

# Physician Preferences Surrounding Urinary Tract Infection Management in Neonates

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## ABSTRACT

**OBJECTIVES:** Variability exists in the treatment of neonates with urinary tract infection (UTI), potentially reflecting an overuse of resources. A cross-sectional vignette survey was designed to examine variability in physician preferences for intravenous (IV) antibiotic duration, genitourinary imaging, and prophylactic antibiotics and to evaluate drivers of resource use.

**METHODS:** The survey was administered to a random sample of pediatricians through the American Medical Association's Physician Masterfile. Respondents were provided with a case vignette of a 2-week-old neonate with a febrile UTI and asked to indicate preferences for IV antibiotic duration and rank drivers of this decision. Respondents were also asked whether they would obtain a voiding cystourethrogram (VCUG) and, regardless of preference, randomly presented with a normal result or bilateral grade II vesicoureteral reflux. The survey was delivered electronically to facilitate skip logic and randomization.

**RESULTS:** A total of 279 surveys were completed. Preference for total IV antibiotic duration differed significantly ( $P < .001$ ) across specialty, with a median duration of 2 days for general pediatricians/hospitalists, 7 days for neonatologists, and 5 days for infectious disease pediatricians. For the 47% ( $n = 131$ ) who did not want a VCUG, 24/61 (39%) wanted prophylactic antibiotics when presented with grade II vesicoureteral reflux ( $P < .001$ ).

**CONCLUSIONS:** Subspecialty status appeared to be the most influential driver of IV antibiotic duration in the treatment of UTI. A substantial proportion of pediatricians who initially expressed a preference against ordering a VCUG wished to prescribe prophylactic antibiotics when results were abnormal, which suggests that even unwanted diagnostic test results drive treatment decisions.

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Variability in the use of health care resources is often a sign of overuse.<sup>1,2</sup> A recent proposal for a research agenda on overuse called for elucidation of its most important drivers.<sup>2</sup> Urinary tract infection (UTI) management in neonates is an attractive candidate for the examination of drivers of usage, because UTI is a common condition, and current evidence has revealed that considerable variability exists around testing and antibiotic treatment durations.<sup>3-8</sup>

American Academy of Pediatrics (AAP) guidelines exist for the evaluation and management of children ages 2 months through 24 months with UTI.<sup>9</sup> Specifically, the authors of these guidelines acknowledge that the initiation of treatment with either oral or intravenous (IV) antibiotics is equally efficacious and advocate for a total duration of 7 to 14 days of antibiotic treatment, without specifying the route of administration. The authors of these national guidelines also suggest a renal bladder ultrasound (RBUS) to evaluate for vesicoureteral reflux (VUR) after a first febrile UTI but state that a voiding cystourethrogram (VCUG) is not indicated after a RBUS with normal results. However, because these guidelines do not include children <2 months of age, there is considerable uncertainty over how best to manage neonates with UTI.

By using a case vignette survey of pediatricians sampled from the American Medical Association (AMA) Physician Masterfile, we aimed to (1) analyze variability and identify drivers of physician preferences regarding the duration of IV antibiotics and (2) examine imaging and prophylactic antibiotic preferences for treatment of a neonate with a UTI.

## METHODS

### Sample

In this cross-sectional study, we surveyed a national sample of pediatricians anonymously. The need for informed consent was waived by the institutional review board at Stanford University. We used the AMA Physician Masterfile, a data set that includes over 1.4 million physicians and medical students in the United States. Both AMA members and nonmembers are included.

## Survey Instrument

The survey consisted of 22 mixed-format questions. We sampled physicians who self-identified in the database as general pediatricians, neonatologists, or pediatric infectious disease (ID) specialists. The sampling and e-mailing was performed by the staff of an independent company, MMS Lists, Inc. The survey was piloted to 23 physicians who provided feedback on content and face validity.

Physicians were provided with a vignette (Box 1) of a 2-week-old term girl hospitalized for a febrile UTI whose urine culture grew *Escherichia coli*. The respondent was instructed that, at 48 hours into the hospital admission, the neonate no longer had a fever, was clinically well-appearing, and had a renal ultrasound with normal results.

