurrent febrile UTIs, and to be considered in infants with dilatation on RBUS while awaiting VCUG.

2.3 | Imaging

The imaging algorithm recommended RBUS examination in all infants after the first UTI. Further renal tract imaging was based on the presence or absence of dilatation on RBUS, the event of a recurrent febrile UTI, or the presence or absence of any of three risk factors: maximum CRP ≥70 mg/L, creatinine >30 μmol/L or non-*E. coli* infection. The guidelines recommended an early DMSA scan for children with risk factors and an additional DMSA scan at least 6 months after the UTI to detect permanent kidney damage in those with parenchymal defects on the initial scan. The same strategy for DMSA scan was recommended to children without risk factors but who experienced a recurrent febrile UTI. VCUG was indicated if dilatation was seen on RBUS, when a relative function below 45% was observed on a DMSA scan, or when a focal uptake defect was detected in a solitary kidney.[8] In some cases, a MAG3 scan was used instead of DMSA and was regarded as equivalent in the analysis. The guidelines also included an alternative imaging algorithm eliminating the demand for early DMSA scans for centres with limited access to scintigraphy.

Adherence to guidelines in the imaging domain was assessed by four criteria (3a–3d), corresponding to the four initial pathways in the guideline algorithm (Figure 1). Overall adherence was considered if the criterion corresponding to any one of these was fulfilled. Not included in the overall adherence analysis in the imaging domain were two criteria assessing adherence to perform a VCUG when a first scintigraphy was abnormal, criterion 3e, and not to perform a VCUG if both RBUS and scintigraphy examinations were normal, criterion 3f. These criteria represented imaging recommendations downstream in the algorithm (Figure 1). Furthermore, we did not assess adherence to the recommendation for a late scintigraphy.

The secondary objectives were assessed by comparing findings on VCUGs and DMSA scans performed according to recommendations with those performed without indication in the guidelines. In this assessment, VUR was graded 1–5 according to the International Reflux Study in Children,[18] and dilating VUR was defined as VUR grade 3–5. On DMSA scan, kidneys with a focal uptake defect or a relative function below 45% were considered abnormal, and the same criteria applied when a MAG3 scan was used. Permanent kidney defect was defined as an abnormal scan 6 months or more after the first UTI. Infants with a normal first scintigraphy and without UTI recurrences were considered to have normal kidneys at follow-up.[19]

To determine predictors of non-adherence, the following variables were used: gender, age at infection, outpatient management only and hospital category.

