[Original Research]

CHEST

Antibiotic Use and Outcomes After Implementation of the Drug Resistance in Pneumonia Score in ED Patients With Community-Onset Pneumonia

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BACKGROUND: To guide rational antibiotic selection in community-onset pneumonia, we previously derived and validated a novel prediction tool, the Drug-Resistance in Pneumonia (DRIP) score. In 2015, the DRIP score was integrated into an existing electronic pneumonia clinical decision support tool (ePNa).

METHODS: We conducted a quasi-experimental, pre-post implementation study of ePNa with DRIP score (2015) vs ePNa with health-care-associated pneumonia (HCAP) logic (2012) in ED patients admitted with community-onset pneumonia to four US hospitals. Using generalized linear models, we used the difference-in-differences method to estimate the average treatment effect on the treated with respect to ePNa with DRIP score on broad-spectrum antibiotic use, mortality, hospital stay, and cost, adjusting for available patient-level confounders.

RESULTS: We analyzed 2,169 adult admissions: 1,122 in 2012 and 1,047 in 2015. A drug-resistant pathogen was recovered in 3.2% of patients in 2012 and 2.8% in 2015; inadequate initial empirical antibiotics were prescribed in 1.1% and 0.5%, respectively ($P = .12$). A broad-spectrum antibiotic was administered in 40.1% of admissions in 2012 and 33.0% in 2015 ($P < .001$). Vancomycin days of therapy per 1,000 patient days in 2012 were 287.3 compared with 238.8 in 2015 ($P < .001$). In the primary analysis, the average treatment effect among patients using the DRIP score was a reduction in broad-spectrum antibiotic use (OR, 0.62; 95% CI, 0.39-0.98; $P = .039$). However, the average effects for ePNa with DRIP on mortality, length of stay, and cost were not statistically significant.

CONCLUSIONS: Electronic calculation of the DRIP score was more effective than HCAP criteria for guiding appropriate broad-spectrum antibiotic use in community-onset pneumonia.

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KEY WORDS: antibiotic; antibiotic resistance; antimicrobial stewardship; health-care associated pneumonia

ABBREVIATIONS: ARR = absolute risk reduction; ATT = average treatment effect in the treated; CAP = community-acquired pneumonia; DRIP = Drug Resistance in Pneumonia; eCURB = electronic CURB-65; ePNa = electronic pneumonia clinical decision support tool; HCAP = health-care-associated pneumonia; MRSA = methicillin-resistant *Staphylococcus aureus*; PCR = polymerase chain reaction

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Previous research has demonstrated that guideline-concordant antibiotic regimens for community-acquired pneumonia (CAP) reduce mortality and length of stay.[1] Less is known, however, about the identification and appropriate treatment of patients at high risk of drug-resistant pathogens. The health-care-associated pneumonia (HCAP) criteria[2] have demonstrated poor specificity for predicting drug resistance.[3-5] Since the introduction of HCAP criteria in 2005, use of vancomycin and broad-spectrum gram-negative antibiotics such as piperacillin-tazobactam in pneumonia has doubled despite stable incidence of drug-resistant pathogens.[6-8] Paradoxically, outcomes among patients with HCAP are not improved with broad-spectrum antibiotics,[3,9] and some data suggest they are worse.[10-15]

In 2011, we deployed a web-based, real-time, electronic pneumonia clinical decision support tool, called ePNa that aids in diagnosis, uses an electronic CURB-65 (eCURB)[16] and other severity criteria to guide appropriate admission decisions, and makes antibiotic recommendations based on HCAP criteria. ePNa was made available to ED physicians at four Salt Lake County Intermountain Healthcare hospitals (Utah), allowing providers to opt-in to ePNa recommendations. We observed lower mortality in patients with CAP compared with three usual care, nearby Intermountain Hospital EDs. However, we found no improvement in outcomes of ED patients treated according to HCAP guideline recommendations.[11] In 2013, we derived and validated a novel method to predict drug resistance, the Drug-Resistance in Pneumonia (DRIP) score.[17] In October 2014, we reprogrammed ePNa to use the DRIP score as the basis for empirical antibiotic recommendations. ePNa logic was otherwise unchanged during the two study periods. Here, we report the impact of integrating the DRIP score into ePNa on broad-spectrum antibiotic use and clinical outcomes.