**Case Vignette:** Jane, a 2-week-old term infant girl, is hospitalized for a febrile UTI. Urinalysis was positive for nitrites, 2+ leukocyte esterase, and 50 white blood cells per high power field. IV antibiotics are administered. At this point, 48 hours into the hospitalization, the urine culture reveals >100 000 colony-forming units/mL of *E coli*, which is pan-sensitive to antibiotics. Blood and cerebrospinal fluid cultures obtained at the time of admission revealed negative results. Jane has always been well-appearing, and is now afebrile and eating well. Jane's family has no strong preferences regarding treatment options. A renal ultrasound was obtained this admission and revealed normal results.

## Outcome Variables

Physicians were asked a series of questions about their preferences in the management of the vignette neonate. The primary outcome of interest was the number of additional days of IV antibiotics beyond the 2 days already given. For the remainder of the article, the duration of IV antibiotics is reported as the total days of IV antibiotics, in which the lowest possible number a respondent could provide is 2. Physicians were asked to use a 5-point Likert scale to indicate the importance of specific

drivers in their decision regarding IV duration and to appraise the current level of evidence applicable to IV duration in this neonate.

Subsequently, physicians were asked whether they would obtain a VCUG for this neonate. Respondents stating "no" were told that, despite their preference, a VCUG was ordered. All respondents, regardless of initial preference for VCUG, were randomly presented with VCUG results showing either (1) bilateral grade II VUR or (2) no signs of reflux. Physicians were then asked to indicate whether they would provide prophylactic antibiotics for the vignette patient.

## Data Collection

All queried physicians were sent an e-mail invitation to participate in the online survey in June 2016. Recipients received an e-mail from "Stanford Pediatrics" with the subject line "Clinical Decision-Making Survey." The e-mail invitation included a brief introduction, along with an electronic link to the Qualtrics (Provo, UT) survey. Three reminder e-mails were sent 6, 13, and 19 days after the original invitation. Participating physicians were offered the chance to enter a drawing for 1 of 2 \$200 gift cards for survey completion. There was no link between the survey responses and the gift card drawing entries.

## Sampling Strategy

Sample size was estimated by using a mean (SD) IV antibiotic duration of 4 (2.5) days,<sup>8,10</sup> a 2-sided  $\alpha$  of .05 and a  $\beta$  of .2. We estimated that 100 responses were needed from both the general pediatrics and neonatology groups to detect a statistically significant difference of  $\geq 1$  day duration of IV antibiotics between these 2 groups. On the basis of an estimated response rate from previous e-mail surveys using the AMA Masterfile of ~8% to 10%,<sup>11,12</sup> we opted to perform a random sample of 2000 general pediatricians (1000 who identified as office-based, 1000 who identified as hospital-based), 1000 neonatologists, and 600 pediatric ID physicians (the entire sample of pediatric ID physicians in the Masterfile). Hospital-based general pediatricians were oversampled to

increase the probability of sampling pediatric hospitalists, because the subspecialty of hospitalist medicine is not specifically identified in the AMA Masterfile. Because some respondents indicated they were both hospitalists and general pediatricians, we opted to combine hospitalists and general pediatricians into 1 category. Successful delivery to active e-mail addresses, unique clicks onto the survey hyperlink, and the proportion of finished surveys were used to calculate participation and completion rates.<sup>13</sup> Unique clicks were defined as those originating from a new Internet protocol address.

### Statistical Analysis

The Kruskal-Wallis test was used to compare median IV antibiotic durations (a nonnormally distributed variable), and a 1-way analysis of variance was used to compare mean scores for the drivers of IV antibiotic duration. A Pearson correlation coefficient was calculated to analyze the association between the drivers of IV duration and the actual duration, with *P* values of <.05 considered statistically significant. A  $\chi^2$  analysis or Fisher's exact test was used, as appropriate, to compare categorical variables. We used a negative binomial regression multivariable model to isolate the effect of specialty (our independent variable of interest) on total days of IV antibiotics (our dependent variable). Because 2 total days was the lowest possible response, we first centered total days on 2 (by subtracting 2). We then used negative binomial regression, because centered days were nonnegative integers (or counts) with a large proportion equal to 0.<sup>14</sup> We uncentered total days for reporting. We constructed our baseline model with specialty as our sole independent variable, coded with indicator variables into 4 categories: general pediatrics or hospital medicine, neonatology, ID, or other. We then constructed our full model in 2 steps.<sup>15</sup> We first added 6 respondent characteristics (respondents' sex, annual experience with UTI, geographic region, years in practice, practice setting, and compensation model) as main effects to remove possible confounding. We then considered each of