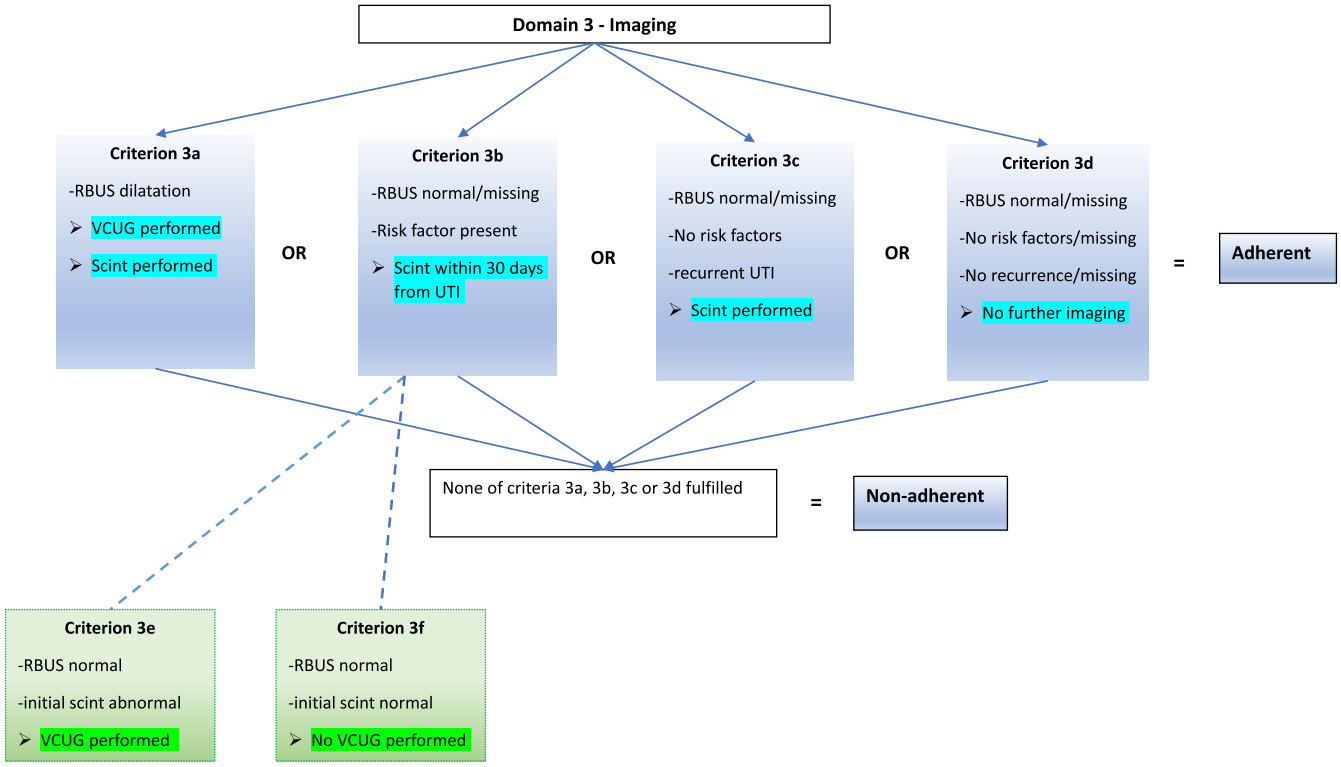

FIGURE 1 Model of the guideline algorithm, used to calculate overall adherence to the imaging domain by adherence to any one of four initial pathways named criteria 3a–3d. Highlighted text represents the recommended action if the above conditions are fulfilled. Two criteria, 3e and 3f, used to assess adherence to recommendations downstream in the imaging algorithm are not included in the overall adherence. RBUS, renal and bladder ultrasound. VCUG, voiding cystourethrography.

2.4 | Statistics

Dichotomous variables for adherence and non-adherence for each of the criteria stated in the guidelines were created. Patient characteristics and adherence rates were summarised using descriptive statistics. Continuous variables, such as age and temperature, were reported as medians with interquartile ranges (IQRs) or means with standard deviations (SDs), depending on the data distribution. Categorical variables were presented as counts and percentages.

Adherence rates calculated per domain and for each criterion were presented as counts and percentages with 95% confidence intervals (CIs). Overall adherence within each domain was defined as adherence to all relevant criteria within that domain. For adherence rates in Domain 3, only centres using the main imaging algorithm were included in the analysis. Univariable logistic regression was used when determining predictors of non-adherence. From these analyses, odds ratios (OR) with 95% CI were presented along with the associated *p*-values. Fisher's exact test was used to assess differences between two groups and binary variables.

A *p*-value of less than 0.05 was considered statistically significant.

2.5 | Statistical software

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 29.0 (IBM Corp., Armonk, NY, USA).

3 | RESULTS

3.1 | Patient characteristics

A total of 1454 infants were enrolled in the study, and of these, 97 (6.7%) were excluded as the presumptive UTI diagnosis was abandoned. The remaining 1357 infants, 629 boys and 728 girls, were diagnosed and treated as having UTI by the managing paediatrician. The median age was 3.9 months (IQR 1.9–6.9) and the mean temperature was 39.2°C (SD 0.9). Exclusively outpatient care was reported in 636 infants (47%) and initial inpatient care in 720 (53%, data missing in one case). Recurrent febrile UTI was reported in 241 infants (18%, data missing in 16 infants).

Adherence rates for the three domains and their underlying criteria are summarised in Table 2.

3.2 | Diagnostic evaluation

Overall adherence with the full set of criteria for the diagnostics domain was 86.1%. Temperature data was recorded in 1318 infants (97.1%). Urine sampling was performed by recommended methods in 1272 of 1285 cases (99.0%, data missing in 72 patients), predominantly by clean catch technique (1188 samples, 92.5%), although SPA, stated in the guidelines as the preferred method for infants under the age of 1 year, was only performed in 64 cases (5.0%) and

TABLE 2 Adherence rates to guideline recommendations per domain and for each criterion.

