Narrow Vs Broad-spectrum Antimicrobial Therapy for Children Hospitalized With Pneumonia

AUTHORS: Derek J. Williams, MD, MPH,^a Matthew Hall, PhD,^b Samir S. Shah, MD, MSCE,^c Kavita Parikh, MD,^d Amy Tyler, MD,^e Mark I. Neuman, MD, MPH,^f Adam L. Hersh, MD, PhD,^g Thomas V. Brogan, MD,^h Anne J. Blaschke, MD, PhD,^g and Carlos G. Grijalva, MD, MPHⁱ

^aDivision of Hospital Medicine, Monroe Carell Jr. Children's Hospital at Vanderbilt, and Department of Pediatrics, Vanderbilt University School of Medicine, Nashville, Tennessee; ^bThe Children's Hospital Association, Overland Park, Kansas; ^cDivisions of Infectious Diseases and Hospital Medicine, Cincinnati Children's Hospital Medical Center, and Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, Ohio; ^dDivision of Hospital Medicine, Children's National Medical Center, and Department of Pediatrics, George Washington University School of Medicine, Washington, District of Columbia; ^eSection of Hospital Medicine, Children's Hospital Colorado, and Department of Pediatrics, University of Colorado School of Medicine, Aurora, Colorado; ^fDivision of Emergency Medicine, Boston Children's Hospital, and Department of Pediatrics, Harvard University School of Medicine, Boston, Massachusetts; ^gDivision of Infectious Diseases, Primary Children's Medical Center, and Department of Pediatrics, University of Utah School of Medicine, Salt Lake City, Utah; ^hDivision of Critical Care, Seattle Children's Hospital, and Department of Pediatrics, University of Washington School of Medicine, Seattle, Washington; ⁱDepartment of Preventive Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee

KEY WORDS

pneumonia, antibiotic use, effectiveness, pediatrics

ABBREVIATIONS

aD—adjusted difference
CAP—community-acquired pneumonia
CI—confidence interval
IDSA—Infectious Diseases Society of America
IQR—interquartile range
LOS—length of stay
PHIS—Pediatric Health Information System
PIDS—Pediatric Infectious Diseases Society

Drs Williams and Grijalva participated in conceptualization and study design, data analysis, interpretation of results, drafting of initial manuscript, and critical review and manuscript revision; Dr Hall participated in conceptualization and study design, data analysis, interpretation of results, and critical review and manuscript revision; Drs Shah, Parikh, Tyler, Neuman, Hersh, Brogan, and Blaschke participated in conceptualization and study design, interpretation of results, and critical review and manuscript revision; all authors reviewed and approved the final manuscript as submitted.

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WHAT'S KNOWN ON THIS SUBJECT: Recent guidelines for the management of childhood pneumonia recommend narrow-spectrum antimicrobial agents (eg, ampicillin) for most children; however, few studies have directly compared the effectiveness of narrow-spectrum agents to the broader spectrum third-generation cephalosporins commonly used among children hospitalized with pneumonia.

WHAT THIS STUDY ADDS: By using data from 43 children's hospitals in the United States, we demonstrate equivalent outcomes and costs for children hospitalized with pneumonia and treated empirically with either narrow- (ampicillin/penicillin) or broad-spectrum (ceftriaxone/cefotaxime) antimicrobial therapy.

abstract

BACKGROUND: The 2011 Pediatric Infectious Diseases Society/Infectious Diseases Society of America community-acquired pneumonia (CAP) guideline recommends narrow-spectrum antimicrobial therapy for most children hospitalized with CAP. However, few studies have assessed the effectiveness of this strategy.

METHODS: Using data from 43 children's hospitals, we conducted a retrospective cohort study to compare outcomes and resource utilization among children hospitalized with CAP between 2005 and 2011 receiving either parenteral ampicillin/penicillin (narrow spectrum) or ceftriaxone/cefotaxime (broad spectrum). Children with complex chronic conditions, interhospital transfers, recent hospitalization, or the occurrence of any of the following during the first 2 calendar days of hospitalization were excluded: pleural drainage procedure, admission to intensive care, mechanical ventilation, death, or hospital discharge.

