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# Antimicrobial Activity of Ceftaroline and Comparator Agents Against Ceftriaxone-Nonsusceptible *Streptococcus pneumoniae* from the United States (2008–2020)

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We evaluated the activity of ceftaroline against clinical isolates of ceftriaxone-nonsusceptible *Streptococcus pneumoniae* from United States medical centers. *Streptococcus pneumoniae* isolates ($n = 21,750$) were consecutively collected from 201 medical centers in 2008–2020 and tested for susceptibility by broth microdilution method. Among these isolates, 1,419 (6.5%) were ceftriaxone-nonsusceptible (ceftriaxone minimum inhibitory concentration [MIC], ≥2 mg/L). Other resistant subgroups analyzed included multidrug-resistant (MDR; nonsusceptibility to ≥3 classes of agents; $n = 4,454$) and extensively drug-resistant (XDR; nonsusceptibility to ≥5 classes; $n = 1,708$) isolates. Ceftriaxone susceptibility increased from 89.0% (2008–2011) to 98.1% (2018–2020). Ceftaroline was active against 99.9% of ceftriaxone-nonsusceptible isolates ($MIC_{50/90}$, 0.25/0.25 mg/L) and retained potent activity against MDR ($n = 4,454$; $MIC_{50/90}$, 0.12/0.25 mg/L; >99.9% susceptible) and XDR ($n = 1,708$; $MIC_{50/90}$, 0.25/0.25 mg/L; 100.0% susceptible) isolates. Only one isolate had a ceftaroline MIC ≥0.5 mg/L. In summary, ceftaroline demonstrated potent and consistent activity over time (2008–2020) against a large collection of *S. pneumoniae* from U.S. medical centers, including ceftriaxone-nonsusceptible, MDR, and XDR isolates

**Keywords:** Pneumococo, PCV, cephalosporin, MDR, ceftaroline, ceftriaxone

## Introduction

*Streptococcus pneumoniae* is a major cause of community-acquired bacterial pneumonia (CABP), meningitis, sepsis, bacteremia, sinusitis, and otitis media in the United States and worldwide. Although the implementation of pneumococcal conjugate vaccines (PCVs) has led to the reduction of pneumococcal resistance to most antimicrobial agents commonly used to treat invasive pneumococcal infections,[1,2] the treatment of infections caused by multidrug-resistant (MDR) *S. pneumoniae* remains a challenge for existing antibacterial agents.[3] Thus, surveillance programs remain important to continue to assess how new and established antibacterial agents perform against MDR subsets of *S. pneumoniae*.[4]

Ceftaroline fosamil is a parenteral prodrug hydrolyzed *in vivo* to release the active agent ceftaroline. Ceftaroline displays broad-spectrum *in vitro* activity against *S. pneumoniae*, including penicillin-resistant and MDR isolates.[4,5] The superior activity of ceftaroline against isolates with elevated minimum inhibitory concentrations (MICs) to other β-lactams has been attributed to its high affinity for the altered penicillin-binding protein (PBPs) targets (PBP-1A, -2B, and -2X) that are associated with β-lactam resistance in *S. pneumoniae*.[6,7] Ceftaroline fosamil is approved by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for the treatment of CABP and acute bacterial skin and skin structure infection (ABSSSI) in adults and children (2 months of age and older for CABP in the United States), including ABSSSI caused by methicillin-resistant *Staphylococcus aureus* (MRSA).[8]

The Assessing Worldwide Antimicrobial Resistance Evaluation (AWARE) Program has monitored ceftaroline activity against bacterial organisms in U.S. medical centers since 2008.[4,5] The aim of the present report is to describe the activity of ceftaroline and comparator agents against ceftriaxone-nonsusceptible *S. pneumoniae* collected from North American medical centers participating in the AWARE Program from 2008 to 2020.