Methods

Study Design

We conducted a quasi-experimental, pre-post implementation study of the impact of redeploying ePNa after changing from HCAP logic (2012) to the DRIP score (2015).

Population

Using a previously validated *International Classification of Diseases, Ninth Revision* code-based strategy, plus additional patients for whom treating physicians completed ePNa,[11] we identified patients admitted to the hospital from the ED with community-onset pneumonia at four Salt Lake County Intermountain Healthcare hospitals during two study periods: ePNa with HCAP (December 1, 2011, to November 30, 2012) and ePNa with DRIP score (October 24, 2014, to September 30, 2015). During both study periods, there were two subgroups of patients: those for whom treating providers used ePNa, which we define as ePNa-HCAP and ePNa-DRIP, depending on the study period, and patients whose providers opted out of ePNa, defined hereafter as usual care patients.

Study investigators reviewed each patient's ED chest imaging radiology report independent of any other health information, excluding those without radiographic confirmation of pneumonia. All patient-level data were electronically captured from the Intermountain Healthcare enterprise data warehouse. Rare missing data were gathered by physician review of dictated notes.

DRIP Score

ePNA was programmed to calculate the DRIP score in real time via an automated query of the electronic health record for the 10 DRIP criteria (Table 1). Providers were able to manually edit criteria in the calculator if they determined the electronic health record data were not accurate or complete. During the study period, the DRIP score was not otherwise available to clinicians who chose not to use ePNa; HCAP criteria were widely recognized by clinicians during both study periods. For patients at low risk for drug-resistant bacteria (DRIP score < 4), ePNa recommended ceftriaxone plus azithromycin. For high-risk patients (DRIP score ≥ 4), ePNa recommended an antipseudomonal beta-lactam, plus vancomycin and azithromycin. Recommendations were modified for documented antibiotic allergy. Actual antibiotic prescribing was ultimately at the discretion of providers, both those opting to use ePNa and those providing usual care.

For patients with a DRIP score ≥ 4 and all patients admitted to an ICU, ePNa also recommended more extensive microbiologic workup.[18] Concurrent with the addition of the DRIP score, we added a recommendation in ePNa to order a nasal swab for methicillin-resistant *Staphylococcus aureus* (MRSA) polymerase chain reaction (PCR) (Cepheid) in patients with high DRIP scores to aid in de-escalation of empirical vancomycin when negative.[19]

Outcomes

The primary outcome was any broad-spectrum antibiotic use within 12 h after presentation to the ED (ie, antibiotics with anti-MRSA or antipseudomonal activity, excluding respiratory

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TABLE 1] Drug Resistance in Pneumonia Score

Factors	Points
Major risk factors	
Antibiotic use, prior 60 d	2
Long-term care resident	2
Tube feeding	2
History of infection with a drug-resistant pathogen (prior 12 mo)	2
Minor risk factors	
Hospitalization, prior 60 d	1
Chronic pulmonary disease	1
Poor functional status	1
Gastric acid suppression	1
Wound care	1
MRSA colonization (prior 12 mo)	1
Total points possible	14

MRSA = methicillin-resistant *Staphylococcus aureus*.

fluoroquinolones, which are also indicated for CAP). Data on total vancomycin use during the admission were also collected to calculate vancomycin usage. We measured usage based on the Centers for Disease Control and Prevention definition for days of therapy per 1,000 patient days, defined as the total number of inpatient calendar days during which any vancomycin had been administered per patient, divided by total inpatient days.[20] Secondary outcomes included 30-day all-cause mortality, hospital length of stay, and total direct cost. For microbiologic outcomes, we included bacteria compatible with a respiratory pathogen other than coagulase-negative staphylococci, *Neisseria* species, *Enterococcus* species, diphtheroids or other oral flora, or non-*Streptococcus pneumoniae* alpha-hemolytic streptococci, except in the setting of putrid lung abscess or empyema. Specimens included cultures of blood, sputum meeting laboratory inclusion criteria, tracheal aspirate, BAL fluid, and pleural fluid. We did not include blood cultures if an extrapulmonary source was more likely. We also included urinary antigen tests for *Legionella pneumophila* and *S pneumoniae*, serologic testing for *Mycoplasma pneumoniae*, and PCR film array for *M pneumoniae* and *Chlamydophila pneumoniae*. Bacteria were defined as drug-resistant pathogens if resistant to CAP guideline-recommended antibiotics (eg, third-generation cephalosporins, respiratory fluoroquinolones). Inadequate initial empirical antibiotic spectrum was defined if any identified respiratory pathogen was outside the spectrum of administered antibiotics.