RESULTS: Overall, 13 954 children received broad-spectrum therapy (89.7%) and 1610 received narrow-spectrum therapy (10.3%). The median length of stay was 3 days (interquartile range 3–4) in the broad- and narrow-spectrum therapy groups (adjusted difference 0.12 days, 95% confidence interval [CI]: –0.02 to 0.26). One hundred fifty-six children (1.1%) receiving broad-spectrum therapy and 13 children (0.8%) receiving narrow-spectrum therapy were admitted to intensive care (adjusted odds ratio 0.85, 95% CI: 0.27 to 2.73). Readmission occurred for 321 children (2.3%) receiving broad-spectrum therapy and 39 children (2.4%) receiving narrow-spectrum therapy (adjusted odds ratio 0.85, 95% CI: 0.45 to 1.63). Median costs for the hospitalization were \$3992 and \$4375 (adjusted difference –\$14.4, 95% CI: –177.1 to 148.3).

CONCLUSIONS: Clinical outcomes and costs for children hospitalized with CAP are not different when treatment is with narrow- compared with broad-spectrum therapy. *Pediatrics* 2013;132:e1141–e1148

The 2011 Pediatric Infectious Diseases Society/Infectious Diseases Society of America (PIDS/IDSA) guideline for the management of children with community-acquired pneumonia (CAP) recommends narrow-spectrum antimicrobial therapy for most hospitalized children.¹ Reasons for this recommendation include the recognition of *Streptococcus pneumoniae* as the leading bacterial pneumonia pathogen among children,^{2–4} reductions in pneumococcal disease caused by penicillin-resistant strains after introduction of pneumococcal conjugate vaccines,^{5–8} and demonstrated effectiveness of higher-dosed penicillin-based therapies for relatively resistant pneumococcal infections outside of the central nervous system.^{9,10} Implicit in these recommendations is also the desire to increase awareness about the epidemic of antimicrobial resistance, due in part to overprescribing of broad-spectrum antibiotics for upper and lower respiratory tract infections.^{11,12} Evidence notwithstanding, the guideline recommendation for parenteral penicillin or ampicillin as empirical therapy for children hospitalized with CAP represents a significant departure from quotidian practice in the United States. A retrospective study of children hospitalized with CAP at 29 US hospitals between 2005 and 2010 demonstrated that <10% received penicillin or ampicillin as empirical therapy.¹³ One argument against the guideline recommendation is that the increased dosing frequency of the relatively inexpensive narrow-spectrum antibiotics may increase hospitalization costs. Another is the perception that broad-spectrum therapy results in faster recovery and better clinical outcomes compared with narrow-spectrum therapy.¹⁴ Nevertheless, few studies have directly compared the effectiveness of narrow-spectrum agents to the broader spectrum third-generation cephalosporins

commonly used among hospitalized children with CAP.

We sought to compare clinical outcomes and resource utilization among children hospitalized with CAP receiving empirical parenteral therapy with either narrow- (ampicillin or penicillin) or broad-spectrum (ceftriaxone or cefotaxime) antimicrobial agents.

METHODS

Data Source and Patient Population

We used data from the Pediatric Health Information System (PHIS) database (Children's Hospital Association, Overland Park, KS). The PHIS administrative database contains clinical and billing data from 43 freestanding, tertiary care children's hospitals and accounts for ~20% of all US pediatric hospitalizations. Data quality is ensured through a joint effort between the Children's Hospital Association and participating hospitals as described previously.¹⁵ In accordance with the Common Rule (45 CFR 46.102(f)), and the policies of the Cincinnati Children's Hospital Medical Center Institutional Review Board, this research, using a deidentified data set, was not considered human subjects research.

Children aged 6 months to 18 years were eligible for inclusion if they were hospitalized between July 1, 2005, and June 30, 2011, with an *International Classification of Diseases, Ninth Revision, Clinical Modification*–coded diagnosis of pneumonia (480–486, 487.1).¹⁶ The lower age limit sought to minimize the inclusion of children with <2 doses of routine childhood immunizations (including *Haemophilus influenzae* and *Streptococcus pneumoniae*). Because there are no validated disease severity measures for childhood CAP, several design restrictions were created to minimize concerns regarding confounding by severity. We excluded children with potentially severe pneumonia or those at

risk for health care–associated infections including children with ≥ 1 complex chronic conditions,¹⁷ interhospital transfers, previous hospitalization at a PHIS hospital within 30 days of the admission date, and children with any of the following during the first 2 calendar days of hospitalization: pleural drainage procedure, admission to intensive care, mechanical ventilation, or death. In addition, to exclude children with mild disease (ie, brief hospitalization) and to ensure a consistent ascertainment of empirical antimicrobial exposures, we also required children to have ≥ 2 calendar days of hospitalization.