Domain/criteria	Adherence rate	95% CI
Domain 1 (diagnostics)		
Overall adherence	1169/1357 (86.1%)	84.2%–87.9%
1a	1318 (97.1%)	
1b[a]	1272/1285 (99.0%)	
1c	1340 (98.7%)	
1d	1337 (98.5%)	
1e	1345 (99.1%)	
1f	1305 (96.2%)	
Domain 2 (treatment)		
2a[b]	1234/1356 (91.0%)	89.4%–92.4%
2b	245/255 (96.1%)	93.2%–98.0%
Domain 3 (imaging)[c]		
Overall adherence	841/1310 (64.2%)	61.6%–66.8%
3a	133/188 (70.7%)	
3b	265/559 (47.4%)	
3c	63/71 (88.7%)	
3d	380/492 (77.2%)	
3e[d]	81/107 (75.7%)	67.0%–83.1%
3f[d]	409/562 (72.8%)	69.0%–76.3%

[a]Missing data in 72.
[b]Missing data in 1.
[c]Only centres using the main imaging algorithm are included ($n = 1310$).
[d]Not included in the overall adherence analysis in the imaging domain.

catheter in 20 (1.6%). Adherence rates for urine dipstick tests (U-Le and U-nitrite), urine culture, plasma CRP, and creatinine were all between 96% and 99%; see Table 2.

3.3 | Treatment

The adherence rate to recommended antibiotics (criterion 2a) was 1234/1356 (91.0%, data missing in one infant). Among 843 infants initially treated with oral antibiotics, 739 (87.7%) were given a third-generation cephalosporin as recommended for empiric treatment in the guidelines while awaiting the urine culture report. Trimethoprim/sulfamethoxazole, recommended only after culture-verified sensitivity testing, was prescribed as initial empiric treatment to 77 (9.1%) orally treated infants. There were no significant differences between infants treated with oral cephalosporine and those treated with trimethoprim/sulfamethoxazole regarding recurrent UTIs or outcome on scintigraphy. Among 513 infants initially treated with intravenous antibiotics, cefotaxime was used in 495 (96.5%) as recommended. The guideline recommendation on 10 days of antibiotic treatment for febrile UTI was followed in 92.5% of cases.

Long-term prophylactic antibiotics were prescribed to 255 infants during the study period, and in 245 (96.1%) of these, the indications were in accordance with guideline recommendations.

3.4 | Imaging investigations

RBUS was performed in 1351 infants (99.6%) of the entire study population as recommended. Forty-seven infants were recruited by six centres with limited access to an early DMSA scan stating the use of an alternative imaging algorithm. These were excluded in the evaluation of adherence to further imaging recommendations, leaving 1310 infants for analysis in this domain. Adherence to further imaging recommendations in the four initial pathways of the algorithm (criterion 3a–3d) is shown in Table 2. The overall adherence rate was 64.2%. The lowest adherence rate was seen in infants with risk factors but no dilatation on RBUS (criterion 3b), where 265 of 559 (47.4%) were investigated with renal scintigraphy within 30 days from the UTI as recommended. Adherence to this criterion was higher in university hospitals (58.3%) than in county hospitals (41.9%, $p < 0.001$). Adherence to not performing any further imaging investigations if RBUS was normal and no risk factors were present (criterion 3d) was observed in 380 of 492 infants (77.2%). Not included in the overall adherence rate in the imaging domain were the two criteria 3e and 3f with adherence rates of 75.7% and 72.8%, respectively.

3.5 | Imaging investigations performed without guideline indication

Findings on imaging performed according to recommendations compared with imaging without indication are presented in Table 3. There were 178 infants investigated with VCUG despite no guideline indication, and 37 had VUR grade 3–5 (16 grade 3, 18 grade 4 and 3 grade 5). VUR grade 3–5 was seen more often in infants with UTI recurrence than in those without recurrence (30/90 vs. 7/88, $p < 0.001$).

Of 492 infants without guideline indication for scintigraphy, 107 (21.7%) were investigated with scintigraphy (104 DMSA and 3 MAG3 scans). Among these, 20 (18.7%) were abnormal compared to 282 of 735 infants (38.4%) with an indication for scintigraphy. Scintigraphy data on permanent kidney abnormalities at least 6 months after the index UTI was available in 639 infants, and abnormal kidneys were seen in 5/95 (5.3%) without indication for scintigraphy compared to 117/544 (21.5%) with indication. None of the abnormal kidneys identified in the group without indication for scintigraphy had a relative function less than 40%, while this was found in 39 (33.3%) of infants with abnormal kidneys investigated on indication.