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A total of 21,750 isolates of *S. pneumoniae* were collected from 201 medical centers that participated in the AWARE Program during 2008 to 2020. The number of medical centers recruited each year varied during the 13-year period of the AWARE Program evaluated in this study. A minimum of 30 medical centers were recruited every year and additional centers (20–120 per year) were recruited in 2009–2017. Each participant center was requested to provide 35 unique, consecutive isolates (a single isolate per patient) *S. pneumoniae* isolates collected from patients with community-acquired respiratory tract infections each year. Moreover, each center collected 60–100 consecutive isolates causing bloodstream infections, from any species, and *S. pneumoniae* isolates were included in this investigation. Only isolates deemed clinically relevant by the submitting laboratory were included (one isolate per patient infectious episode). Isolates were submitted to the central monitoring laboratory (JMI Laboratories, North Liberty, IA) for identification by matrix-assisted laser desorption/ionization, optochin test, and bile solubility and for susceptibility testing by broth microdilution method. Among these isolates, 1,419 (6.5%) were ceftriaxone nonsusceptible (MIC, ≥2 mg/L).

Broth microdilution tests were conducted at the central reference laboratory according to Clinical and Laboratory Standards Institute (CLSI) methods to determine the susceptibility of these isolates to ceftaroline and comparator antimicrobial agents.[9] Validated MIC panels were manufactured at JMI Laboratories (2015–2020) or by Thermo Fisher Scientific (2008–2014) (Cleveland, OH). *Streptococcus pneumoniae* isolates were tested in cation-adjusted Mueller-Hinton broth supplemented with 2.5–5% lysed horse blood according to the CLSI M07 document.[10] The quality control strain *S. pneumoniae* ATCC 49619 was tested concurrently with clinical isolates.

Susceptibility determinations and the quality assurance of MIC results were based on CLSI guidelines. CLSI and European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoint criteria published in 2021 were applied for ceftaroline and comparator agents for the entire collection of organisms independent of the year the organism was isolated. Both CLSI and EUCAST breakpoints can be applied for interpretation of the results since CLSI and EUCAST recommendations for testing *S. pneumoniae* isolates by broth microdilution are identical.[9,11]

MDR status was determined based on the nonsusceptibility of an isolate to ≥3 classes of the following antimicrobial agents: penicillin (MIC, ≥4 mg/L), ceftriaxone (MIC, ≥2 mg/L), erythromycin (MIC, ≥0.5 mg/L), clindamycin (MIC, ≥0.5 mg/L), levofloxacin (MIC, ≥4 mg/L), tetracycline (MIC, ≥2 mg/L), and trimethoprim-sulfamethoxazole (MIC, ≥1 mg/L). Extensively drug-resistant (XDR) status was determined based on an isolate's nonsusceptibility to ≥5 classes as described by Golden *et al.*[12]

Ceftaroline was active against 99.9% of ceftriaxone-nonsusceptible *S. pneumoniae* at the CLSI and U.S. FDA susceptible breakpoint of ≤0.5 mg/L ($MIC_{50/90}$, 0.25/0.25 mg/L); only one isolate had a ceftaroline MIC >0.5 mg/L (Table 1). The ceftaroline-nonsusceptible strain was isolated in Texas in 2014 and has been described previously.[13] This Texas isolate was MDR, with MIC values of 1 mg/L for ceftaroline, 8 mg/L for penicillin and ceftriaxone, 8 mg/L for erythromycin, >4 mg/L for trimethoprim–sulfamethoxazole, >8 mg/L for amoxicillin–clavulanate, and 1 mg/L for meropenem. A molecular characterization of the isolate showed multiple substitutions in the PBPs, mainly PBP2X, compared with reference sequences. Additionally, it showed 31 amino acid alterations in MurM.[13] Moreover, 91.3% of ceftriaxone-nonsusceptible isolates were inhibited at ≤0.25 mg/L of ceftaroline, which is the EUCAST susceptible breakpoint.

Linezolid ($MIC_{50/90}$, 0.5/1 mg/L), vancomycin ($MIC_{50/90}$, 0.25/0.5 mg/L), and meropenem (only as per EUCAST criteria for indications other than meningitis; $MIC_{50/90}$, 1/1 mg/L) showed complete activity (100.0% susceptible; Table 1). Levofloxacin was active against 98.1% of isolates ($MIC_{50/90}$, 1/1 mg/L) as per CLSI and U.S. FDA criteria, whereas tigecycline was active against 95.5% as per U.S. FDA criteria; all other compounds tested were active against ≤17.7% of isolates as per CLSI, U.S. FDA, or EUCAST criteria (Table 1). Ceftriaxone-nonsusceptible isolates exhibited high resistance rates to amoxicillin–clavulanate ($MIC_{50/90}$, >4/>4 mg/L; 86.7% resistance as per CLSI), azithromycin ($MIC_{50/90}$, >4/>4 mg/L; 98.2% resistance per CLSI), doxycycline ($MIC_{50/90}$, >1/> 1 mg/L; 88.1% resistance as per CLSI), and meropenem ($MIC_{50/90}$, 1/1 mg/L; 82.1% resistance as per CLSI; Table 1).