Analyses

Because some providers likely opted out of ePNa for sicker patients, we recognized the possibility of indication bias in the comparison of ePNa with DRIP score vs usual care, for which we might not be able to sufficiently control. For the primary and secondary analyses, we therefore used the difference-in-differences method[21] to estimate the average treatment effect in the treated (ATT)[22] for DRIP-ePNa. This was done by estimating the temporal change in outcome between patients in ePNa-HCAP and ePNa-DRIP groups and subtracting the temporal change in outcome between patients in the usual care groups. For these analyses, we selected appropriate interaction terms within generalized linear models using binomial distributions with logit link functions for binary outcomes (broad-spectrum antibiotics, mortality) and gamma distributions with log link functions for positive, numerical outcomes (length of stay, total cost). As sensitivity analyses, we also fit multilevel/hierarchical models using generalized linear mixed models with provider-level random intercepts to account for provider variability in overall broad-spectrum use rates.

Because broad-spectrum antibiotic prescribing decisions are known to be influenced by severity, ED busyness (ratio of ED patients to physicians immediately before ED admission),[23] and HCAP criteria, we chose to include the following patient-level confounders in the multivariable regression for the primary analysis: ED busyness, number of minor severe CAP criteria present,[24] and binary indicators of intubation, vasopressors, and HCAP. For the secondary outcomes, we included eCURB, Pao_2/Fio_2, and binary indicators of sex, pleural effusion, and HCAP as adjustor variables in the regression models. Pao_2/Fio_2 was calculated for all patients, using a previously validated method to calculate from Spo_2 when arterial blood gas was not available.[25] Simple two-way comparisons were conducted using Pearson χ^2 or Fisher exact test for categorical variables and the Wilcoxon rank-sum test for continuous variables. Hypothesis tests were two-tailed, significant if $P \leq .05$.

We calculated the test performance characteristics of the DRIP score to predict the recovery of a drug-resistant pathogen at various scoring thresholds in ePNa-DRIP group, and we also calculated test performance analysis in the subgroup of patients who received complete microbiologic testing (eg, patients who underwent all of the following: blood culture, an appropriate respiratory culture, and urine antigen testing). Sensitivity, specificity, and predictive values were calculated using a conventional 2 × 2 table. The percent of patients who would have received inadequate therapy had DRIP score recommendations been followed strictly was calculated by summing the patients with a DRIP score at each cut point in whom a drug-resistant pathogen was recovered. Likewise, the percent of patients who would have received broad-spectrum antibiotics under strict DRIP score recommendations was calculated as all patients with a DRIP score at each cut point. The area under the receiver operator characteristic curve was calculated by plotting the DRIP score for each patient in each group against whether or not a drug-resistant pathogen was recovered.

We assessed calibration of binomially distributed models with a calibration plot and discrimination per receiver operating characteristics. Diagnostics for gamma-distributed models were assessed by interpreting quantile-quantile plots. Diagnostics of the primary model appeared well calibrated. Diagnostics of the secondary models were mixed. Calibration of the mortality model suggested overpredicting mortality among the sickest patients. Both the primary and mortality models had reasonable discriminatory ability, each with about 75% area under the curve. The quantile-quantile plots of the length of stay and cost models indicated right-skewed residuals and the cost model had higher residual variance, resulting from a handful of extreme observations.

Statistical analyses were conducted using R version 3.5.1 (The R Foundation) unless otherwise noted. Approval for the study was granted by the institutional review board of Intermountain Healthcare (study 1050074).

