# Antimicrobial Activity of Aztreonam-**Avibactam and Other β-Lactamase** Inhibitor Combinations Tested against Enterobacterales Isolates from Pediatric Patients from United States Medical Centers (2019 - 2023)

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# CONCLUSIONS



ATM-AVI, CAZ-AVI, and MEM-VAB were highly active against pediatric Enterobacterales isolates from all age groups and infection types.



Susceptibility differences were observed among age groups and infection types for some comparator agents.



Bacterial isolates from pediatric patients were generally slightly more susceptible than those from adults.

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# INTRODUCTION

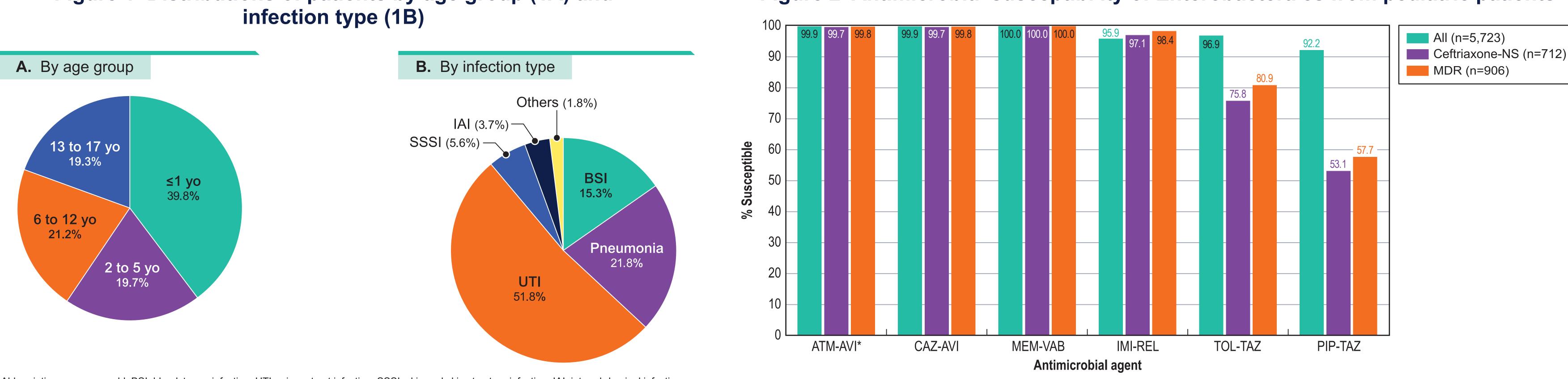
- Aztreonam-avibactam (ATM-AVI) is under development in the United States (US) to treat infections caused by Gram-negative bacteria, including metalloβ-lactamase (MBL) producers.
- Results from clinical trials indicated that ATM-AVI is effective and well-tolerated, with no new safety findings and a similar safety profile to aztreonam alone.
- Moreover, ATM-AVI has been recently approved by the European Medicine Agency (Emblaveo®) to treat adults who have complicated intra-abdominal infections (IAI), hospital-acquired pneumonia (including ventilator-associated pneumonia), and complicated urinary tract infections (UTI; including pyelonephritis), as well as infections caused by aerobic Gram-negative organisms in patients who have limited treatment options.
- We evaluated the activities of ATM-AVI, ceftazidime-avibactam (CAZ-AVI), meropenem-vaborbactam (MEM-VAB), imipenem-relebactam (IMI-REL), ceftolozane-tazobactam (TOL-TAZ), and comparators against Enterobacterales isolates causing infection in pediatric patients.

## METHODS

- Among 43,325 Enterobacterales (1/patient) collected in 2019–2023 via the INFORM Surveillance Program, 5,723 (13.2%) were from pediatric patients (≤17 years old [yo]).
- The isolates were consecutively collected from 81 US medical centers and susceptibility tested by CLSI broth microdilution method. • Only isolates determined to be significant by local criteria as the reported probable cause of an invasive infection were included in the program. • Susceptibility was stratified by infection type and patient age:  $\leq 1$  yo (n=2,275), 2–5 yo (n=1,130), 6–12 yo (n=1,213), and 13–17 yo (n=1,105) and
- compared to adults (18–64 yo; *n*=17,712) (Figure 1A).
- Multidrug-resistant (MDR) phenotype was defined as non-susceptibility to at least one drug in  $\geq$ 3 classes.

