

# Clinical Impact of an Antimicrobial Stewardship Program on Pediatric Hospitalist Practice, a 5-Year Retrospective Analysis

Russell J. McCulloh, MD,<sup>a</sup> Mary Ann Queen, MD,<sup>a</sup> Brian Lee, PhD,<sup>a</sup> Diana Yu, PharmD,<sup>b</sup> Leslie Stach, PharmD,<sup>c</sup> Jennifer Goldman, MD,<sup>a</sup> Angela Myers, MD,<sup>a</sup> Brian Pate, MD,<sup>d</sup> Jason G. Newland, MD<sup>a</sup>

**BACKGROUND AND OBJECTIVES:** Hospitalists increasingly serve as the primary physicians for children hospitalized with infections. Consequently, hospitalists frequently interact with institutional antimicrobial stewardship programs (ASPs). Understanding how these services interact can inform ongoing practice improvement efforts. The objectives of this study were to identify factors associated with ASP recommendations among hospitalist-managed children, and to determine the association of ASP interventions with clinical outcomes for hospitalist-managed patients.

**METHODS:** We retrospectively analyzed ASP reviews of hospitalist patients from a children's hospital from March 2008 to June 2013. Clinical factors associated with an ASP recommendation were determined. Length of stay and 30-day readmission were compared between cases of agreement and disagreement with ASP recommendations.

**RESULTS:** The ASP reviewed 2163 hospitalist patients, resulting in 350 recommendations (16.2% of reviews). Hospitalists agreed with ASP recommendations in 86.9% of cases. The odds of an ASP recommendation decreased during the study period. Ceftriaxone was the most common antibiotic associated with a recommendation (154/350, 44.0%); community-acquired pneumonia was the most common diagnosis (105/350, 30.0%). Antibiotic discontinuation was the most often recommendation; hospitalists most often disagreed with consulting infectious diseases. Disagreement with ASP recommendations was associated with a decreased length of stay of 15.4 (95% confidence interval -33.2 to 1.1) hours but not 30-day readmission prevalence.

**CONCLUSIONS:** Pediatric hospitalists and ASPs can form an effective collaboration that improves antibiotic use while providing safe care. Better characterization of the areas of disagreement between hospitalists and ASPs is needed. Future studies are needed to identify ASP strategies that will be beneficial in other hospitalist settings.

## ABSTRACT

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Address correspondence to Russell J. McCulloh, MD, Children's Mercy Hospital, 2401 Gillham Rd, Kansas City, MO 64108. E-mail: rmcculloh@cmh.edu

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<sup>a</sup>Departments of Pediatrics, and  
<sup>b</sup>Pharmacy, Children's Mercy Hospital, Kansas City, Missouri;  
<sup>c</sup>Department of Pharmacy, Ann & Robert H. Lurie Children's Hospital, Chicago, Illinois; and <sup>d</sup>Department of Pediatrics, University of Kansas School of Medicine Wichita, Kansas

Antimicrobial stewardship programs (ASPs) have been shown to decrease antibiotic use with the hope of decreasing the rates of antimicrobial resistance.<sup>1,2</sup> In 2007, the Infectious Disease Society of America developed guidelines for the development of ASPs in all hospitals.<sup>3</sup> The guidelines recommend routine review of antimicrobial use for hospitalized patients to help clinicians provide optimal treatment strategies that result in the most appropriate, efficacious, and cost-effective antimicrobial agents. ASPs use varying strategies in an attempt to improve antimicrobial use, including prospective-audit with feedback, previous approval, and/or clinical guidelines for specific conditions.<sup>4</sup> In freestanding children's hospitals, these efforts are typically led by pharmacists and/or physicians with subspecialty training in infectious diseases (ID).<sup>4</sup>

Hospitalist programs are rapidly expanding in both community and tertiary settings,<sup>5</sup> resulting in a growing proportion of children hospitalized for infectious conditions being treated by pediatric hospitalists. Consequently, hospitalists increasingly manage patients who may undergo ASP review. The goals of hospital medicine and ASPs are broadly congruent. Hospitalists have been shown to decrease length of stay (LOS) and total hospital costs,<sup>6</sup> and to more closely adhere to evidence-based guidelines.<sup>7,8</sup> Given their central role in the management of hospitalized children, the American Academy of Pediatrics Section on Hospital Medicine recommends that pediatric hospitalists establish collaborative relationships with other pediatric subspecialists.<sup>9</sup> The Institute of Medicine has long recommended that "clinicians and institutions should actively collaborate and communicate to ensure an appropriate exchange of information and coordination of care."<sup>10</sup> However, little is known regarding the specific recommendations by ASPs in hospitalist-managed patients, the acceptability of recommendations to pediatric hospitalists, or the associated clinical outcomes among hospitalist-managed children for whom a recommendation is given.