Ceftriaxone susceptibility rates varied from 86.9% in 2009 to 98.8% in 2019 and increased from 89.0% in 2008–2011 to 98.1% in 2018–2020 (Fig. 1 and Supplementary Fig. S1). Similarly, amoxicillin–clavulanate susceptibility rates increased from 82.4% in 2008–2011 to 96.1% in 2018–2020 (Fig. 1). To evaluate if these results could have been affected by the fact that some medical centers did not participate during the entire period of the study, we recalculated ceftriaxone and amoxicillin-clavulanate susceptibility rates in these two periods (2008–2011 and 2018–2020) using only data from medical centers that participated in both periods. The results were similar and indicated that susceptibility to ceftriaxone increased from 90.0% to 98.2% and susceptibility to amoxicillin–clavulanate increased from 83.3% to 96.2% (data not shown).

Overall, 20.5% of isolates were MDR and 7.9% were XDR. MDR and XDR rates decreased from 24.4% and 13.5% in 2008–2011 to 16.8% and 2.4% in 2018–2020, respectively (Fig. 2). Ceftaroline retained potent activity against MDR ($MIC_{50/90}$, 0.12/0.25 mg/L; >99.9% susceptible as per CLSI and U.S. FDA) and XDR ($MIC_{50/90}$, 0.25/0.25 mg/L; 100.0% susceptible as per CLSI and U.S. FDA) isolates. Ceftriaxone exhibited limited activity against both MDR ($MIC_{50/90}$, 1/2 mg/L; 68.9% susceptible as per CLSI) and XDR ($MIC_{50/90}$, 2/2 mg/L; 26.7% susceptible as per CLSI) isolate subsets (Table 1). Amoxicillin–clavulanate also showed limited activity against MDR ($MIC_{50/90}$, 0.25/>4 mg/L; 55.9% susceptible as per CLSI) and XDR ($MIC_{50/90}$, >4/>4 mg/L; 3.8% susceptible as per CLSI) isolate subsets. Levofloxacin and tigecycline retained good activity against MDR and XDR isolates with >95% susceptibility as per CLSI and/or U.S. FDA criteria (Table 1).

The AWARE Surveillance Program has been monitoring the *in vitro* activity of ceftaroline and comparator antimicrobial agents against *S. pneumoniae* and other bacterial pathogens collected from episodes of community-acquired respiratory tract infection, health care-associated pneumonia, bloodstream infections, and other infection types

Table 1. Antimicrobial Activity of Ceftaroline and Comparator Agents Against Ceftriaxone-Nonsusceptible, Multidrug-Resistant, and Extensively Drug-Resistant *Streptococcus pneumoniae* from North American Medical Centers (2008–2020)