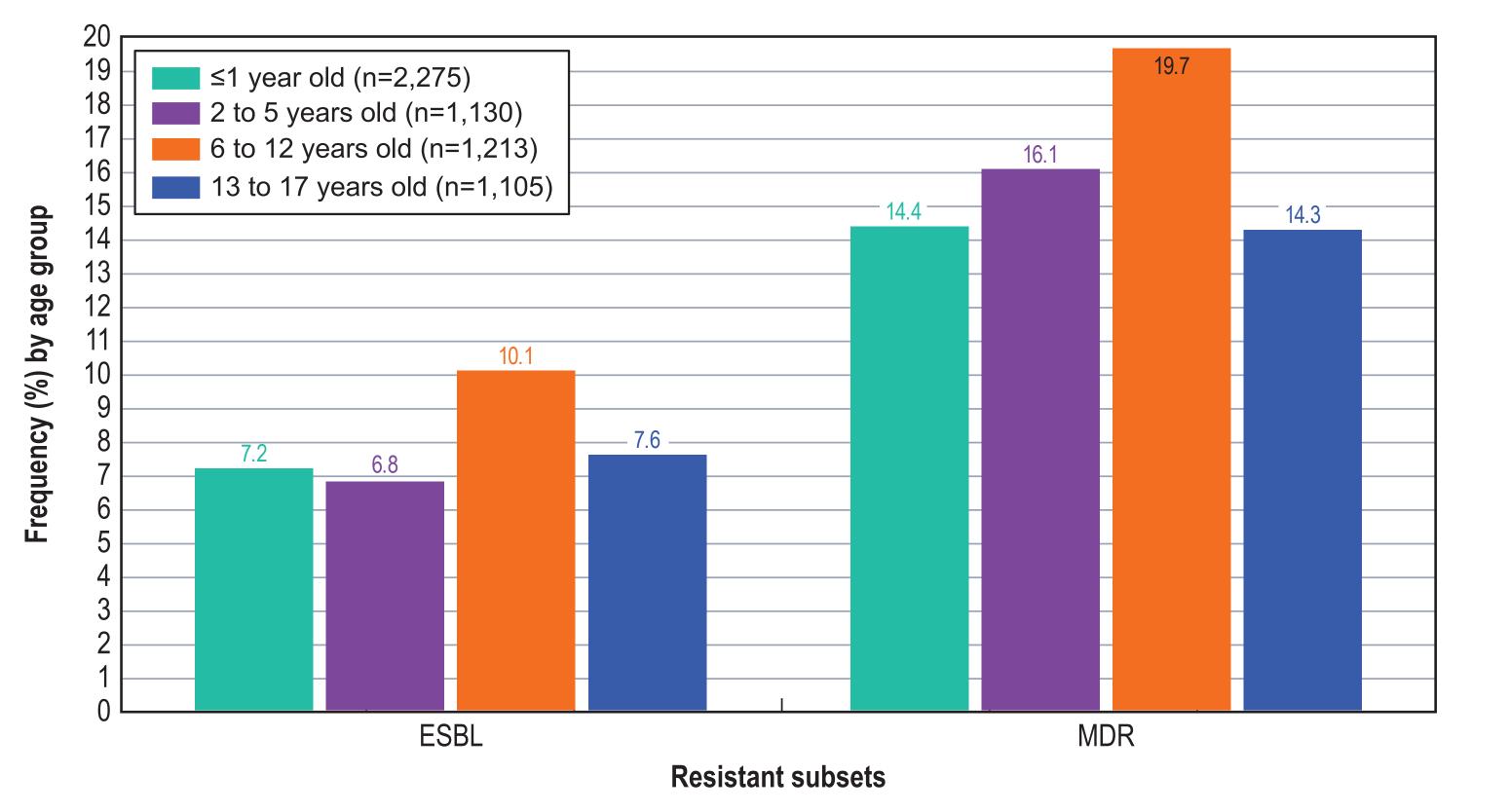


### Figure 1. Distributions of patients by age group (1A) and infection type (1B)



), vears old: BSI, bloodstream infection: UTI, urinary tract infection: SSSI, skin and skin structure infection: IAI, intra-abdominal infection