In the current study, we aimed to characterize the patient-level factors associated with ASP-recommended changes for patients admitted to pediatric hospital medicine services at our tertiary care children's hospital. Our second aim was to determine associations between agreement with ASP recommendations and clinical outcomes for our cohort.

## METHODS

A retrospective study was conducted using clinical data from an existing ASP data repository at Children's Mercy Hospital—Kansas City from March 3, 2008, to June 30, 2013. The hospital is a freestanding children's hospital with 354 pediatric beds. The ASP program began in 2008 led by a board-certified pediatric infectious disease physician and clinical pharmacist. The ASP uses a system of prospective-audit with feedback to track the use of selected antibiotics for appropriateness of use, dose, and duration after a patient has been receiving the antibiotic for at least 2 calendar days (Table 1).<sup>11</sup> Clinical pharmacists and pediatric ID specialists discuss antibiotic choices with patient care teams and attending physicians and make recommendations for all reviewed antimicrobial prescriptions as necessary. Potential ASP recommendations include the following: stop antibiotics, optimize therapy (eg, dose-adjust, interval adjust), modify therapy (eg, change antibiotic to narrow or broad spectrum, convert intravenous to oral therapy), and infectious disease consultation. No recommendation is made in cases in which the patient is already on

appropriate therapy at the time of ASP review. Data on all ASP reviews, recommendations, and monitoring events are stored in a data repository.

Children admitted to an inpatient service staffed by a pediatric hospitalist between March 2008 and June 2013 and who had an ASP review during the course of their hospital stay were included for analysis. A patient may have received >1 ASP review during hospitalization, which may lead to a situation in which the same patient receives an intervention for one review but not for a subsequent review. This introduces complexity when determining which clinical characteristics had a significant influence on LOS and readmission. Consequently, we included only those patients with 1 review during the hospital stay, which represented nearly 90% of the original hospitalist sample.

Data collected for each patient from the ASP data repository included clinical service, antibiotic(s) prescribed, antibiotic indication, length of therapy, recommendations made by the ASP, and agreement and adherence with recommendations. In situations in which an ASP clinician made a recommendation, the recommendations were discussed between ASP staff and the hospitalist caring for the patient. Agreement with ASP recommendations was documented at this time and confirmed based on review of medical management after recommendations were discussed.

The Pediatric Health Information System database was used to obtain consistent data on readmissions and the presence of a complex chronic condition (CCC) for propensity scoring.<sup>12</sup> The Pediatric Health Information System database is an administrative database that contains inpatient, emergency department, ambulatory surgery, and observation encounter-level data from >45 not-for-profit, tertiary care pediatric hospitals in the United States, including our center. These hospitals are affiliated with the Children's Hospital Association (Overland Park, KS). For the purposes of external benchmarking, participating hospitals provide discharge/encounter data, including

**TABLE 1** ASP-Monitored Antibiotics

Ceftazidime	Amoxicillin/Clavulanate
Cefepime	Ampicillin/Sulbactam
Ceftriaxone	Piperacillin/Tazobactam
Cefotaxime	Ticarcillin/Clavulanate <sup>a</sup>
Meropenem	Ciprofloxacin
Imipenem/cilastatin <sup>a</sup>	Moxifloxacin <sup>a</sup>
Atreonam	Levofloxacin <sup>b</sup>
Amikacin <sup>b</sup>	Daptomycin <sup>a</sup>
Tobramycin	Vancomycin
Colistimethate <sup>b</sup>	Linezolid <sup>b</sup>

<sup>a</sup> Nonformulary items.

<sup>b</sup> Require previous approval.

demographics, diagnoses, and procedures. Data are de-identified at the time of data submission, and data are subjected to a number of reliability and validity checks before being included in the database. Children's Mercy Hospital institutional review board approved this study with an informed consent exemption. The ASP data repository is maintained under separate approval from the institutional review board.