these characteristics as second-order interaction terms with specialty and each other, by using backward selection with a *P* value  $\leq .2$  as our cut point for retention. From this strategy, our full model included specialty, 6 additional respondent characteristics as main effects, and 2 interaction terms: respondent sex by compensation model and respondent sex by geographic region.

Statistical computations were performed by using Stata 14.2 (StataCorp, College Station, TX).

### RESULTS

The survey was sent out in 4 rounds. It was delivered to 3528 out of 3600 physicians, because 72 e-mail addresses from the original sample were deemed inactive at the time of the first round. Like the creators of other online surveys, we determined participation and completion rates in place of traditional response rates.<sup>13,16</sup> The participation rate was 12.4%, calculated as the proportion of opened surveys to e-mails sent (438/3528). The completion rate was 63.7%, reflecting 279 completed surveys out of the 438 opened surveys. Respondent demographics are summarized in Table 1.

There was considerable variation in physician preferences for total duration of IV antibiotics (median: 3 days, interquartile range [IQR]: 1–6 days). The median and IQR of the duration of IV antibiotics differed significantly (*P* < .001) across pediatric subspecialties: a median of 2 days and an IQR of 2–7 days for general pediatricians/hospitalists, a median of 7 days and an IQR of 3–7 days for neonatologists, and a median of 5 days and an IQR of 2–7 days for ID specialists (Table 2). There was no significant difference in the median duration from responses across the 4 separate e-mail rounds (*P* = .46) or from respondents who finished the survey and those who answered the IV duration question but did not complete the remainder of the survey (*P* = .64).

There are 2 main findings from the multivariable model (Fig 1). First, even after adjustment for respondent characteristics, the effect of specialty was associated with IV

**TABLE 1** Characteristics of Physicians Completing Study Survey

Characteristic	<i>n</i> (%)
<b>Specialty</b>	
General pediatrics	129 (46) <sup>a</sup>
Neonatology	81 (29)
ID	52 (19)
Other <sup>b</sup>	17 (6)
<b>No. UTI cases managed</b>	
12+ cases/y	45 (16)
6–12 cases/y	49 (19)
1–5 cases/y	123 (44)
<1 case/y	62 (22)
<b>Sex</b>	
Male	117 (42)
Female	156 (56)
Declined to state	6 (2)
<b>Geography</b>	
West	73 (26)
Central	60 (22)
South	61 (22)
Northeast	84 (30)
Other	1 (0.4)
<b>Still in training</b>	
Yes	13 (5)
No	266 (95)
<b>Years in practice<sup>c</sup></b>	
1–5 y	36 (14)
6–10 y	46 (17)
11–15 y	48 (18)
16+ y	136 (51)
<b>Practice setting</b>	
Solo/stand-alone	11 (4)
Group	67 (24)
University-based	105 (38)
Hospital-based, community	85 (30)
Other	11 (4)
<b>Compensation</b>	
Salary without incentive	123 (44)
Salary with incentive	101 (36)
Self-employment practice income	23 (8)
Productivity model	21 (8)
Other	11 (4)
<b>Total</b>	<b>279 (100)</b>

<sup>a</sup> Out of 129 general pediatricians, 30 described themselves as hospitalists.

<sup>b</sup> Other specialists included pediatric emergency medicine (*n* = 7), both general pediatrics and ID (*n* = 2), pediatric cardiology (*n* = 1), developmental pediatrics (*n* = 1), pediatric critical care (*n* = 1), pediatric endocrinology (*n* = 1), genetics (*n* = 1), public health (*n* = 1), research (*n* = 1), and unspecified (*n* = 1).

<sup>c</sup> Excludes trainees.