### Figure 3. Frequency of ESBL producers and isolates with a multidrug-resistant (MDR) phenotype stratified by age group

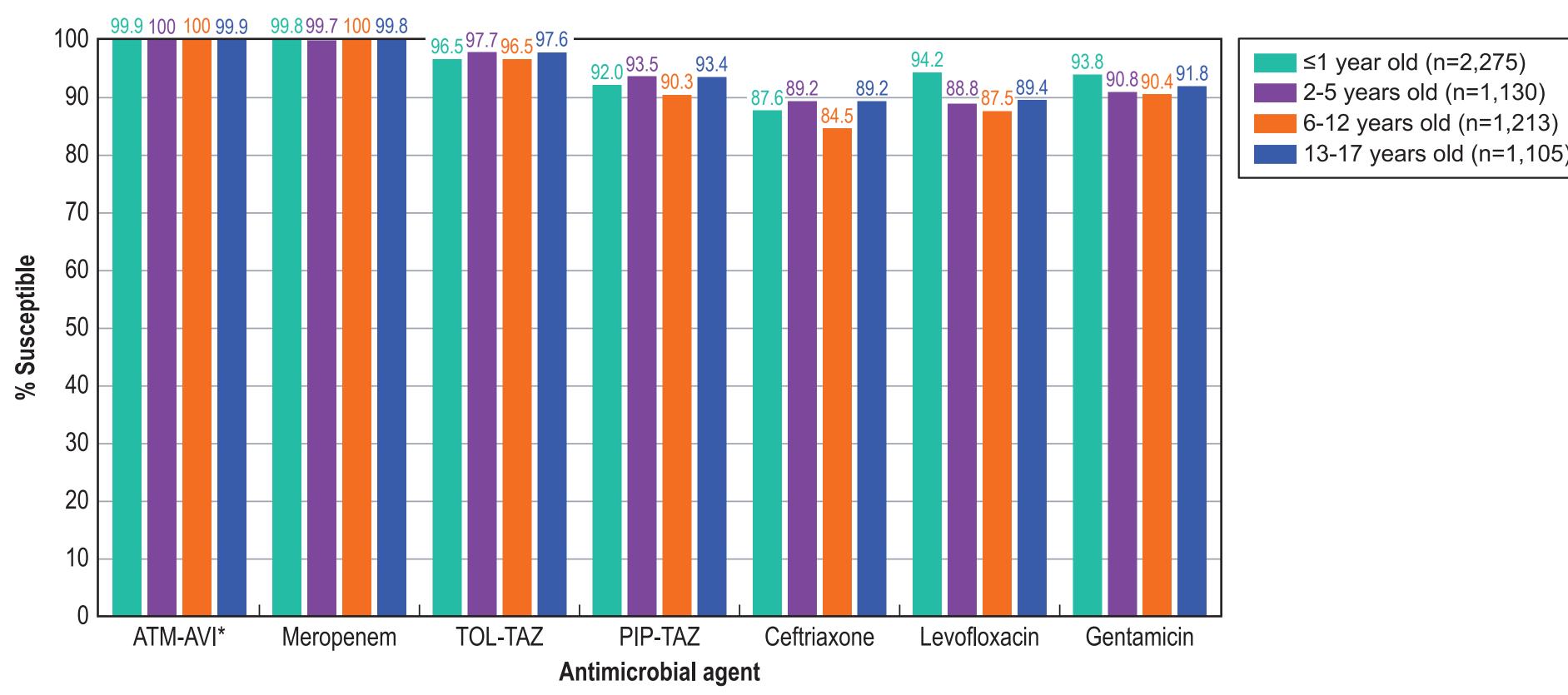


Abbreviations: ESBL, extended-spectrum  $\beta$ -lactamase; MDR, multidrug-resistant.