| | | *MIC (mg/L)* | | *CLSI*[a] | | | *EUCAST*[a] | | |
|---|---|---|---|---|---|---|---|---|---|
| *Antimicrobial agent* | *No. of isolates* | $MIC_{50}$ | $MIC_{90}$ | *%S* | *%I* | *%R* | *%S* | *%I* | *%R* |
| Ceftriaxone-nonsusceptible | | | | | | | | | |
| Ceftaroline | 1,419 | 0.25 | 0.25 | 99.9 | | | 91.3 | | 8.7 |
| Ceftriaxone | 1,419 | 2 | >2 | 0.0[b] | 84.8[b] | 15.2[b] | 0.0[b] | 84.8 | 15.2[b] |
| | | | | 0.0[c] | 0.0[c] | 100.0[c] | 0.0[c] | | 100.0[c] |
| Amox–clav (2:1 ratio) | 1,418 | >4 | >4 | 7.3 | 6.0 | 86.7 | [d] | [d] | 97.9 |
| Azithromycin[e] | 558 | >4 | >4 | 1.1 | 0.7 | 98.2 | 0.0 | 0.2 | 99.8 |
| Clindamycin | 1,418 | >2 | >2 | 17.3 | 0.4 | 82.3 | 17.7 | | 82.3 |
| Doxycycline | 1,122 | >1 | >1 | 11.2 | 0.6 | 88.1 | 12.4 | 4.0 | 82.5 |
| Erythromycin | 1,419 | >16 | >16 | 1.9 | 0.1 | 98.0 | 1.9 | 0.1 | 98.0 |
| Levofloxacin | 1,419 | 1 | 1 | 98.1 | 0.3 | 1.6 | [f] | 98.1 | 1.9 |
| Linezolid | 1,418 | 0.5 | 1 | 100.0 | | | 100.0 | | 0.0 |
| Meropenem[g] | 1,209 | 1 | 1 | 2.5 | 15.5 | 82.1 | 100.0[b] | | 0.0[b] |
| | | | | | | | 2.5[c] | | 97.5[c] |
| Penicillin | 1,415 | 4 | >4 | 10.2[b] | 78.7[b] | 11.1[b] | 0.0[b] | 10.2[b] | 89.8[b] |
| | | | | 0.0[c] | | 100.0[c] | 0.0[c] | | 100.0[c] |
| Tetracycline | 1,418 | >4 | >4 | 10.0 | 0.1 | 89.9 | 10.0 | 0.1 | 89.9 |
| Tigecycline | 1,407 | 0.03 | 0.06 | 95.5[f] | | | | | |
| TMP–SMX | 1,419 | >4 | >4 | 3.0 | 1.7 | 95.3 | 3.7 | 0.9 | 95.3 |
| Vancomycin | 1,419 | 0.25 | 0.5 | 100.0 | | | 100.0 | | 0.0 |
| MDR | | | | | | | | | |
| Ceftaroline | 4,454 | 0.12 | 0.25 | >99.9 | | | 97.2 | | 2.8 |
| Ceftriaxone | 4,454 | 1 | 2 | 68.9[b] | 19.4[b] | 4.7[b] | 49.4[b] | 45.9[b] | 4.7[b] |
| | | | | 49.4[c] | 26.4[c] | 31.1[c] | 49.4[c] | | 50.6[c] |
| Amox–clav (2:1 ratio) | 4,451 | 0.25 | >4 | 55.9 | 6.4 | 37.7 | | | 49.7 |
| Azithromycin[e] | 2,198 | >4 | >4 | 0.5 | 0.6 | 98.9 | 0.1 | 0.2 | 99.6 |
| Clindamycin | 4,452 | >1 | >1 | 20.6 | 1.3 | 78.1 | 21.9 | | 78.1 |
| Doxycycline | 2,856 | >1 | >1 | 6.6 | 0.6 | 92.8 | 8.5 | 3.7 | 85.0 |
| Erythromycin | 4,454 | >16 | >16 | 0.2 | | 99.4 | 0.2 | 0.4 | 99.4 |
| Levofloxacin | 4,453 | 1 | 1 | 97.4 | 0.2 | 2.4 | [f] | 97.4 | 2.6 |
| Linezolid | 4,452 | 0.5 | 1 | 100.0 | | | 100.0 | | 0.0 |
| Meropenem[g] | 3,756 | 0.5 | 1 | 49.9 | 14.0 | 36.1 | 100.0[b] | | 0.0[b] |
| | | | | | | | 49.9[c] | | 50.1[c] |
| Penicillin | 4,454 | 1 | 4 | 60.3[b] | 40.5[b] | 3.7[b] | 10.5[b] | 49.8[b] | 39.7[b] |
| | | | | 10.5[c] | | 89.5[c] | 10.5[c] | | 89.5[c] |
| Tetracycline | 4,451 | >4 | >4 | 5.1 | 0.4 | 94.6 | 5.1 | 0.4 | 94.6 |
| Tigecycline | 4,427 | 0.03 | 0.06 | 96.9[f] | | | | | |
| TMP–SMX | 4,453 | >2 | >2 | 22.7 | 20.0 | 57.4 | 32.1 | 10.6 | 57.4 |
| Vancomycin | 4,454 | 0.25 | 0.5 | 100.0 | | | 100.0 | | 0.0 |
| XDR (1,708) | | | | | | | | | |
| Ceftaroline | 1,708 | 0.25 | 0.25 | 100.0 | | | 94.3 | | 5.7 |
| Ceftriaxone | 1,708 | 2 | 2 | 26.7[b] | 25.1[b] | 10.0[b] | 1.6[b] | 88.4[b] | 10.0[b] |
| | | | | 1.6[c] | 63.3[b] | 73.3[c] | 1.6[c] | | 98.4[c] |
| Amox–clav (2:1 ratio) | 1,707 | >4 | >4 | 3.8 | 6.8 | 89.4 | [d] | [d] | 98.6 |
| Azithromycin[e] | 714 | >4 | >4 | 0.3 | 0.3 | 99.4 | 0.1 | 0.1 | 99.7 |
| Clindamycin | 1,708 | >2 | >2 | 5.0 | 0.5 | 94.5 | 5.5 | | 94.5 |
| Doxycycline | 1,300 | >2 | >2 | 1.8 | 0.2 | 97.9 | 2.7 | 4.3 | 91.7 |
| Erythromycin | 1,708 | >16 | >16 | 0.0 | | 100.0 | 0.0 | | 100.0 |
| Levofloxacin | 1,708 | 1 | 1 | 96.7 | 0.4 | 2.9 | [f] | 96.7 | 3.3 |
| Linezolid | 1,708 | 0.5 | 1 | 100.0 | | | 100.0 | | 0.0 |
| Meropenem[g] | 1,431 | 1 | 1 | 1.5 | 14.0 | 84.4 | 100.0[b] | | 0.0[b] |
| | | | | | | | 1.5[c] | | 98.5[c] |
| Penicillin | 1,708 | 4 | 4 | 4.9[b] | 1.2[b] | 9.0[b] | 0.2[b] | 4.7[b] | 95.1[b] |
| | | | | 0.2[c] | | 99.8[c] | 0.2[c] | | 99.8[c] |
| Tetracycline | 1,707 | >4 | >4 | 1.6 | 0.1 | 98.4 | 1.6 | 0.1 | 98.4 |
| Tigecycline | 1,695 | 0.03 | 0.06 | 95.9[f] | | | | | |