## Statistical Analyses

We examined 2 primary outcomes for this study: (1) the LOS, which was defined as the total hours between admission and discharge from the hospital; and (2) readmission to the hospital within 30 days of discharge for the same all patient refined diagnosis-related groups (APR-DRG). Previous research has examined condition-specific readmission rates and shown interhospital variations as well as the level of cost attributable to readmissions.<sup>13,14</sup> We hypothesized a readmission for the same APR-DRG as the index hospitalization could indicate incomplete clinical care. We examined differences in both LOS and readmission outcomes based on 2 explanatory variables. The first was whether the ASP made a recommendation. The second, which was specific to those with a recommendation, was based on whether the attending disagreed with the recommendations. For the unadjusted analyses, the median LOS was calculated and the Wilcoxon rank-sum test used to determine statistical significance, whereas the prevalence of readmission was compared using the Fisher exact test. We defined statistical significance as a 2-sided  $P < .05$ . We reported the difference in median LOS and difference in proportion readmitted, with SEs calculated using bootstrap estimations.

Because both explanatory variables could be considered differing levels of "treatment," which were assigned in a nonrandom fashion, we then used propensity scoring matching as a means to control for confounding by indication.<sup>15,16</sup> This approach was also selected to observe any covariate imbalance, as well as establishing the level of exchangeability

between groups.<sup>17</sup> The propensity score was calculated using multiple factors that were hypothesized to be related to an ASP intervention: (1) patient's age, (2) year since the ASP program was implemented, (3) principal diagnosis for antibiotic treatment, (4) the antibiotic(s) currently prescribed, and (5) whether the patient had any CCC. Matching was performed using a 1:2 ratio (recommendation:no recommendation disagreed:agreed) based on the propensity score. In an effort to minimize bias, the caliper was restricted to 0.02 to help ensure a nearly identical probability of receiving treatment, as well as sampling with replacement. The matched analysis was also restricted to include only those patients with common support, which implies that a patient must have at least 1 control within their caliper to be included. After matching, covariate balance was completed to assess if the matching process was sufficient. Sensitivity analyses were performed on hospital readmission using adjusted logistic regression and the same covariates used in propensity score-matching. All analyses were completed with Stata software (version 13.1; Stata Corp, College Station, TX). The PSMATCH2 package was used for propensity scoring.

## RESULTS

### ASP Recommendation Prevalence and Clinical Factors Associated With Recommendations

A total of 2178 hospitalist patients underwent a single ASP review during the study period. We excluded 15 (0.7%) records for missing data on specific intervention and clinical indications leaving 2163 hospitalist-managed patients in our final sample. Overall, the ASP agreed with initial hospitalist antibiotic prescription choices in 1828 patients (83.8%). The proportion of patients receiving ASP recommendations varied by year (eg, 23.5% for year 1 compared with 12.1% for year 3), and the proportion of ASP recommendations among hospitalist patients decreased from year 1 to year 5 ( $P < .001$ ). Agreement with ASP recommendations was relatively high ( $n = 291/335$  [86.9%]). The most commonly given recommendation was to stop antibiotic