### Figure 2. Antimicrobial susceptibility of Enterobacterales from pediatric patients

 aztreonam-avibactam: CAZ-AVI. ceftazidime-avibactam: MEM-VAB. meropenem-vaborbactam; IMI-REL, imipenem-relebactam; TOL-TAZ, ceftolozane-tazobactam; PIP-TAZ, piperacillin-tazobactam; NS, nonsusceptible MDR, multidrug-resistant \* % inhibited at ≤8 mg/L.

### Figure 4. Antimicrobial susceptibility of pediatric isolates stratified by age



• Pediatric isolates were mainly from pneumonia (21.8%), bloodstream (BSI; 15.3%), and urinary tract infections (UTI; 51.8%; Figure 1B). • ATM-AVI inhibited >99.9% of pediatric isolates at  $\leq 8 \text{ mg/L}$  (Table 1 and Figure 2).

- adult isolates (Figure 3).
- (Table 1 and Figure 4).



RESULTS

Abbreviations: ATM-AVI, aztreonam-avibactam; TOL-TAZ, ceftolozane-tazobactam; PIP-TAZ, piperacillin-tazobactam. \* % inhibited at  $\leq 8$  mg/L.

• CAZ-AVI and MEM-VAB were active against >99.9% and 100.0% of pediatric isolates, respectively, whereas IMI-REL (95.9% susceptible [S]) and TOL-TAZ (96.9%S) were slightly less active (Table 1 and Figure 2).

• Meropenem, ceftriaxone, and gentamicin were active against 99.8%, 87.6%, and 92.1% of pediatric isolates, respectively (Table 1).

• The frequencies of MDR phenotype varied from 14.3% (13–17 yo) to 19.7% (6–12 yo) among pediatric isolates (15.8% overall) and was 20.7% among

• TOL-TAZ and piperacillin-tazobactam (PIP-TAZ) exhibited limited activity against ceftriaxone-nonsusceptible and MDR isolates (Figure 2). • Ceftriaxone susceptibility ranged from 84.5% (6–12 yo) to 89.2% (2–5 and 13–17 yo) among pediatric isolates and was 81.5% against adult isolates

• Ceftriaxone was active against 86.0%, 87.3%, and 88.4% of pediatric isolates from pneumonia, BSI, and UTI, respectively (Figure 5).

• Carbapenem resistance rate was markedly lower among pediatric isolates (0.1%) compared to adult isolates (1.3%).

• Susceptibility rates for most comparators were higher among pediatric than adult isolates, including ceftriaxone (87.6% vs. 81.5%), PIP-TAZ (92.2% vs. 88.0%), TOL-TAZ (96.9% vs. 93.9%), and levofloxacin (90.8% vs. 82.1%; Table 1).

### Table 1. Antimicrobial activity of aztreonam-avibactam and comparator agents tested against Enterobacterales isolates stratified by patient age group

Organism/antimicrobial agent	% Susceptible by age group <sup>a</sup>					A de la b
	≤1 yo	2–5 уо	6–12 yo	13–17 yo	All Peds	Adults <sup>b</sup>
<i>Enterobacterales</i> (no. of isolates)	(2,275)	(1,130)	(1,213)	(1,105)	(5,723)	(17,712)
Aztreonam-avibactam <sup>c</sup>	>99.9 °	100.0 <sup>c</sup>	100.0 °	99.9 <sup>c</sup>	>99.9°	>99.9 °
Ceftazidime-avibactam	100.0	99.9	100.0	99.9	>99.9	99.7
Meropenem-vaborbactam	100.0	100.0	100.0	100.0	100.0	99.6
Imipenem-relebactam	98.1	92.7	95.3	94.6	95.9	93.1
Ceftolozane-tazobactam	96.5	97.7	96.5	97.6	96.9	93.9
Piperacillin-tazobactam	92.0	93.5	90.3	93.4	92.2	0.88
Ceftriaxone	87.6	89.2	84.5	89.2	87.6	81.5
Meropenem	99.8	99.7	100.0	99.8	99.8	98.6
Levofloxacin	94.2	88.8	87.5	89.4	90.8	82.1
Gentamicin	93.8	90.8	90.4	91.8	92.1	91.2
Amikacin	96.0	95.0	94.6	98.5	95.5	95.0