**TABLE 2** Effect of Specialty on 279 Pediatricians' Planned IV Antibiotic Durations Beyond 48 Hours in a Febrile Neonate With UTI

Specialist	n	Actual Average Additional Days, d (95% CI)	Expected Effect of Specialist Versus General Pediatrician on Additional Days <sup>a</sup>	
			Baseline Model, d (95% CI) <sup>b</sup>	Full Model, d (95% CI) <sup>c</sup>
General pediatrician	129	2.4 (1.9 to 3.0)	Referent	Referent
Neonatologist	81	4.2 (3.0 to 5.4)	+1.7 (+0.4 to +3.0)	+2.2 (+0.8 to +3.7)
ID specialist	52	2.7 (1.7 to 3.7)	+0.3 (-0.8 to +1.4)	+1.2 (-0.4 to +2.8)
Other specialist	17	2.0 (0.7 to 3.3)	-0.4 (-1.9 to +1.0)	-0.5 (-1.8 to +0.8)

<sup>a</sup> Negative binomial regression model with the dependent variable of total days of IV antibiotics beyond 48 h.

<sup>b</sup> Baseline model included specialty, coded into the 4 categories listed in the first column.

<sup>c</sup> In addition to specialty, the full model included the following respondent characteristics from Table 1 as main effects. Nominal characteristics (sex, years in practice, location, proportion of clinical time managing inpatients, practice setting, and compensation) were coded with indicator variables. Annual experience with UTI was entered as an ordinal variable (<1 case = 0, 1–5 cases = 1, 6–12 cases = 2, and 12 or more cases = 3). In addition, backward selection of candidate interaction terms led to retention of sex by compensation model and sex by location.

reports),  $n = 35$  (12.5%); Level X (exceptional situations),  $n = 2$  (0.7%); and "I don't know,"  $n = 62$  (22.2%). There was no significant correlation ( $P = .49$ ) between appraised level of current evidence and IV antibiotic duration. Physician demographics, including sex, geographical location, trainee status, years in practice, practice setting, or compensation model were not associated with IV antibiotic duration preferences on bivariate analysis.

A total of 148/279 (53%) respondents reported wanting to order a VCUg, and 73/279 (26%) wished to provide prophylactic antibiotics. For those respondents who wanted a VCUg, 4/68 (6%) wanted prophylactic antibiotics when told the results of the VCUg were normal, whereas 45/80 (56%) wanted prophylactic antibiotics when the VCUg showed grade II VUR ( $P < .001$ ). For those respondents that did not want a VCUg, 0/70 (0%) wanted prophylactic antibiotics when told that the VCUg results were normal, whereas 24/61 (39%) wanted prophylactic antibiotics when the VCUg showed grade II VUR ( $P < .001$ ).

## DISCUSSION

In this national cross-sectional survey of pediatricians, we demonstrate several important findings to help understand practice patterns and variation in the treatment of neonates with UTI. Specialty type appears to be a strong driver of IV antibiotic duration, with the median duration of IV antibiotics being ~3 times as long for neonatologists and approximately twice as long for ID physicians compared to the median duration for general pediatricians/hospitalists. We also demonstrate that a substantial proportion of physicians who did not wish to obtain a VCUg wanted to start prophylactic antibiotics when presented with abnormal VCUg results, indicating that physicians feel compelled to react to abnormal results from tests they would not have ordered.

Most UTIs can be treated with oral antibiotics, as recommended by the AAP<sup>9</sup>; this recommendation is supported by the authors of recent Cochrane reviews<sup>17,18</sup> and by the authors of additional studies<sup>19–21</sup> who demonstrate that longer IV courses provide

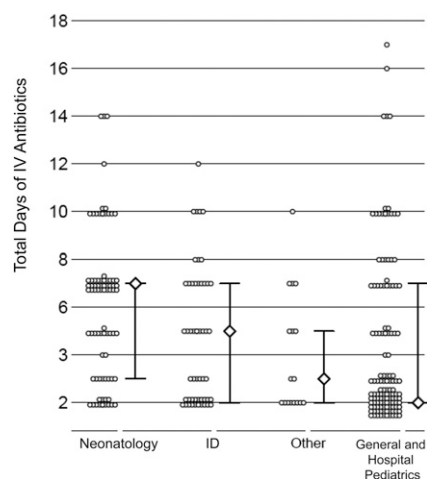
antibiotic duration by a statistically significant measure ( $P = .019$  in baseline model and  $P = .003$  in full model). Second, the magnitude of the effect of being a neonatologist (a 2-day increase in total IV antibiotic duration) remained statistically significant in the fully adjusted model.