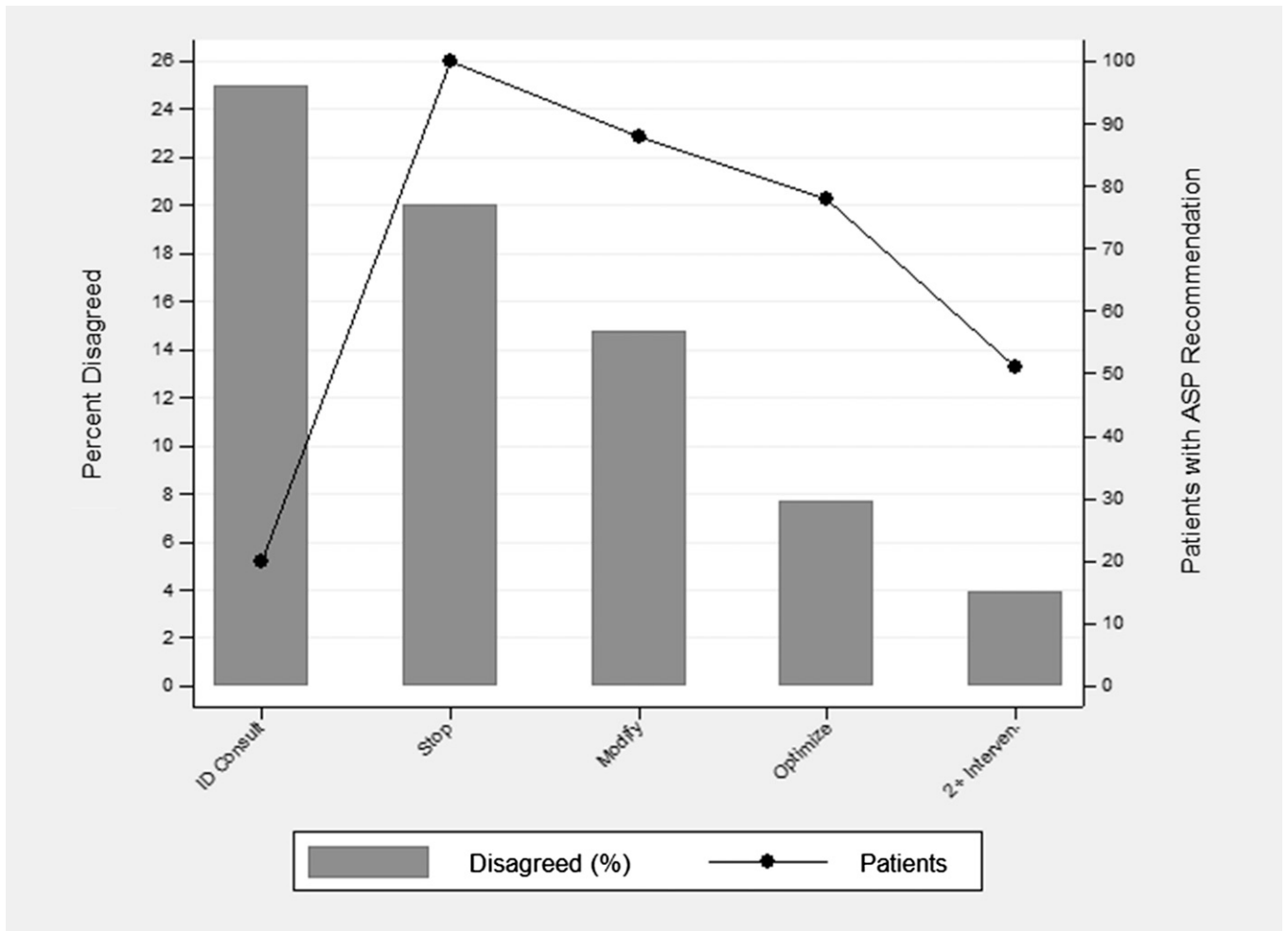
therapy ( $n = 100$ , 28.6%); however, disagreement with a recommendation was highest for ID consultation (25%) (Fig 1).

Several clinical factors were found to be significantly associated with ASP recommendations (Table 2). Community-acquired pneumonia (CAP) was the most prevalent diagnosis ( $n = 105$ , 30.0%) among hospitalist patients with a recommendation, whereas only 10.2% of patients with no recommendations were being treated for CAP. Similarly, the prevalence of an ASP-monitored drug in combination with clindamycin was 2 times greater in the recommendation group (25.1% vs 12.2%). Patients with an ASP recommendation were also more likely to have a CCC (22.0% vs 14.9%). Fifty percent of disagreed records were being treated for CAP.

### Clinical Outcomes Associated With ASP Recommendation

In unadjusted analysis, we observed that patients who had a recommendation had a significantly longer median LOS when compared with those who did not receive a recommendation (85.5 vs 63.3 hours, respectively;  $P < .001$  [Table 3]). Although the median LOS for agreed recommendations was 13 hours longer (87.9 vs 74.3 hours) when compared with disagreed recommendations, this did not reach statistical significance ( $P = .123$ ). We did not observe any significant differences in readmission in unadjusted analysis (Table 4).