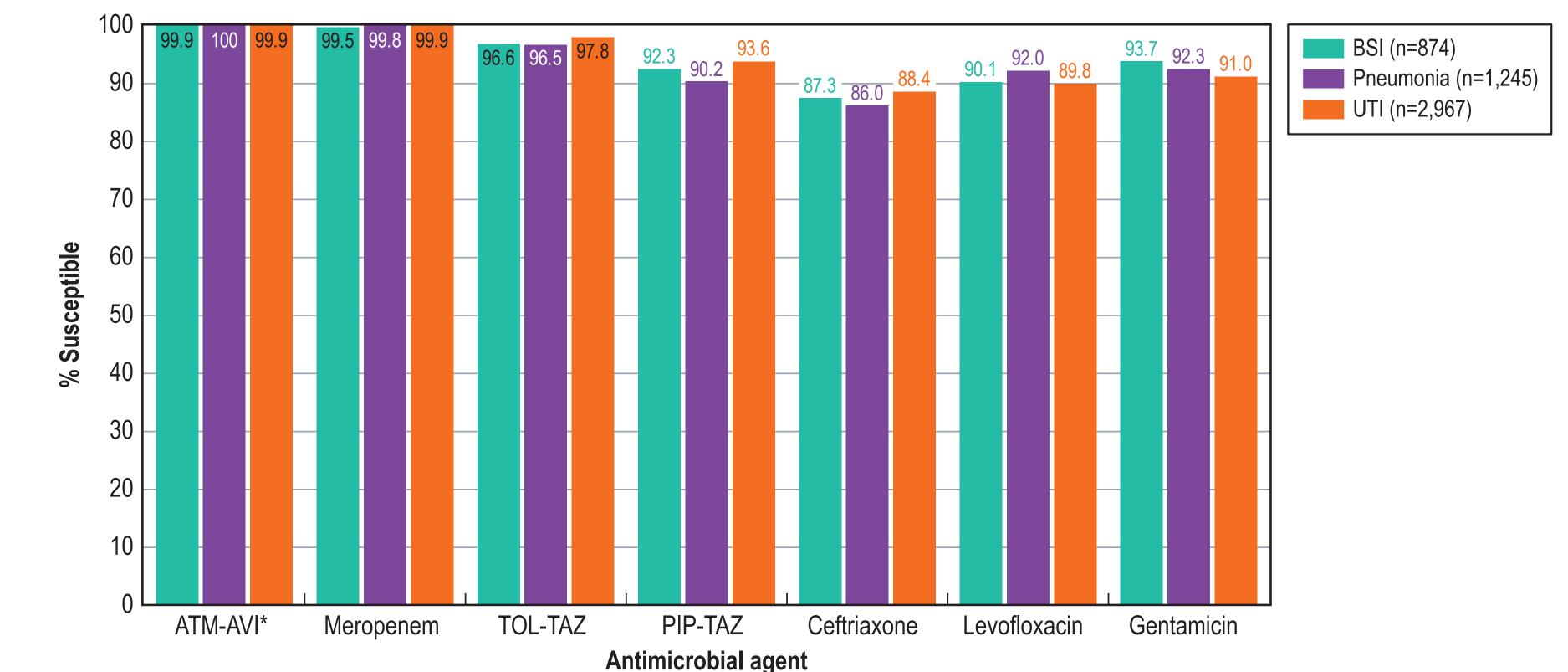
<sup>a</sup> Criteria as published by CLSI.

2-5 years old (n=1,130)

6-12 years old (n=1,213

<sup>b</sup> 18–64 years old. <sup>c</sup> Percentage inhibited at  $\leq 8$  mg/L.

Abbreviations: yo, year(s) old; Peds, pediatric



### Figure 5. Antimicrobial susceptibility of pediatric isolates stratified by infection type

Abbreviations: ATM-AVI, aztreonam-avibactam; TOL-TAZ, ceftolozane-tazobactam; PIP-TAZ, piperacillin-tazobactam; BSI, bloodstream infection; UTI, urinary tract infection.