Results

We observed 2,169 patients, 1,122 in ePNa with HCAP logic period (2012) and 1,047 in ePNa with DRIP score period (2015). Demographic data and clinical characteristics of the two periods are displayed in Table 2. The two cohorts had similar eCURB mean predicted 30-day mortality (5.9% vs 6.1%), vasopressor use (5.1% vs 6.6%), and mechanical ventilation (5.6% vs 7.4%), respectively. Fewer patients met HCAP criteria in 2012 (15.3%) than in 2015 (20.8%). Local influenza incidence was 4.16 per 10,000 in 2012 vs 4.99 per 10,000 in 2015.[26] ED clinicians used ePNa for 73.4% of patients in 2012 and for 71.3% of patients in 2015. There were some differences in severity between usual care and ePNa cohorts during both study intervals (Table 3).

TABLE 2] Demographics and Clinical Characteristics by Year

Characteristics	2012 (HCAP Logic) (n = 1,122)	2015 (DRIP Score) (n = 1,047)
Age, y	65 (51-79)	67 (54-78.5)
Female	589 (52.5)	530 (50.6)
Charlson Comorbidity Index score	3 (1-4)	3 (2-5)
Diabetes mellitus	436 (40.9)	384 (40.9)
COPD	696 (65.4)	657 (69.9)
Congestive heart failure	399 (37.5)	350 (37.2)
Cognitive impairment	60 (5.6)	48 (5.1)
Renal disease	290 (27.2)	295 (31.4)
HCAP	172 (15.3)	218 (20.8)
eCURB, mean % predicted 30-d mortality ± SD	5.9 ± 9	6.1 ± 8.5
Vasopressor use	57 (5.1)	69 (6.6)
Intubation	63 (5.6)	78 (7.4)
Pleural effusion	288 (25.7)	244 (23.3)
Severe CAP minor criteria	1 (1-2)	2 (1-3)
Respiratory rate ≥ 30 breaths/min	122 (10.9)	122 (11.7)
Pa_{O_2}:F_{IO_2} ratio	260.5 (215.7-319.1)	260.5 (201.9-303.8)
Multilobar infiltrates	486 (43.3)	521 (49.8)
Confusion	135 (12.0)	71 (6.8)
BUN ≥ 20 mg/dL	581 (51.8)	508 (48.5)
WBC count < 4,000/mm^3	32 (2.9)	33 (3.2)
Platelet count < 100,000/mm^3	42 (3.7)	56 (5.3)
Hypothermia (temperature < 36°C)	151 (13.5)	123 (11.7)
Systolic BP < 90 mm Hg	49 (4.4)	55 (5.3)
ePNa tool use	824 (73.4)	746 (71.2)
Any broad-spectrum antibiotic	450 (40.1)	345 (33.0)
Antipseudomonal beta-lactam	334 (29.8)	219 (20.9)
Anti-MRSA	390 (34.8)	308 (29.4)
Vancomycin DOT	3 (2-4)	2 (1-4)
Vancomycin, DOT/1,000 patient days	287.3	238.8
Inadequate initial empirical antibiotic spectrum	12 (1.1)	5 (0.5)
Length of stay, d	2.9 (1.8-4.8)	3.0 (1.9-9.5)
30-d all-cause mortality	91 (8.1)	104 (9.9)
Clostridioides difficile infection	14 (1.2)	14 (1.3)
Total cost (thousands)	$6.9 ($4.4-$13.2)	$7.5 ($4.9-$13.9)

Values are No. (%), median (25%-75% interquartile range), or as otherwise indicated. CAP = community-acquired pneumonia; DOT = days of (antibiotic) therapy per 1,000 patient days; DRIP = Drug Resistance in Pneumonia; eCURB = electronic CURB-65; ePNa = electronic pneumonia clinical decision support tool; HCAP = health-care-associated pneumonia. See Table 1 legend for expansion of other abbreviation.