Exposures

Antimicrobial therapy was classified as narrow- or broad-spectrum based on antimicrobial agents received during the first 2 calendar days of hospitalization. Narrow-spectrum therapy was defined by the exclusive use of parenteral penicillin or ampicillin, and broad-spectrum therapy was defined by the exclusive use of parenteral ceftriaxone or cefotaxime. With the exception of macrolides or oseltamivir, children receiving other antimicrobial agents during the first 2 calendar days of hospitalization were excluded, as were those with antibiotic class switching (eg, from ceftriaxone to ampicillin) because antimicrobial changes during the first 2 days of therapy are likely not related to treatment failure.

Outcomes

The main outcome measure was total hospital length of stay (LOS) for the index hospitalization. Additional outcomes included admission to intensive care (after the first 2 calendar days), 14-day all-cause readmission, and total costs for the admission and the entire episode of illness (accounting for 14-day readmissions). Cost data were estimated using hospital-specific cost-to-charge ratios and adjusted for hospital

location using the Centers for Medicare and Medicaid price/wage index.

Covariates

Model covariates included patient demographics (age, gender, race/ethnicity, payer); calendar time (hospitalization year and month); hospitalization at PHIS hospital within the preceding 6 months; asthma comorbidity (asthma-related hospitalization within the preceding 6 months or use of chronic asthma controller medications on the first day of hospitalization)¹⁷; and resource utilization during the first 2 calendar days of hospitalization, including oxygen therapy, advanced imaging (ultrasound or computed tomography), blood gas analysis, receipt of blood products, or receipt of other selected medications (macrolides, oseltamivir, bronchodilators, and corticosteroids).

Analysis

Characteristics of the exposure groups were summarized using frequencies and percentages for categorical variables and median and interquartile ranges (IQRs) for continuous variables. Bivariate comparisons used χ^2 and rank-sum tests as appropriate. Multivariable linear and logistic regression models evaluated the association between narrow- versus broad-spectrum antimicrobial use and outcomes while accounting for study covariates. Continuous outcomes with nonnormal distributions were log transformed, and normality was verified before model fitting with appropriate back transformation for reporting.

To further address the possibility of residual confounding by indication, we applied a propensity score matching strategy. Study covariates were used in the calculation of a propensity score by using a multivariable logistic regression model with antibiotic therapy (narrow versus broad spectrum) as the dependent variable (model *c* statistic

= 0.68). Observations from exposure groups were matched 1:1 on propensity score using nearest-neighbor matching with a caliper set at one-quarter of the SD of the logit of the propensity scores.¹⁸ Visual inspection of the distribution of propensity scores between antibiotic groups revealed good overlap after matching.

A planned subgroup analysis for children with and without acute wheezing was also performed for LOS. Children presenting with acute wheezing and concurrent evidence of pneumonia impose clinical uncertainty regarding the diagnosis (eg, pneumonia versus atelectasis in the setting of acute asthma) and the potential etiology (viral or atypical pathogens versus typical bacterial pathogens). Children with wheezing are also often treated with bronchodilators and corticosteroids, which may hasten recovery and influence outcomes. For this analysis, bronchodilator therapy was considered a proxy for acute wheezing. Children receiving bronchodilator therapy on the first 2 calendar days of hospitalization were categorized as having acute wheezing.

RESULTS

Study Population

There were 149 853 children hospitalized with CAP during the study period. After exclusion criteria were applied (Fig 1), 15 564 children remained and constituted the study population. Broad-spectrum therapy was administered to 13 954 (89.7%) children, and 1610 (10.3%) children received narrow-spectrum therapy. Children receiving broad-spectrum therapy were slightly older and more likely to be male, of non-Hispanic white or Hispanic race/ethnicity, and to have private insurance compared with children receiving narrow-spectrum therapy. Those receiving broad-spectrum therapy were

also more likely to receive advanced imaging, blood gas analysis, and macrolides but were less likely to have had a recent hospitalization, a history of asthma, or to receive bronchodilator or corticosteroid therapy (Table 1). Only 1 child died.