(*continued*)

Table 1. (Continued)

| Antimicrobial agent | No. of isolates | MIC (mg/L) | | CLSI[a] | | | EUCAST[a] | | |
|---|---|---|---|---|---|---|---|---|---|
| | | $MIC_{50}$ | $MIC_{90}$ | %S | %I | %R | %S | %I | %R |
| TMP–SMX | 1,708 | >4 | >4 | 0.4 | 1.2 | 98.4 | 1.1 | 0.5 | 98.4 |
| Vancomycin | 1,708 | 0.25 | 0.5 | 100.0 | | | 100.0 | | 0.0 |

[a]Criteria as published by CLSI[9] and EUCAST[11].
[b]Using non-meningitis breakpoints.
[c]Using meningitis breakpoints.
[d]An arbitrary susceptible breakpoint of ≤0.001 mg/L has been published by EUCAST indicating that susceptible should not be reported for this organism–agent combination and intermediate should be interpreted as susceptible-increased exposure.
[e]Azithromycin was not tested in 2011–2013 and was tested only against isolates from community-acquired respiratory tract infections in 2008 and 2009.
[f]U.S. FDA breakpoints were applied.
[g]Meropenem was not tested in 2015.
Amox–clav, amoxicillin–clavulanate; CLSI, Clinical and Laboratory Standards Institute; EUCAST, European Committee on Antimicrobial Susceptibility Testing; MDR, multidrug-resistant; MIC, minimum inhibitory concentration; TMP–SMX, trimethoprim–sulfamethoxazole; XDR, extensively drug-resistant.



since 2008.[4,5] As seen in the present investigation, ceftaroline demonstrated potent and consistent *in vitro* activity (≥99.9% susceptibility) over time (2008–2020) against a large collection of *S. pneumoniae* from North American medical centers, including ceftriaxone-nonsusceptible, MDR, and XDR isolates.