3.6 | Predictors of non-adherence

Univariate analysis of predictors for non-adherence is summarised in Table 4. Within the diagnostic domain, the only significant predictor of non-adherence was hospital category, where county hospitals were twice as likely to be non-adherent compared to university

	With indication	Without indication
VUR grade 3–5	78/218 (35.8%)[a]	37/178 (20.8%)[b]
Abnormal 1st scintigraphy	282/735 (38.4%)	20/107 (18.7%)
Permanent kidney defects	117/544 (21.5%)[c]	5/95 (5.3%)[d]

Abbreviation: VUR, vesicoureteral reflux.

[a]19 VUR grade 3 (24%), 35 grade 4 (45%) and 24 grade 5 (31%).

[b]16 VUR grade 3 (43%), 18 grade 4 (49%) and 3 grade 5 (8%).

[c]26 discrete (relative function ≥45%), 52 moderate (relative function 40%–44%), 20 pronounced (relative function 30%–39%) and 19 severe (relative function <30%).

[d]4 discrete and 1 moderate.

TABLE 3 VUR status ($n = 396$) and findings on renal scintigraphy ($n = 842$) performed with and without indication according to the UTI guidelines. Scintigraphy data for evaluation of permanent kidney damage are available in 639 infants.

Variable	Values	*n*	Non-adherent (%)	OR (95% CI)	*p*-value
Domain 1 (diagnostic evaluation)					
Gender	Boys	629	87 (13.8)	ref.	
	Girls	728	101 (13.9)	1.00 (0.74–1.37)	1.000
Age at infection	≤median	680	90 (13.2)	ref.	
	>median	677	98 (14.5)	1.11 (0.82–1.51)	0.530
Management[a]	Inpatient	720	101 (14.0)	ref.	
	Outpatient	636	87 (13.7)	0.97 (0.71–1.32)	0.875
Hospital category	University	437	39 (8.9)	ref.	
	County	920	149 (16.2)	1.97 (1.36–2.86)	<0.001
Domain 2 (treatment)					
Gender	Boys	629	59 (9.4)	ref.	
	Girls	727	63 (8.7)	0.92 (0.63–1.33)	0.704
Age at infection	≤median	680	46 (6.8)	ref.	
	>median	676	76 (11.2)	1.75 (1.19–2.56)	0.004
Management[a]	Inpatient	720	43 (6.0)	ref.	
	Outpatient	636	79 (12.4)	2.23 (1.51–3.29)	<0.001
Hospital category	University	437	34 (7.8)	ref.	
	County	919	88 (9.6)	1.26 (0.83–1.90)	0.311
Domain 3 (imaging)					
Gender	Boys	615	204 (33.2)	ref.	
	Girls	695	265 (38.1)	1.24 (0.99–1.56)	0.065
Age at infection	≤median	661	227 (34.3)	ref.	
	>median	649	242 (37.3)	1.14 (0.91–1.42)	0.274
Management	Inpatient	689	286 (41.5)	ref.	
	Outpatient	621	183 (29.5)	0.59 (0.47–0.74)	<0.001
Hospital category	University	437	140 (32.0)	ref.	
	County	873	329 (37.7)	1.28 (1.01–1.64)	0.050

[a]Data missing in one infant.

TABLE 4 Univariable analysis of predictors of non-adherence.

hospitals. In the treatment domain, non-adherence to recommended empiric antibiotics was more prevalent in infants above the median age than below it and was also more common in infants exclusively managed as outpatients compared to initial inpatient management. In the imaging domain, non-adherence was associated with inpatient management and county hospital care.

4 | DISCUSSION

In this prospective observational multicentre study on the management of infants with first-time UTIs, adherence to the recommended diagnostic procedures was high at 86.1%, indicating careful and thorough evaluation when diagnosing UTIs in infants.

However, although the guidelines include clean catch as an approved sampling method, the preferred recommended method in infants was SPA. This was only performed in 5.0% of the population, more often in university hospitals than in county hospitals. Although not studied in detail, infants exposed to SPA were younger and had more severe outcomes on DMSA scans suggesting that they were more severely ill. Interestingly, an American survey among 155 paediatricians asked about their preferred method of urine sampling for culture in febrile children aged 2–24 months with suspicion of UTI and concluded that up to 18% would use bagged urine, against recommendations in the 2011 AAP guidelines.[20] Likewise, an Italian multicentre survey conducted in 2021 found that bagged urine was commonly used for culture in children aged 2 months to 3 years.[21] Clearly, guideline recommendations on SPA or urethral catheterisation for urine sampling pose significant challenges when it comes to clinical practice.