LOS

The median LOS for the study population was 3 days (IQR 3–4). The median LOS was shorter among those receiving narrow-spectrum therapy compared with those receiving broad-spectrum therapy in bivariate analysis; however, these differences were not significant after adjustment for potential confounders (adjusted difference [aD] 0.12 days, $P = .11$; Table 2).

Intensive Care Admission and 14-Day Readmission

One hundred and fifty six (1.1%) children receiving broad-spectrum therapy and 13 (0.8%) children receiving narrow-spectrum therapy were admitted to intensive care after the first 2 days of hospitalization ($P = .26$). Readmissions within 14 days of discharge did not differ between those receiving broad-spectrum therapy ($n = 321$, 2.3%) and narrow-spectrum therapy ($n = 39$, 2.4%; $P = .76$). In multivariable analyses, the odds of admission to intensive care and 14-day readmission did not significantly differ between children treated with broad- versus narrow-spectrum antimicrobial therapy (Table 2).

Costs

Unadjusted costs were higher among those receiving narrow-spectrum therapy for both the index hospitalization (median costs \$4375 vs \$3992, $P < .001$) and the total episode of illness (\$4407 vs \$4036, $P < .001$). However, in adjusted analyses, differences in costs were not statistically significant (aD -\$14.4, $P = .78$ for index hospitalization; aD -\$19, $P = .71$ for episode of illness; Table 2).

FIGURE 1

Study population. ICD-9-CM, *International Classification of Diseases, Ninth Revision, Clinical Modification*.^a See reference Feudtner et al.¹⁷ ^b Among these children, 59% received broad-spectrum therapy alone, 13% narrow-spectrum therapy alone, and 28% other antimicrobial agents.

Propensity Score-Matched Cohort

Propensity score matching retained 1044 children in each exposure group. There were no baseline differences in characteristics of the study population between the 2 groups (Table 1). Results of the matched analysis did not differ from those of the primary analyses. There were no significant differences between groups with respect to LOS (aD 0.01 days, $P = .71$), admission to intensive care (adjusted odds ratio 1.0, $P = .43$), 14-day readmission (adjusted odds ratio 1.0, $P = .48$), or costs (aD

−\$109, $P = .71$ for index hospitalization; aD −\$47, $P = .2$ for episode of illness; Table 3).

Subgroup Analysis

There were 4876 children in the broad-spectrum therapy group (34.9%) and 476 in the narrow-spectrum therapy group (29.6%) with acute wheezing. Children in the acute wheezing subgroup had similar median LOS compared with the nonwheezing subgroup (3 days [IQR 3–4] vs 4 days [IQR 3–4], $P = .71$). We observed no significant

differences in LOS between antibiotic exposure groups in both the acute wheezing (aD 0.1 days, $P = .5$) and nonwheezing (aD 0.15 days, $P = .21$) subgroups.

DISCUSSION

Among >15 000 children hospitalized with CAP, there were no differences in LOS, costs, need for intensive care, or readmissions between those treated with parenteral ampicillin or penicillin and those treated with broader spectrum third-generation cephalosporin therapy. Our findings suggest that the effectiveness of narrow-spectrum therapy is similar to that of broad-spectrum therapy for children hospitalized with CAP and provides new evidence to support the 2011 PIDS/IDSA CAP management guideline. The low frequency of narrow-spectrum therapy usage observed in our study highlights a substantial opportunity to promote greater use of narrow-spectrum antimicrobial agents for children hospitalized with CAP.