Ceftaroline was the most potent β-lactam tested, showing MIC values at least eightfold lower than ceftriaxone in a collection of isolates with elevated MIC values for ceftriaxone ($MIC_{50}$, 2 mg/L), amoxicillin–clavulanate ($MIC_{50}$, >4 mg/L), meropenem ($MIC_{50}$, 1 mg/L), and penicillin ($MIC_{50}$, 4 mg/L) (Table 1). Resistance to β-lactam agents in *S. pneumoniae* is mediated by successive alterations in essential PBPs. Unlike other β-lactams, ceftaroline maintains high affinity for PBP-2X mutants and displays low MIC values against penicillin- and cephalosporin-resistant *S. pneumoniae*.[6,7]

The yearly frequency of *S. pneumoniae* isolates nonsusceptible to ceftriaxone is shown in Fig. 1 and Supplementary Fig. S1, which illustrate a continuous decline in the isolation of ceftriaxone-nonsusceptible *S. pneumoniae* from 2011 through 2015. The frequency of ceftriaxone-nonsusceptible *S. pneumoniae* then remained low from 2015 to 2020, varying from a high of 3.3% in 2017 to a low of 1.2% in 2019. A decline on antimicrobial resistance among *S. pneumoniae* causing invasive infections has been reported by other investigators and has been attributed to the introduction and spread of the PCV13.[14–16] A similar decline was observed with the introduction of the PCV7 in 2000; however, resistance rates increased again after a few years due to the development of antimicrobial resistance in serotypes not covered by PCV7.[4,17,18] In contrast, the results of this investigation indicated that antimicrobial resistance remained low for at least 6 years (2015–2020) after an important decline attributed to PCV13 (Figs. 1 and 2, and Supplementary Fig. S1).

The surveillance data we present in this report have limitations. The fact that the number of medical centers recruited each year varied during the 13-year period of the investigation may have introduced bias in the analysis of the yearly frequency of ceftriaxone-nonsusceptible isolates. However, it is very unlikely that these limitations have influenced the assessment of the susceptibility profile

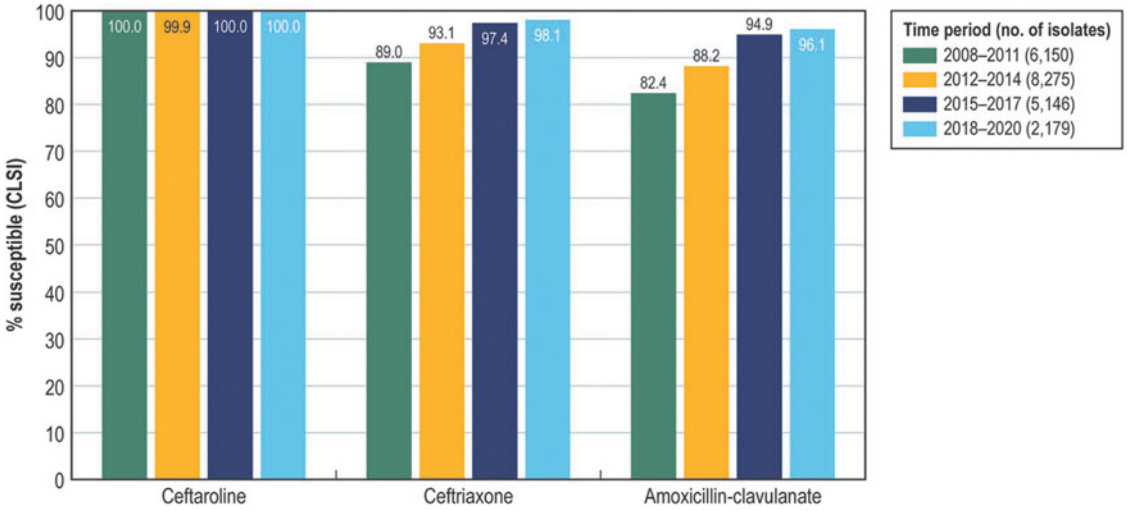


**FIG. 1.** Percentages of *Streptococcus pneumoniae* inhibited at ceftaroline MIC of ≤0.5 mg/L, ceftriaxone MIC of ≤1 mg/L, and amoxicillin–clavulanate MIC of ≤2/1 mg/L over 2008–2020. MIC, minimum inhibitory concentration.