TABLE 3] Selected Clinical Data by Usual Care and ePNa Use for Each Time Period

Characteristic	2012 Usual Care (n = 298)	2012 ePNa (n = 824)	2015 Usual Care (n = 301)	2015 ePNa (n = 746)
Age, y	67 (54-81)	64.5 (50-78)	66 (51-78)	68 (54.2-79)
Female	159 (53.4)	430 (52.2%)	159 (52.8)	371 (49.7)
Charlson Comorbidity Index score	3 (2-5)	3 (1-4)	3 (2-5)	3 (2-5)
Vasopressors	32 (10.7)	25 (3)	26 (8.6)	43 (5.8)
Intubation	36 (12.1)	27 (3.3)	47 (15.6)	31 (4.2)
Pao_2:Fio_2	256.4 (207.7-319.1)	264.2 (220.9-319.1)	244.8 (190.5-303.8)	260.5 (210.4-303.8)
Severe CAP minor criteria	2 (1-3)	1 (1-2)	2 (1-3)	1 (1-2)
HCAP	60 (20.1)	112 (13.6)	52 (17.3)	166 (22.3)

Values are No. (%), median (25%-75% interquartile range), or as otherwise indicated. See Table 2 legend for expansion of abbreviations.

In the overall cohort, blood cultures were obtained in 84.0% of patients, a laboratory-acceptable respiratory culture in 31.2%, and urine antigen testing in 41.3%. A bacterial pathogen was identified in 12.7% of admissions in 2012 and 15.8% of admissions in 2015 (see Table 4 for microbiology results). A drug-resistant pathogen was recovered from 3.2% of patients in 2012 and 2.8% of patients in 2015. Inadequate initial empirical antibiotics were prescribed in 1.1% of patients in 2012 compared with 0.5% of patients in 2015 ($P = .12$). Among all patients with a microbiologic diagnosis, inadequate initial empirical antibiotics were associated with increased mortality (6/17 [35.3%] vs 51/296 [17.2%]) and did not differ significantly between years (4/12 in 2012, 2/5 in 2015, $P > .99$).

An initial broad-spectrum antibiotic was administered in 40.1% of admissions in 2012 vs 33.0% of admissions in 2015 (absolute risk reduction [ARR], 7.2%; 95% CI, 3.1-11.2; $P < .0001$). Antipseudomonal therapy was prescribed in 29.8% of 2012 patients vs 20.9% of 2015 patients (ARR, 8.9%; 95% CI, 5.2-12.5; $P < .0001$), and anti-MRSA therapy decreased from 34.8% in 2012 to 29.4% in 2015 (ARR, 5.3%; 95% CI, 1.4%-9.2%; $P = .01$). Compared with vancomycin, linezolid comprised only a fraction (3.6% in 2012 and 2.9% in 2015) of anti-MRSA therapy. Total vancomycin days of therapy per 1,000 patient days were 287.3 in 2012 vs 238.8 in 2015 (ARR, 16.9%; $P < .001$).

In the primary analysis (Table 5), the average treatment effect on the treated for ePNa-DRIP patients was to reduce broad-spectrum antibiotic prescription (OR, 0.62; 95% CI, 0.39-0.98; $P = .039$). In the secondary analyses, the ATT estimates for ePNa-DRIP for mortality (OR, 0.84; 95% CI, 0.43-1.6; $P = .59$), length of stay (OR, 0.98; 95% CI, 0.82-1.2; $P = .81$), and cost (OR, 0.93; 95% CI, 0.75-1.1; $P = .47$) were not statistically significant.

In 2015, an admission nasal swab for MRSA PCR was performed in 120 patients (11.5%). Median time to result was 4.2 h (25%-75% interquartile range, 2.1-22.5). Anti-MRSA antibiotics were discontinued within 24 h in 74.6% of patients with a negative result, with 29.8% of these receiving only a single dose in the ED. Overall median time to anti-MRSA de-escalation was 20.8 h (25%-75% interquartile range, 9.4-27.6).

In ePNa-DRIP patients for whom the DRIP score was calculated, test performance characteristics for predicting drug-resistant pathogens are displayed in Table 6. A scoring cut point of ≥ 4 optimized sensitivity (70.6) and specificity (82.2), with positive and negative predictive values of 8.4 and 99.2, respectively, and an area under the receiver operating characteristic curve of 0.79 (95% CI, 0.65-0.93). In this group, where prevalence of drug resistance was 2.3%, the predicted rate of inadequate treatment had prescribing strictly followed ePNa recommendations was 0.66% (95% CI, 0.24-1.6), whereas predicted broad-spectrum use was 18.9% (95% CI, 16.3-21.9). In a subgroup of patients for whom a complete microbiologic workup was performed, sensitivity was 85.7 and specificity 73.9 at the ≥ 4 cut point (Table 6).