The effectiveness of narrow- versus broad-spectrum antimicrobial therapy for pediatric CAP that required hospitalization has been compared in a few small, randomized trials, but no large-scale randomized controlled trial has conclusively addressed this question. A randomized trial that studied 154 children <5 years of age hospitalized with severe CAP in Brazil found that empirical therapy with parenteral amoxicillin/clavulanic acid was as efficacious as combination therapy with oxacillin and ceftriaxone. The study demonstrated no differences in the time to stability (duration of fever or supplemental oxygen requirement) or the need for expanded antimicrobial coverage between the 2 treatment groups.¹⁹ In fact, children treated with amoxicillin/clavulanic acid had a shorter duration of tachypnea and shorter hospital LOS. In a similar study, 154 Finnish children with pneumonia,

TABLE 1 Characteristics of the Study Population

	Unmatched Cohort (n = 15 564)			Propensity Score Matched Cohort (n = 2088)		
	Ceftriaxone/Cefotaxime (n = 13 954)	Penicillin/Ampicillin (n = 1610)	P	Ceftriaxone/Cefotaxime (n = 1044)	Penicillin/Ampicillin (n = 1044)	P
Demographics						
Age, y	2 [1–5]	2 [1–4]	.003	2 [1–4]	2 [1–4]	.54
Male gender	7216 (51.7)	785 (48.8)	.025	497 (47.6)	494 (47.3)	.90
Race/ethnicity						
NH white	5584 (42.7)	481 (33.5)	<.001	208 (19.9)	224 (21.5)	.47
NH African American	3619 (27.7)	574 (39.9)		479 (45.9)	491 (47)	
Hispanic	3199 (24.5)	286 (19.9)		264 (25.3)	256 (24.5)	
Asian	382 (2.9)	70 (4.9)		56 (5.4)	47 (4.5)	
Other	280 (2.1)	26 (1.8)		37 (3.5)	26 (2.5)	
Payer						
Government	7075 (70.9)	1021 (87.3)	<.001	900 (86.2)	905 (86.7)	.92
Private	1586 (15.9)	92 (7.9)		89 (8.5)	88 (8.4)	
Other	1316 (13.2)	57 (4.9)		55 (5.3)	51 (4.9)	
Asthma	5226 (37.5)	696 (43.2)	<.001	514 (49.2)	484 (46.4)	.19
Previous hospitalization	1049 (7.5)	162 (10.1)	<.001	101 (9.7)	120 (11.5)	.18
Resource utilization ^a						
Oxygen therapy	4880 (35)	532 (33)	.124	396 (37.9)	403 (38.6)	.75
Blood products	17 (0.1)	2 (0.1)	.979	0 (0)	1 (0.1)	.32
Chest CT	173 (1.2)	10 (0.6)	.029	7 (0.7)	4 (0.4)	.36
Chest ultrasound	150 (1.1)	5 (0.3)	.003	0 (0)	1 (0.1)	.32
Blood gas analysis	1577 (11.3)	77 (4.8)	<.001	63 (6)	59 (5.7)	.71
Medications ^a						
Macrolide	2607 (18.7)	216 (13.4)	<.001	149 (14.3)	147 (14.1)	.90
Bronchodilator	8296 (59.5)	1025 (63.7)	.001	722 (69.2)	701 (67.1)	.32
Corticosteroid	4698 (33.7)	653 (40.6)	<.001	473 (45.3)	471 (45.1)	.93
Oseltamivir	520 (3.7)	73 (4.5)	.109	41 (3.9)	42 (4)	.91

Data presented as n (%) or median [IQR]. CT, computed tomography; NH, non-Hispanic.

^a Resource utilization and medication variables limited to first 2 calendar days of hospitalization.

TABLE 2 Outcomes Among Children Hospitalized With CAP According to Empiric Antimicrobial Therapy (N = 15 564)

	Ceftriaxone/Cefotaxime (n = 13 954)	Penicillin/Ampicillin (n = 1,610)	Adjusted MD or OR (95% CI)
LOS, d	3 [3–4]	3 [3–4]	MD 0.12 (−0.02 to 0.26)
Cost (\$), index hospitalization	3992 [2895–5713]	4375 [3390–5805]	MD −14.4 (−177.1 to 148.3)
Cost (\$), episode of illness	4036 [2919–5857]	4407 [3405–5913]	MD −18.6 (−194 to 156.9)
ICU admission	156 (1.1)	13 (0.8)	OR 0.85 (0.27 to 2.73)
14-day readmission	321 (2.3)	39 (2.4)	OR 0.85 (0.45 to 1.63)