The drivers of the IV antibiotic duration decision are summarized in Table 3. There

was a positive correlation between IV duration and the "standard of care at hospital" ( $r = 0.18$ ,  $P = .003$ ) and "medicolegal concerns" ( $r = 0.2$ ,  $P < .001$ ) drivers. There was a negative correlation between IV duration and "evidence from medical literature" ( $r = -0.15$ ,  $P = .01$ ), "concerns about harms from treatment" ( $r = -0.25$ ,  $P < .001$ ), and "financial costs of treatment" ( $r = -0.26$ ,  $P < .001$ ) drivers.

Neonatologists ranked standard of care at hospital higher than general pediatricians by 0.32 (95% confidence interval [CI] for difference: 0.05 to 0.60), whereas ID physicians ranked this driver lower than general pediatricians by -0.66 (95% CI: -0.98 to -0.34). ID physicians ranked medicolegal concerns lower than general pediatricians by -0.48 (95% CI: -0.90 to -0.06). In comparison with general pediatricians, neonatologists ranked concerns about harm from treatment lower by -0.39 (95% CI: -0.70 to -0.07), whereas ID physicians ranked it higher by 0.39 (95% CI: 0.02 to 0.75).

There was minimal consensus over the quality of the available evidence to assist with the IV antibiotic duration decision, with a breakdown of respondents' appraisals as follows: Level A (well-designed trials),  $n = 54$  (19.4%); Level B (trials with minor limitations),  $n = 70$  (25.1%); Level C (single or few observational studies),  $n = 56$  (20.1%); Level D (expert opinion, case



**FIGURE 1** Effect of respondent specialty on IV antibiotic duration. Circles represent physicians' responses for total days of IV antibiotics (which includes the 2 days already provided). The diamonds represent the medians, and the vertical lines with caps represent the IQRs of these responses, grouped by specialty.

**TABLE 3** Physician Ranking of Drivers as Related to IV Antibiotic Duration Preference in Case Vignette Neonate

Driver	Mean (Likert Scale, 1–5, 5 = Strongly Agree)	Statistically Significant Correlations With IV Antibiotic Duration ( <i>r</i> ) <sup>a</sup>
Evidence from the medical literature	4.2	−0.15
Standard of care at hospital	3.7	0.18
Concerns about harm from treatment	3.2	−0.25
Medicolegal concerns	2.9	0.20
Previous UTIs with bad outcomes	2.6	None
Financial costs of treatment	2.6	−0.26
Concerns about peer review and/or being negatively judged	2.2	None

<sup>a</sup> Measuring strength of linear association between driver and IV antibiotic duration. "None" indicates that there was no statistically significant correlation between the 2 variables.

no benefit over shorter IV courses or oral-only courses. However, few studies specifically focus on infants <2 months of age, an age range in which there is evidence of substantial variability in IV antibiotic duration decisions.<sup>3,5,8,10</sup> Because of this documented variability, we opted to examine IV duration decisions in neonates and to explore potential drivers of these decisions.

On the basis of our survey, specialty type appears to be a main driver of IV antibiotic duration. Although variability in NICU antibiotic use has been characterized previously,<sup>22</sup> we are unaware of any other investigators who have shown increased IV antibiotic use in neonatology compared with other services for similar clinical conditions. Presumably, neonatologists encounter more severe cases of UTI than do general pediatricians and hospitalists, which may bias preferences toward longer IV durations, although the subject in our case vignette was not severely ill. Additionally, neonatologists ranked the standard of care at hospital driver more highly than other specialties, and this driver was positively associated with IV duration, indicating that the practice of providing a longer IV course may be entrenched in the specialty. The authors of studies from adult medicine have previously described regional variations in care that are explained in part by physician specialty and have noted that this variation is not correlated with outcome.<sup>23,24</sup>