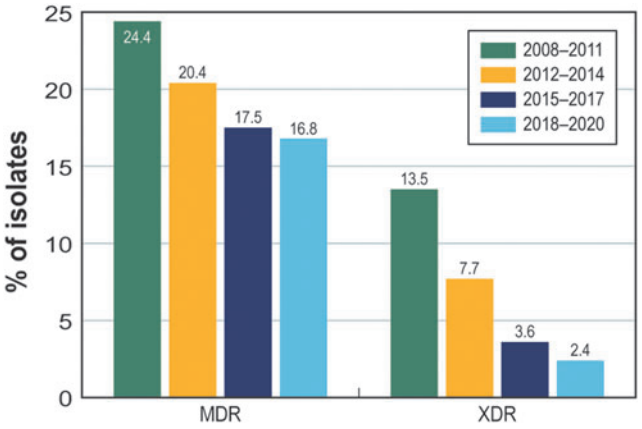


**FIG. 2.** Frequencies of MDR and XDR phenotypes. MDR, multidrug-resistant; XDR, extensively drug-resistant.



of ceftriaxone-nonsusceptible, MDR, or XDR subsets. Moreover, susceptibility rates for key antimicrobial agents, such as ceftriaxone and amoxicillin–clavulanate, were re-evaluated using data from medical centers that participated during the entire period of the study and results were comparable to those generated for the entire organism collection.

In conclusion, ceftaroline demonstrated potent activity and almost complete coverage against *S. pneumoniae* from U.S. medical centers, including ceftriaxone-nonsusceptible, MDR, and XDR isolates. Moreover, ceftaroline has consistently retained potency against isolates obtained following its introduction for clinical use in the United States.

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### Authors' Contributions

H.S.S.: conceptualization, data curation, formal analysis, funding acquisition, visualization, writing—original draft, and writing—review and edit. M.C.: methodology, formal analysis, investigation, data curation, software, validation, supervision, and writing—review and edit. C.G.C.: methodology, formal analysis, data curation, project administration, methodology, software, and validation. S.J.R.A.: methodology, formal analysis, investigation, and data curation. R.E.M.: conceptualization, validation, resources, visualization, supervision, funding acquisition, and writing—review and edit.

### Disclosure Statement

JMI Laboratories contracted to perform services in 2021 for AbbVie, Inc., Affinity Biosensors, AimMax Therapeutics, Inc., Alterity Therapeutics, Amicrobe, Inc., Arietis Pharma, Armata Pharmaceuticals, Inc., Astrellas Pharma, Inc., Basilea Pharmaceutica AG, Becton, Dickinson and Company (BD), bioMérieux, Inc., Boost Biomes, Brass Dome Ventures Ltd., Bravos Biosciences, Bugworks Research, Inc., Centers for Disease Control and Prevention, Cerba Research, Cidara Therapeutics, Cipla Ltd., Contra-Fect Corp., CXC7, DiamondV, Enveda Biosciences, Fedora Pharmaceuticals, Inc., Fimbrion Therapeutics, First Light Diagnostics, Forge Therapeutics, Inc., Fox Chase Cancer Center, GlaxoSmithKline plc (GSK), Harvard University, Institute for Clinical Pharmacodynamics (ICPD), International Health Management Associates (IHMA), Inc., Iterum Therapeutics plc, Janssen Research & Development, Johnson & Johnson, Kaleido Biosciences, Inc., Laboratory Specialists, Inc., (LSI), Meiji Seika Pharma Co., Ltd., Melinta Therapeutics, Menarini Group, Merck & Co., Inc., MicuRx Pharmaceuticals, Inc., Mutabilis, Nabriva Therapeutics, National Institutes of Health, Novome Biotechnologies, Omnix Medical Ltd., Paratek Pharma, Pattern Bioscience, Pfizer, Inc., Prokaryotics, Inc., Pulmocide Ltd., QPEX Biopharma, Inc., Roche Holding AG, Roivant Sciences, SeLux Diagnostics, Inc., Shionogi, Inc., Sinovent Pharmaceuticals, Inc., SNIPR Biome ApS, Spero Therapeutics, Summit Therapeutics, Inc., T2 Biosystems, Ten-Nor Therapeutics, Thermo Fisher Scientific, University of Southern California, University of Wisconsin, USCAST, U.S. Food and Drug Administration, Venatorx Pharmaceutics, Inc., Weill Cornell Medicine, and Wockhardt Ltd.

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