For our adjusted analyses, which were conducted to account for imbalanced covariates and confounding of treatment by indication, we observed a 96% bias reduction following propensity score calculations, suggesting we had improved covariate balance.<sup>15,17</sup> There was no significant difference in median LOS based on recommendation status (difference in median: 4.0 [95% CI -4.5 to 13.7] hours [Table 3]) in propensity score-matched analysis. Disagreement with ASP recommendations had a shorter LOS (difference in median LOS -15.4 [95% CI -33.2 to 1.1] hours). Although the 30-day readmission percentage was less when the hospitalist agreed with the ASP recommendation (1.1% [95% CI 0 to 3.3%] vs



**FIGURE 1** Proportion of ASP-recommended intervention and hospitalist disagreement by category.

2.2% [95% CI 0.1 to 11.5%]), this was not statistically significant (Table 4), which was confirmed on sensitivity analysis.

## DISCUSSION

In this study, we provide the first reported evaluation of an ASP on pediatric hospitalist practice and associated patient outcomes. Our evaluation of 2163 ASP reviews of hospitalist-managed patients over a 5-year period found that hospitalist patients received an ASP recommendation in 16.2% of reviews. This rate of ASP recommendation is consistent with our previously reported overall rate of recommendations for all inpatient service lines combined (16.1%).<sup>18</sup> Community-acquired pneumonia was the most common diagnosis, and antibiotic discontinuation

was the most common recommendation. The ASP recommendation that hospitalists were most likely to disagree with was to consult ID; however, the number of recommendations by the ASP decreased over time. Finally, in adjusted analysis, agreement with an ASP recommendation was not associated with an increase in readmissions but was associated with a longer median LOS (median difference 15.4 hours).

The high level of ASP-concordant antibiotic use is likely in part due to the presence of institutional clinical practice guidelines (CPGs) that provide explicit antimicrobial usage recommendations for common pediatric illnesses (eg, CAP, evaluation of the febrile infant). However, the fact that CAP, the most common antibiotic indication

associated with an ASP recommendation, had a CPG available highlights the known limitation of CPGs to influence physician practice,<sup>19–21</sup> the marked variation in care in the management of CAP also found nationally,<sup>22</sup> and the usefulness of ASPs to support the practice improvement goals that underpin CPG creation.<sup>23,24</sup> We also found that the ASP recommended an intervention in 105 (36.2%) of 290 reviewed CAP cases, suggesting that evidence-based guidelines for antibiotic use in CAP may not have been followed before ASP review in many cases. These results are in contrast to previous studies that have reported enhanced hospitalist adherence to evidence-based guidelines reported from observational studies<sup>7,25</sup> as well as surveys of physician knowledge, skills, and

**TABLE 2** Factors Evaluated for Association With ASP Recommendation (*n* = 2163)

Factor	Recommendation, <i>n</i> = 350, <i>n</i> (%)	No Recommendation, <i>n</i> = 1813, <i>n</i> (%)	<i>P</i>
Age			<.001
0–5 mo	101 (28.9)	978 (53.9)	
6–17 mo	54 (15.4)	184 (10.1)	
18–59 mo	86 (24.6)	230 (12.7)	
5–12 y	75 (21.4)	285 (15.7)	
≥13 y	34 (9.7)	136 (7.5)	
Review year			<.001
1	123 (35.1)	400 (22.1)	
2	74 (21.1)	440 (24.3)	
3	50 (14.3)	363 (20.0)	
4	56 (16.0)	323 (17.8)	
5	47 (13.4)	287 (15.8)	
Presence of CCC	77 (22.0)	270 (14.9)	.001
Antibiotic Indication			<.001
Bacteremia	14 (4.0)	49 (2.7)	
CAP	105 (30.0)	185 (10.2)	
CNS infection	10 (2.9)	92 (5.1)	
ENT	42 (12.0)	179 (9.9)	
Genitourinary infection	81 (23.1)	277 (15.3)	
Respiratory (not CAP)	10 (2.9)	34 (1.9)	
SSTI	25 (7.1)	89 (4.9)	
Surgical site infection	2 (0.6)	18 (1.0)	
Suspected sepsis	25 (7.1)	536 (29.6)	
2 or more diagnoses	19 (5.4)	57 (3.1)	
Other indication	17 (4.9)	297 (16.4)	
Monitored antibiotic or group <sup>a</sup>			<.001
β-lactam/inhibitor	21 (6.0)	103 (5.7)	
Carbapenem	3 (0.9)	7 (0.4)	
Ceftriaxone	154 (44.0)	599 (33.0)	
Fluoroquinolone	1 (0.3)	26 (1.4)	
Other cephalosporin	16 (4.6)	140 (7.7)	
Vancomycin	2 (0.6)	25 (1.4)	
2+ monitored antibiotics	8 (2.3)	80 (4.4)	
Monitored + clindamycin	88 (25.1)	222 (12.2)	
Monitored + metronidazole	2 (0.6)	9 (0.5)	
Monitored + penicillins	37 (10.6)	532 (29.3)	
Other	18 (5.1)	70 (3.9)	