The evidence from the medical literature driver was ranked most highly by

pediatricians and was negatively associated with IV antibiotic duration (the higher this driver was ranked, the shorter the duration). However, when asked to appraise the strength of the available evidence to drive the IV antibiotic duration decision, there was little agreement, reflecting general unfamiliarity either with the evidence in this area or with classification systems for evidence grading. Nonetheless, because of the fact that medical evidence is perceived to be an important driver, we suggest that further dissemination of current literature, targeted evidence-based educational efforts, or additional studies in this age group may help change clinical practice. Interestingly, medicolegal concerns, often cited as a driver of high usage, was ranked relatively low in comparison with other drivers. Financial costs of treatment was ranked lower than concerns about harm from treatments, suggesting that emphasis on harm may be more effective than emphasis on cost in limiting overuse.

Just over half of respondents expressed a preference for a VCUG, indicating a lack of consensus in the pediatric community over imaging in this age group. Although the AAP guidelines do not include infants <2 months, the authors of other published national guidelines that do include young infants suggest obtaining a VCUG only if the RBUS results are abnormal or if the UTI is caused by an atypical organism.<sup>25</sup>

By providing VCUG results regardless of respondent preference for ordering the

study, and by randomly assigning respondents to normal versus abnormal VCUG results, we were able to explore how physicians respond to abnormal results from a test that they would not have ordered. This phenomenon is encountered by most practitioners on a regular basis because patient care is often fragmented, particularly for hospitalized patients who are likely to encounter numerous providers at different stages of care. Our results were striking in that 39% of physicians who did not wish to order a VCUG expressed a preference for prophylactic antibiotics when informed that the VCUG had revealed bilateral grade II VUR, whereas none of the physicians who did not wish to order a VCUG desired prophylactic antibiotics if the VCUG revealed no evidence of VUR. These findings are noteworthy, given that the pretest probability of VUR in a neonate with UTI is fairly high (21%–52%),<sup>26–30</sup> and although this probability is lower if the results of a RBUS are normal, it is still reported to be in the 18% to 24% range.<sup>26,27</sup> Therefore, it is somewhat counterintuitive that a respondent would not want a VCUG but would then want prophylactic antibiotics when presented with an abnormal VCUG result. More broadly, the fact that physicians feel compelled to react to abnormal results from a test that they would not have ordered has implications in terms of potential educational interventions focusing both on test ordering and test interpretation.

There are several limitations to this study. Reported as a proportion of respondents who clicked on the survey link in the e-mail, our survey completion rate (63.7%) was reasonable, but the participation rate (completed surveys out of e-mails sent) was low (12.4%), although not dissimilar to other published articles for electronic surveys.<sup>12,13,30</sup> Mail surveys have higher response rates, but our survey needed to be conducted electronically because of skip logic and randomization for the VCUG and prophylactic antibiotic questions. To minimize the potential for response bias, we attempted to make the subject line of the e-mail neutral (ie, Clinical Decision-Making Survey). We were reassured that the median IV duration response was not significantly different over the 4 e-mail rounds or in

comparing partially completed versus fully completed surveys. Nonetheless, the low participation rate does limit the generalizability of our findings. Similarly, although case vignettes are often used in research to ascertain practice patterns, responses from surveys may not align with decision-making in actual clinical practice. A common “wait and watch” approach to neonatal UTI is oftentimes applied with regards to obtaining a VUCG and providing prophylactic antibiotics, which we did not directly address in our survey. Likewise, there are likely other drivers of decision-making in UTI treatment duration and imaging preferences that were not captured in this study.

## CONCLUSIONS

There is considerable variability in reported physician preferences for IV antibiotic duration when treating a febrile UTI in a 2-week old neonate. Physician specialty type appears to be strongly associated with IV antibiotic duration preferences. A substantial proportion of pediatricians who did not wish to order a VUCG chose to provide prophylactic antibiotics in reaction to findings of VUR, demonstrating that results from unwanted tests often influence decision-making.

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