Discussion

The DRIP score is a cumulative, probabilistic model for predicting risk of pneumonia because of drug-resistant pathogens based on well-established host risk factors. In

TABLE 4] Microbiology Results

Result	2012	2015
Bacterial pathogen identified	140 (12.5)	164 (15.8)
Drug-resistant pathogens	35 (3.1)	29 (2.8)
MRSA	16 (1.4)	15 (1.4)
Resistant gram-negative organisms	21 (1.9)	15 (1.4)
Gram positive		
Streptococcus pneumoniae	74	62
Staphylococcus aureus	36	39
Methicillin-sensitive	20	24
MRSA	16	15
Viridans streptococci	2	13
Group A beta-hemolytic streptococcus	3	5
Group B beta-hemolytic streptococcus	0	2
Group F beta-hemolytic streptococcus	0	2
Gram negative		
Pseudomonas aeruginosa	11	8
Haemophilus influenzae	8	6
Haemophilus species	2	6
Escherichia coli	9	5
Klebsiella pneumoniae	4	5
Klebsiella oxytoca	0	1
Proteus mirabilis	0	4
Enterobacter aerogenes	1	2
Enterobacter cloacae	1	2
Stenotrophomonas maltophilia	1	2
Roseomonas species	0	1
Achromobacter xylosoxidans	0	1
Serratia marcescens	0	1
Citrobacter koseri	0	1
Morganella morganii	1	0
Moraxella catarrhalis	1	1
Capnocytophaga canimorsus	0	1
Pasteurella multocida	0	1
Neisseria meningitidis	0	1
Fusobacterium species	0	2
Atypical		
Mycoplasma pneumoniae	0	7
Legionella pneumophila	3	3
Chlamydophila pneumoniae	0	1

Values are No. (%) or No. See Table 1 legend for expansion of abbreviation.

an observational validation cohort of patients with a microbiologic etiology identified, we previously showed that DRIP score more effectively differentiated high and low probability of drug-resistant pathogens than HCAP criteria.[17] In this prospective, electronic DRIP score implementation in a multicenter ED population, we now report effective reduction in broad-spectrum antibiotic prescribing.

Similar to other reported US trends, broad-spectrum antibiotic use was very common in our cohort, and 10-fold higher than the incidence of drug-resistant pathogens. These results underscore a general tendency of clinicians to overestimate the risk of antibiotic resistance in pneumonia and reflect consequences of the HCAP guidelines on practice. This is of particular importance considering that unnecessary antibiotics are associated with increased cost,[10,27] length of stay,[10,28,29] drug toxicity,[30-33] *Clostridioides difficile* infection,[34] disruption of the microbiome,[35] and resistance.[36] Better methods of predicting drug-resistant pathogens while limiting unnecessary use of extended-spectrum antibiotics are needed.

When integrated into an existing ePNa, and after accounting for temporal trends, the DRIP score significantly decreased broad-spectrum antibiotic utilization compared with ePNa containing HCAP logic. This corroborates observations made in a previous implementation study in a different center,[37] and confirms the improved specificity of DRIP score compared with HCAP criteria. Despite this, predicted unnecessary broad-spectrum use data (18.9% vs actual use of 33%) suggest that the reduction would be greater had clinicians followed the tool recommendations explicitly. As with any stewardship intervention, this is likely to improve with more provider education and

TABLE 5] Generalized Linear Regression Model for the Average Treatment Effect Among ePNA-DRIP on Broad-Spectrum Antibiotic Use

Variable	OR	95% CI	*P* Value
ePNA with DRIP implementation	0.62	0.39-0.98	.039
ePNA tool use	1.47	1.08-2.02	.015
2015	0.8	0.54-1.17	.25
ED busyness	1.03	0.93-1.13	.556
Intubation	2.26	1.4-3.66	< .001
Vasopressors	4.9	2.93-8.46	< .001
Severe CAP minor criteria	1.31	1.2-1.43	< .001
HCAP	7.79	6.0-10.17	< .001

See Table 2 legend for expansion of abbreviations.

familiarity. Initial broad-spectrum gram-negative antibiotic use decreased more than anti-MRSA therapy (8.9% vs 5.3%, respectively), but coupling the DRIP score with an MRSA nasal swab PCR-guided de-escalation strategy produced additional reductions in anti-MRSA therapy (16.9% reduction in total vancomycin days of [antibiotic] therapy per 1,000 patient days) after the initial ED dose.