CNS, central nervous system; ENT, otolaryngologic infection; SSTI, skin and soft tissue infection.

<sup>a</sup> Full list of monitored antibiotics detailed in Table 1.

attitudes.<sup>26,27</sup> Thus, our findings suggest that, even for common infections associated with existing institutional CPGs, ASPs can play a role in optimizing hospitalist prescribing practices.

The odds of a patient cared for by a hospitalist to have the ASP make a recommendation steadily dropped over

the study period. This finding may represent increasing hospitalist familiarity with institutional and national CPGs for the treatment of common infectious entities.

This finding may also represent behavioral changes in hospitalist antibiotic prescription practices in response to ongoing interactions and education from

the ASP. Our ASP uses prospective audit-with-feedback strategy (ie, active audit of monitored drugs followed by feedback to the prescribing clinician) to help optimize antimicrobial prescription practices.

Previous studies have demonstrated that physician behavior changes significantly under the pressure of explicit external

**TABLE 3** Unadjusted and Propensity Score–Matched Difference in Length of Stay (in Hours) Based on Intervention and Recommendation Agreement Statuses

	Unadjusted			1:2 Matched <sup>a</sup>		
	Median (95% CI)	<i>n</i>	<i>P</i> <sup>b</sup>	Median (95% CI)	Difference in Medians (95% CI)	<i>n</i>
Intervened	85.5 (79.0 to 89.4)	350	<.001	84.7 (76.2 to 88.9)	4.0 (−4.5 to 13.7)	343
No intervention	63.3 (61.9 to 65.2)	1813		80.7 (71.4 to 85.2)		686
Agreed	87.9 (80.8 to 90.8)	291	.123	89.7 (74.4 to 107.3)		88
Disagreed	74.3 (67.2 to 87.6)	46		74.3 (67.2 to 87.6)	−15.4 (−33.2 to 1.1)	46

<sup>a</sup> *P* values are not included in this aspect of the table as the statistical methodology using propensity scores does not make this feasible.

<sup>b</sup> Obtained using Wilcoxon rank-sum test.

**TABLE 4** Unadjusted and Propensity Score–Matched Comparison of 30-Day Readmission Based on Intervention and Recommendation Agreement Status

	Unadjusted			1:2 Matched <sup>a</sup>		
	Percent Readmit (95% CI)	<i>n</i>	<i>P</i> <sup>b</sup>	Percent Readmit (95% CI)	Difference in Percent (95% CI)	<i>n</i>
Intervened	3.1 (1.7 to 5.6)	350	.587	3.2 (1.6 to 5.7)	−1.0 (−3.3 to 1.5)	343
No intervention	2.6 (1.9 to 3.4)	1813		4.2 (2.7 to 5.7)		686
Agreed	3.4 (1.8 to 6.3)	291	.999	1.1 (0 to 3.3)		88
Disagreed	2.2 (0.3 to 14.2)	46		2.2 (0.1 to 11.5)	1.1 (−3.2 to 6.5)	46

<sup>a</sup> *P* values are not included in this aspect of the table as the statistical methodology using propensity scores does not make this feasible.

<sup>b</sup> Obtained using Fischer's exact test.

observation,<sup>28</sup> and it is possible that the ASP supplies the impetus for a Hawthorne effect in antimicrobial prescription practices over time.<sup>29</sup>

Our finding of antibiotics discontinuation as the most common ASP recommendation is not surprising, given recent reports of the effect of pediatric ASPs on antimicrobial use.<sup>30</sup> Previous studies of the impact of ASPs on antimicrobial use have reported decreases both in overall antibiotic use as well as the use of broad-spectrum antimicrobial agents.<sup>1,2,23,30</sup> Decreasing unnecessary antimicrobial use can have far-reaching effects for patients through decreased costs and avoidance of adverse effects from antibiotics,<sup>31</sup> as well as for the community through reducing the risk of developing antimicrobial resistance.<sup>32</sup> In this respect, ASPs provide value to inpatient pediatric care that is both complementary and additive to the value provided by hospitalists.