Data presented as median [IQR] or n (%). Models adjusted for age, gender, race/ethnicity, payer, asthma comorbidity, previous hospitalization, month and year, resource utilization (oxygen therapy, blood products, chest ultrasound and computed tomography, blood gas analysis), and concomitant medication use (macrolides, bronchodilators, corticosteroids, oseltamivir). CI, confidence interval; MD, mean difference; OR, odds ratio.

sepsis, or other acute invasive bacterial infection requiring hospitalization were randomized to receive either parenteral penicillin or cefuroxime. Of the included children, 47% were diagnosed with pneumonia and nearly 40% had evidence of *S pneumoniae* infection. There were no differences in outcomes (time to recovery, normalization of laboratory parameters, or

treatment failure) between the 2 antibiotic treatment groups.²⁰ These small trials were conducted in regions with relatively low rates of pneumococcal resistance to penicillins compared with the United States or were not limited to CAP. Thus, their findings may not be directly applicable to children hospitalized with CAP in the United States.

Observational studies have also assessed the effectiveness of narrow-spectrum antimicrobial therapy for the treatment of CAP in children. A study among 319 Israeli children <2 years of age hospitalized with CAP demonstrated no differences in duration of oxygen requirement, hospital LOS, or treatment failures between children receiving parenteral aminopenicillins (n = 66) and those receiving parenteral cefuroxime (n = 253).²¹ After the implementation of an antibiotic stewardship program and a local practice guideline in a tertiary US children's hospital, Newman et al demonstrated a significant increase in use of ampicillin from 15% to 60%, a corresponding decrease in ceftriaxone use, and no significant difference in the rate of treatment failure among >1000 children hospitalized with uncomplicated CAP.²² That study was conducted in an

TABLE 3 Outcomes Among Children Hospitalized With CAP According to Empiric Antimicrobial Therapy, Propensity Score Matched Cohort (*n* = 2088)

	Ceftriaxone/Cefotaxime (<i>n</i> = 1044)	Penicillin/Ampicillin (<i>n</i> = 1044)	Adjusted MD or OR (95% CI)
LOS, d	3 [3–5]	3 [3–4]	MD 0.01 (–0.22 to 0.24)
Cost (\$), index hospitalization	4017 [2872–5908]	4255 [3302–5651]	MD –108.8 (–393.4 to 175.9)
Cost (\$), episode of illness	4106 [2898–6057]	4274 [3305–5752]	MD –46.9 (–349.9 to 265.1)
ICU admission	14 (1.3)	11 (1.1)	OR 1.0 (0.996 to 1.01)
14-day readmission	28 (2.7)	25 (2.4)	OR 1.0 (0.994 to 1.01)

Data presented as median [IQR] or *n* (%). Variables used to estimate propensity score included age, gender, race/ethnicity, payer, asthma comorbidity, previous hospitalization, month and year, resource utilization (oxygen therapy, blood products, chest ultrasound and computed tomography, blood gas analysis), and concomitant medication use (macrolides, bronchodilators, corticosteroids, oseltamivir). Propensity score matching (1:1) retained 1044 children in the narrow-spectrum therapy group (64.8%), model *c* statistic 0.68. CI, confidence interval; MD, mean difference; OR, odds ratio.

area with a relatively high rate of pneumococcal resistance to penicillin (~25% of isolates). Using PHIS data from 2006 to 2008, Ambroggio et al compared the effectiveness of β -lactam monotherapy versus a β -lactam in combination with a macrolide, and demonstrated shorter LOS for those receiving macrolide combination therapy in children aged ≥ 6 years.¹⁷ A subgroup analysis comparing narrow-versus broad-spectrum β -lactam monotherapy showed no differences in LOS or readmissions. However, that study included children with short LOS (eg, admitted and discharged on the same day) and those receiving oral therapy only and did not exclude children with early antimicrobial class switching (eg, ceftriaxone for ampicillin). In contrast, our study focused on the direct comparison of specific parenteral antibiotic regimens and excluded children with mild disease.

Antimicrobial selection for treatment of pediatric CAP is nearly always made without direct knowledge of the causative microorganism. The findings from our study suggest that narrower-spectrum therapies are not inferior to broader-spectrum therapies. Although the importance of viruses as causes of CAP among children is increasingly recognized,^{23–28} distinguishing viral from bacterial etiologies is difficult. Without rapid and sensitive

bacterial diagnostics at the point of care or trials demonstrating the efficacy of no treatment, our findings indicate therapy with narrow-spectrum antibiotics is effective for most children hospitalized with CAP, as recommended by the PIDS/IDSA CAP management guideline.