Reductions in broad-spectrum antibiotic use were accompanied by a reduction in inadequate initial empirical therapy, an important point considering that inadequate initial therapy was associated with increased crude mortality in this cohort. Although secondary outcomes were not statistically significant, the directionality did not suggest harm. However, definitively measuring the effect on clinical outcomes would require a much larger sample size. For example, to estimate the minimum sufficient sample size to achieve 80% power for the ATT effect on mortality, we computed a post hoc power analysis using 10,000 iterations of bootstrapped Monte Carlo simulations and estimated that as many as 44,000 patients might be needed to demonstrate efficacy on mortality, assuming our data are representative of the larger population.

Although the DRIP score is now available for manual calculation on other web-based platforms,[38] calculation is facilitated by electronic capture of criteria. However, even within ePNa, the DRIP score still requires clinician review to add elements not available in the electronic medical record (eg, nonprescription proton pump inhibitors). Although some of the observed use of broad-spectrum antibiotics use in this study was attributable to ED physicians opting not to use ePNa (and therefore the DRIP score), additional broad-spectrum use beyond DRIP recommendations is likely because of reluctance to use CAP-guideline concordant therapy in patients with severe pneumonia despite data suggesting that severity alone is not a predictor of drug-resistant bacterial pneumonia.[39,40]

The primary limitation of this study was confounding by indication, a limitation of any study in which treatment choice depends partially on factors related to the outcome. This meant that we could not measure the unbiased effect of DRIP score implementation in the full population. Although the difference-in-differences approach allowed us to measure the average treatment effect on the treated (ie, the effect only among patients treated using ePNA with DRIP score), we were unable to assess the unbiased effect of ePNa with DRIP score

TABLE 6] Test Performance Characteristics in Patients for Whom DRIP Score Was Calculated

2015 ePNa-DRIP	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
All patients (N = 740, DRP prevalence 2.3%)				
Cut point ≥ 3 points	82.2 (55.8-95.3)	54.4 (50.7-58.0)	4.0 (2.3-6.8)	99.3 (97.7-99.8)
Cut point ≥ 4 points	70.6 (44.0-88.6)	82.3 (79.3-84.9)	8.4 (4.6-14.5)	99.2 (98.0-99.7)
Full microbiologic workup (n = 194, DRP prevalence 7.2%)				
Cut point ≥ 3 points	85.7 (56.2-97.5)	63.9 (56.4-70.8)	15.6 (8.7-26.0)	98.3 (93.3-99.7)
Cut point ≥ 4 points	85.7 (56.2-97.5)	73.9 (66.7-80.0)	20.3 (11.4-33.2)	98.5 (94.2-99.7)

DRP = drug-resistant pathogen; NPV = negative predictive value; PPV = positive predictive value. See Table 2 legend for expansion of other abbreviations.

vs usual care, the counterfactual of perhaps greater interest to the clinician. Although a cluster randomized controlled trial with mandatory tool use by clinicians would potentially solve this limitation, such a study is not feasible.

Conclusions

Electronic implementation of DRIP score reduced initial empirical broad-spectrum antibiotic use without increasing inadequate empirical antibiotic therapy or mortality. When coupled with a MRSA nasal swab PCR-based strategy for de-escalation, reduction in overall vancomycin use was realized. Compared with HCAP criteria, the DRIP score is a more effective tool to assist clinicians in accurately identifying the risk of drug-resistant pathogens in pneumonia. Nevertheless, significant opportunities for improvement remain to reduce unnecessary antibiotic use in pneumonia. We plan to reexamine broad-spectrum antibiotic use in the same four EDs 3 years after DRIP deployment, hypothesizing that further reductions will be detected after both the DRIP score and MRSA nasal swab strategies are more familiar to clinicians. Further evaluation of DRIP score in other EDs with varying patient demographics and resistance patterns is warranted.

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