In our study, urine dipstick tests and urine culture were performed in more than 98% of the patients. Other studies have reported far less adherence to recommendations on performing urinalysis and urine culture in young children with presumed UTI. Copp et al. reported that 32% of outpatient children <2 years who were prescribed antibiotics for a primary diagnosis of UTI had neither urinalysis nor culture performed.[11] The high adherence rate in our study is likely to be explained in part by the differences in methodology, as the study by Copp et al. was a retrospective outpatient study, whereas 53% of the subjects in our cohort were initially managed as inpatients.

In the treatment domain, adherence to the recommended antibiotics for empiric treatment was 91% for infants with initial oral medication. Almost all cases of non-adherence in this group were attributed to the use of trimethoprim-sulfamethoxazole. This was formerly the first-line antibiotic for oral treatment of UTI in young children but, due to increasing resistance rates to trimethoprim, was displaced in the UTI guideline to be used only when proof of sensitivity was available on an antibiogram. However, during the study period, the recommended third-generation oral cephalosporins (ceftibuten and cefixime) were only available on special licence which could have impeded the use of these. In a study on antibiotic prescriptions to children with UTIs in Taiwan the overall non-adherence rate to guideline recommendations was 20.1%.[22] However, when looking at prescriptions only by paediatricians, the non-adherence rate was 13.2%, and for infants less than 1 year of age, it was 8.6%, similar to our results.

The overall adherence rate in the imaging domain, 64.2%, was significantly lower than in the diagnostics and treatment domains. This was the most challenging domain to analyse due to a relatively complicated algorithm including several risk factors guiding the further imaging strategy. This algorithm was not entirely clear regarding which pathway to choose in cases with both dilatation on RBUS and the presence of one or more risk factors that could have influenced the adherence analysis. The guidelines also included an alternative algorithm for centres with limited access to scintigraphy. Centres that declared the use of this alternative algorithm, however, were few and included only 47 infants of the study population. Hence, analysing differences in adherence between the algorithms was not meaningful due to this low number. There were, however, no significant differences in the rate of VUR grade 3–5 identified on VCUGs or the rate of permanent kidney damage on renal scans between these groups.

The guideline algorithm for imaging recommended that infants with dilatation of the renal pelvis with an anteroposterior diameter (APD) ≥10 mm on RBUS should be investigated by VCUG and scintigraphy of the kidneys (criterion 3a). The APD, however, was inconsistently reported. Therefore, we used only reported presence or absence of dilatation on RBUS as an indication for further imaging in the analysis of adherence to this criterion. This carries a risk of overestimating the number of infants with significant dilatation of the renal pelvis and thereby falsely decreasing the adherence rate to criterion 3a. Therefore, it is likely that the true overall adherence in the imaging domain was underestimated.

The lowest adherence rate in the imaging domain, 47.4%, was seen in the recommendation to perform a DMSA scan within 1 month from the first UTI if a risk factor was present (criterion 3b). The guideline imaging algorithm represents a top-down model where, ideally, the scan should be performed within a few days from the UTI. This approach is based on studies showing that children with a normal early DMSA scan rarely have dilating VUR, thus making a VCUG unnecessary.[23–25] However, the timing of the scan will affect the detection rate of abnormalities since it has been shown that acute renal involvement on a DMSA scan sometimes resolves within weeks from the UTI.[26,27] Consequently, a delayed early renal scintigraphy could affect the decision to perform a VCUG and the possibility to detect VUR. The ability of the top-down approach to identify children with dilating VUR has also been disputed,[28] and our findings raise concerns regarding the guidelines' timing of a DMSA scan and its usefulness in everyday clinical practice. Clearly, there were barriers in the process of performing a scintigraphy within the one-month time limit, illustrated by an increase in adherence to this criterion to 73.9% if the time limit was extended to 60 days. Furthermore, adherence to this criterion was significantly lower at county hospitals compared to university hospitals, implying that this imaging strategy might not be fitted to the prerequisite at smaller hospitals. The Swedish UTI guidelines include an alternative imaging algorithm where a late DMSA scan only, 6–12 months after the UTI, is recommended for children with risk factors, which might be a more appropriate approach for hospitals struggling with access to an early DMSA scan.