Previous surveys of pediatric prescribers' perceptions of ASPs has found that the services provided by these programs are perceived to be valuable,<sup>33</sup> which may in part explain the overall high rate of agreement with ASP recommendations found in our study (86.4%). ID consultation

was proportionally the most common recommendation where disagreement occurred. However, ID consultation constituted only 10% of all recommended interventions, and the underlying reason for recommending ID consultation was not available for review. Thus, we were unable to determine if disagreement with ID consultation may have been due to extenuating circumstances not captured in the database. For example, it is possible that ID consultation could have been recommended for issues unrelated to acute inpatient management (eg, facilitating outpatient follow-up for a diagnosed and appropriately treated osteomyelitis), or the hospitalist may have made antimicrobial changes that obviated the need for ID consultation.

We were surprised to find that LOS was increased in cases in which hospitalists agreed with ASP recommendations, given that the most common ASP recommendation was antibiotic discontinuation. However, the significance of this finding is uncertain, as the difference represents less than a full hospital day. The difference in LOS also should be balanced against the lack of difference in 30-day readmission rates. Differences in

readmission rates would be reasonably expected to occur if ASP recommendations resulted in inappropriate management of infections. Because the most common recommendation was to stop an antibiotic, the lack of difference in readmission rates provides further reassurance that ASP recommendation was not associated with adverse events. These findings taken together suggest that improving the judicious use of antibiotics does not result in worse patient outcomes.

Our study has a few limitations. First, we analyzed retrospective data, which limited our ability to infer causation for changes in prescription practices. Additionally, the ASP repository did not include all potentially relevant clinical information, which could result in the development of a propensity score that further biased results. However, given our use of clinical indication, age, and antimicrobial agents monitored, we were able to base the development of this score on the most clinically relevant factors to the ASP-hospitalist interaction. Findings regarding nonadherence to ASP recommendations may have been biased toward the null due to small sample size, despite our use of data from more than 5 years of ASP-reviewed patients. We chose

to use 30-day readmission for the same APR-DRG as our readmission metric, which can certainly be debated. However, we also examined all-cause 30-day readmission in propensity score–matched analysis and did not observe any significant differences, which was confirmed in sensitivity analysis. Finally, our study excluded some of the most complex patients from analysis by limiting eligible patients to those who received only 1 ASP review. However, excluding such complex patients from analysis allowed us to minimize overrepresentation of individual patients in the included sample as well as unmeasured confounding from variables that would inevitably be a part of these patients' more complicated clinical courses.

This study was conducted at a tertiary pediatric medical center with available pediatric ID and pharmacy support. However, pediatric hospitalists practice in a variety of inpatient settings, including smaller community hospitals and medical centers that may not have such subspecialty service available. Previous studies have reported successful incorporation of adult hospitalists into ASP programs,<sup>34</sup> and national initiatives have been established to promote and advance the role of hospitalists in ASPs.<sup>34,35</sup> The role of the pediatric hospitalist, as outlined by the American Academy of Pediatrics Section on Hospital Medicine, highlights hospitalist participation in ongoing hospital committees and initiatives.<sup>36</sup> The results of our study suggest that ASPs provide additional benefits to the management of children hospitalized for infection beyond those provided by pediatric hospitalists alone. Components of an ASP (eg, automatic hard stops for antibiotics, CPGs, computer entry order sets with optimal antibiotics) could be incorporated by pediatric hospitalists into ongoing initiatives at medical centers lacking on-site support from ID subspecialists to optimize care delivery, and is an area being actively pursued by some health systems.<sup>37</sup>

## CONCLUSIONS

Pediatric hospitalists and ASPs can form an effective collaboration that improves antibiotic use while providing safe care. A better characterization of the areas of

disagreement between hospitalists and ASPs is needed to further improve this collaboration. Finally, studies are needed to identify ASP strategies that will be beneficial in other hospitalist settings.

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