Optimizing antimicrobial usage is important for minimizing the spread of antimicrobial resistance on a global scale. More than 150 000 US children are hospitalized with CAP annually, making it among the most common indications for hospitalization in childhood.²⁹ Discouraging the use of unnecessarily broad-spectrum antimicrobial agents for children hospitalized with CAP therefore has the potential to markedly reduce selective pressure for antimicrobial resistance. Our study noted that only 10% of study children received empirical therapy with penicillin or ampicillin. Wide variation in prescribing of antimicrobial agents for children hospitalized with CAP has been observed across PHIS hospitals, although <5% of children with CAP receive narrow-spectrum therapy at most hospitals.¹³ Thus, although some institutions often used narrow-spectrum therapy for uncomplicated CAP, most did not, highlighting an important opportunity for improvement in antimicrobial selection. Previous studies have demonstrated the feasibility

and effectiveness of stewardship programs and dissemination of local practice guidelines on changing antimicrobial selection for CAP management.^{22,30–33} The publication of the first consensus guidelines for childhood CAP management could serve as a catalyst for these initiatives.

The overall cost of hospitalization did not differ between children treated with narrow- versus broad-spectrum antimicrobial therapy in our study. This finding suggests that routine use of penicillin or ampicillin does not contribute to substantial increases in hospitalization costs despite the increased dosing frequency of these medications compared with some third-generation cephalosporins, such as once-daily ceftriaxone. Although pharmacy costs may differ in local environments, differences are likely small and not a major driver of hospital costs. Thus, other cost-saving measures, such as promoting early transition to oral therapy, improving diagnostics to facilitate reduced antimicrobial use, or interventions to reduce hospital LOS, may prove more effective in minimizing total hospital costs.^{34,35}

Limitations of the study are largely related to the observational study design and include the potential for confounding by indication, absence of etiologic and other clinical data, and a relative lack of objective outcome measures. In the absence of large randomized efficacy trials, well-designed observational studies provide valuable data on the effectiveness of therapies and interventions on a large scale. Several steps were taken to reduce potential confounding due to differential use of narrow- or broad-spectrum therapy based on illness severity. First, we excluded children with indicators of severe disease at or near the time of presentation (eg, admission to intensive care). We also excluded children with indicators of particularly mild disease (eg, receipt of oral

antimicrobial agents on the first hospital day or hospital LOS <2 calendar days). Second, a number of factors that may influence antimicrobial selection, including proxy measures of disease severity, were accounted for in our multivariable analyses. Furthermore, our propensity score matched analysis, which substantially minimized the differences between exposure groups, also produced results similar to those from the unmatched cohort, lending further support to our study's primary results. Although we cannot eliminate residual confounding due to unmeasured covariates, the careful selection of our study population as well as the use of robust modeling techniques minimizes this concern. The

distinction between bacterial and viral causes of CAP in children is difficult, even in prospective studies. Residual misclassification after application of selection criteria in this regard would be expected to be nondifferential between the 2 empirical treatment groups, favoring the null hypothesis. Although the PHIS database does not contain results of microbiologic testing, our study was restricted to children who received antimicrobial therapy, which suggests clinical suspicion of and treatment of bacterial pneumonia. Similarly, hospital-specific data, such as the presence or absence of local practice guidelines or stewardship programs was not available. Finally, our assessment focused on the

evaluation of empirical antimicrobial treatments but did not characterize antimicrobial class switching after the first 2 days of hospitalization.

CONCLUSIONS

Clinical outcomes and costs for children hospitalized with CAP are not different when empirical treatment is with narrow-spectrum compared with broad-spectrum therapy. Few institutions used narrow-spectrum therapy routinely before publication of the PIDS/IDSA CAP management guidelines. Programs promoting guideline implementation and targeting judicious antibiotic selection for CAP are needed to optimize management of childhood CAP in the United States.

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Address correspondence to Derek J. Williams, MD, MPH, 1161 21st Ave South, CCC 5311 Medical Center North, Nashville, TN 37232. E-mail: derek.williams@vanderbilt.edu
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