Non-adherence in the imaging domain was more often caused by performing imaging without guideline recommendation than by refraining from recommended imaging. There were 178 infants without indication for VCUG yet exposed to this investigation. The reason for this is unclear, but an observation was that a focal uptake defect on scintigraphy with a normal relative function might have been the reason, although not stated as an indication for VCUG in the guidelines. Furthermore, we speculate that recurrent UTIs, despite risk factors and other imaging investigations being normal, in some cases have triggered investigations by VCUG, as 50% of these

infants had recurrences. In children with recurrent febrile UTIs, the guidelines recommend prophylactic antibiotic treatment and management on an individual basis but provide no advice on further imaging in this situation. A conceivable modification of the imaging algorithm could be to recommend a VCUG in infants with recurrent UTIs regardless of other risk factors.

One hundred seven infants were investigated with scintigraphy despite no guideline indication. Although not studied systematically, comments on RBUS investigations, such as suspicion of duplex collecting system, horseshoe kidney, or calyceal dilatation, indicate that in some cases there were valid reasons for scintigraphy other than those recommended in the guidelines. It is also possible that uncertainty on the diagnosis or severe illness could have motivated a scintigraphy investigation. However, the reason for scintigraphy in many cases remains unclear, and the abnormalities found on scans performed without indication were fewer and less severe than findings on scans with indication (Table 3).

Regarding our secondary objective to identify predictors of non-adherence, we found that county hospitals were less adherent to diagnosis and imaging recommendations. The latter is probably explained by less accessible scintigraphy service than in university hospitals, while reasons for lower adherence to diagnostic recommendations are more uncertain. In the treatment domain, outpatient management was a predictor of non-adherence, most likely linked to limited access to recommended third-generation oral cephalosporins during the study period.

There are few published studies on adherence to paediatric UTI guidelines, and to our knowledge, all are retrospective, and most studies are either questionnaires to practitioners or audits at a specific institution or healthcare region. Comparing adherence rates is problematic due to differences in healthcare systems, populations, age spans and methodology. We conducted a nationwide study where adherence to the Swedish UTI guidelines was evaluated prospectively at paediatric hospital departments. The strengths of this study were the size, multicentre participation, prospective methodology and the evaluation of the entire chain of care from diagnostics to follow-up. On the other hand, a prospective study where physicians are aware of the participation in a study might also influence them to be more meticulous in their management, thus falsely increasing adherence rates. A limitation with the study was the lack of information on infants missed for inclusion or who declined participation in the study. Also, we did not study the management of UTI in older children since the study was limited to infants <1 year. This, however, was justified by the fact that the highest incidence of UTI in childhood is during the first year of life and the guidelines' main focus was on management of the first UTI. Furthermore, a few infants might have been managed in primary care or in private paediatric clinics, thus not invited to participate in this study. We have not explored this in detail, but by information from representatives in our paediatric nephrology network, we believe that this number was negligible.

In conclusion, we found adherence to the guidelines in diagnostic evaluation and treatment to be satisfactorily high while adherence to imaging recommendations was significantly lower. In particular, early DMSA scans within a month from the first UTI seem to be hard to achieve. Non-adherence in the imaging domain included both withholding recommended imaging and, probably of greater concern, a substantial number of investigations performed without indication, imposing radiation exposure, discomfort for the child, and costs. A number of infants considered to be at low risk were exposed to a VCUG without guideline indications, revealing a surprisingly high rate of dilating VUR. Among these, recurrent UTIs were common and associated with dilating VUR, raising the question of whether more specific recommendations regarding imaging in children with recurrent UTIs should be included in the guidelines. The results from this study will be a valuable basis for an upcoming revision of the guidelines.

When developing clinical guidelines, it is important to consider not only the scientific evidence for recommendations but also the practical aspects of implementation and barriers to executing these recommendations in everyday clinical practice. We hope that this study will inspire developers of paediatric UTI guidelines to review adherence to their recommendations and adjust them to fit into the setting for which they are aimed.

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CONFLICT OF INTEREST STATEMENT

The authors have no competing interests to declare that are relevant to the content of this article.

ETHICS STATEMENT

The study was approved by the research ethics committee at Lund University (EPN 2015–884, 2016–799, 2016–912 and 2017–164). Written informed consent was obtained from all guardians of participants included in the study.

ORCID

Magnus Lindén https://orcid.org/0000-0002-5592-1267

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