

Epidemiology and Susceptibility Profiles of ST131-O25b *Escherichia coli* Detected Among Cephalosporin- and/or Carbapenem-Resistant Isolates Collected in United States Hospitals

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Introduction

- The ST131 *E. coli* clone has spread across numerous countries in Asia, Europe, and North America and has been identified as an endemic organism that colonizes humans and causes human infections.
- These extra-intestinal *E. coli* (ExPEC) isolates belong to the phylogroup B2 and exhibit true virulence factors, including adhesions, capsules, invasins, lipopolysaccharides, proteases, and toxins.
- Most ST131 *E. coli* exhibit serotype O25b, which emerged as a fluoroquinolone resistance lineage that later acquired *bla*_{CTX-M-15}, conferring resistance to cephalosporins as well as other resistance genes.
- We evaluated the prevalence of ST131 and the antigen O25b among the *E. coli* isolates collected in US hospitals during 2017 and 2018 and analyzed the susceptibility patterns of the isolates that belonged to these groups.

Materials and Methods

- A total of 6,768 *E. coli* isolates were recovered from documented infections in 74 US hospitals during 2017 and 2018 according to a common surveillance design.
- All isolates were tested for antimicrobial susceptibility using broth microdilution methodology per CLSI M07 (2018) guidelines.
- MIC values were validated by concurrently testing CLSI-recommended M100 (2021) quality control (QC) reference strains.
 - QC ranges for tested reference strains were approved or published by CLSI in the M100 (2021).
- All categorical interpretations used were published by CLSI in the M100 (2021) or were from the US Food and Drug Administration criteria for tigecycline.
- A total of 1,154 *E. coli* isolates were submitted to WGS and analysis, including:
 - Isolates displaying MIC values ≥ 2 mg/L for at least 2 of the following β -lactams: ceftazidime, ceftriaxone, aztreonam, or ceftipime and
 - Isolates displaying MIC values ≥ 2 mg/L for imipenem and/or meropenem.
- The housekeeping genes *adk*, *fumC*, *gyrB*, *icd*, *mdh*, *purA*, and *recA* were analyzed to detect ST131 and a single loci variant (SLV; 1 allele difference).
- ST131 and the SLV were evaluated for the presence of the O25b antigen using the EcOH database, the SRST2 software package, and by submitting a *de novo* assembly of quality-trimmed WGS reads to SerotypeFinder 2.0.
 - The SerotypeFinder database compared sequences to *wzx*, *wzy*, *wzm*, and *wzt* for O-groups and *fljC*, *flkA*, *flmA*, *flnA*, and *fljA* for H-types.
- If no O-antigen was observed in the *in silico* search, the isolate was submitted to a PCR reaction that was specific for O25b antigen, as described elsewhere.
 - PCR also was used if there was disagreement between the *in silico* and WGS approaches.

Results

- A total of 47.8% of the 1,154 sequenced *E. coli* isolates were collected from urinary tract infections (552 isolates).
 - The remaining isolates were recovered from bloodstream infections (257 isolates), isolates deemed as cause of pneumonia in hospitalized patients (159 isolates), skin/soft tissue infections (115 isolates), and intra-abdominal infections (71 isolates).
 - 65 isolates that caused bloodstream infections had a primary source from urinary tract infections.

- Among 1,154 *E. coli* isolates, 627 belonged to ST131 or were SLVs that contained 1 allele of the MLST scheme difference with ST131 (Figure 1).
 - ST131 and SLV (ST131 herein) isolates were similarly distributed in 2017 and 2018. In 2017, 324 (52.0%) isolates were identified. In 2018, 303 (56.1%) isolates were identified.
 - Among the US Census Bureau divisions, the occurrence of ST131 was lowest in the Mountain region (37.9%) and highest in the Mid-Atlantic (60.4%; Figure 2).
- A total of 586 *E. coli* isolates belonged to the O25b serotype, which corresponded to 93.5% of the ST131 isolates and 50.8% of the sequenced isolates (Figure 1).
 - Serotype O16 was detected in 40 isolates and a variant of O153 was detected in 1 isolate of the 627 isolates evaluated.
- The prevalence of ST131-O25b *E. coli* in the US Census Divisions ranged from 36.2% to 58.7% among the sequenced isolates.
 - The highest occurrence of ST131-O25b was in isolates from the South Atlantic region (Figure 2).
- ST131 *E. coli* isolates were considerably more resistant compared to the isolates that did not belong to the ST131 clade (Figure 3).
 - Ceftriaxone, cefepime, the fluoroquinolones, tobramycin, and trimethoprim-sulfamethoxazole had $\geq 5\%$ (range 6.1% to 35.8%) higher resistance rates in the ST131 group when compared to the non-ST131 group.
- ST131 (49.0%) and ST131-O25b (51.5%) isolates had higher multidrug resistant (MDR; resistant to ≥ 3 antimicrobial classes) rates compared to all *E. coli* isolates (7.3%), sequenced isolates (41.4%), and isolates that did not carry these traits (32.4% for non-ST131 and 12.2% for non-O25b; Figure 4).

Conclusions

- This study highlights the widespread distribution of ST131-O25b *E. coli* in the US hospitals and documents the high resistance rates among these isolates, including multidrug resistance.
- Monitoring *E. coli* O25b-ST131 is critical as it can cause severe infections and there are limited treatment options active against these isolates.

Acknowledgements

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Figure 1. Prevalence of ST131 *Escherichia coli* isolates and O serotypes collected from US hospitals during 2017 and 2018

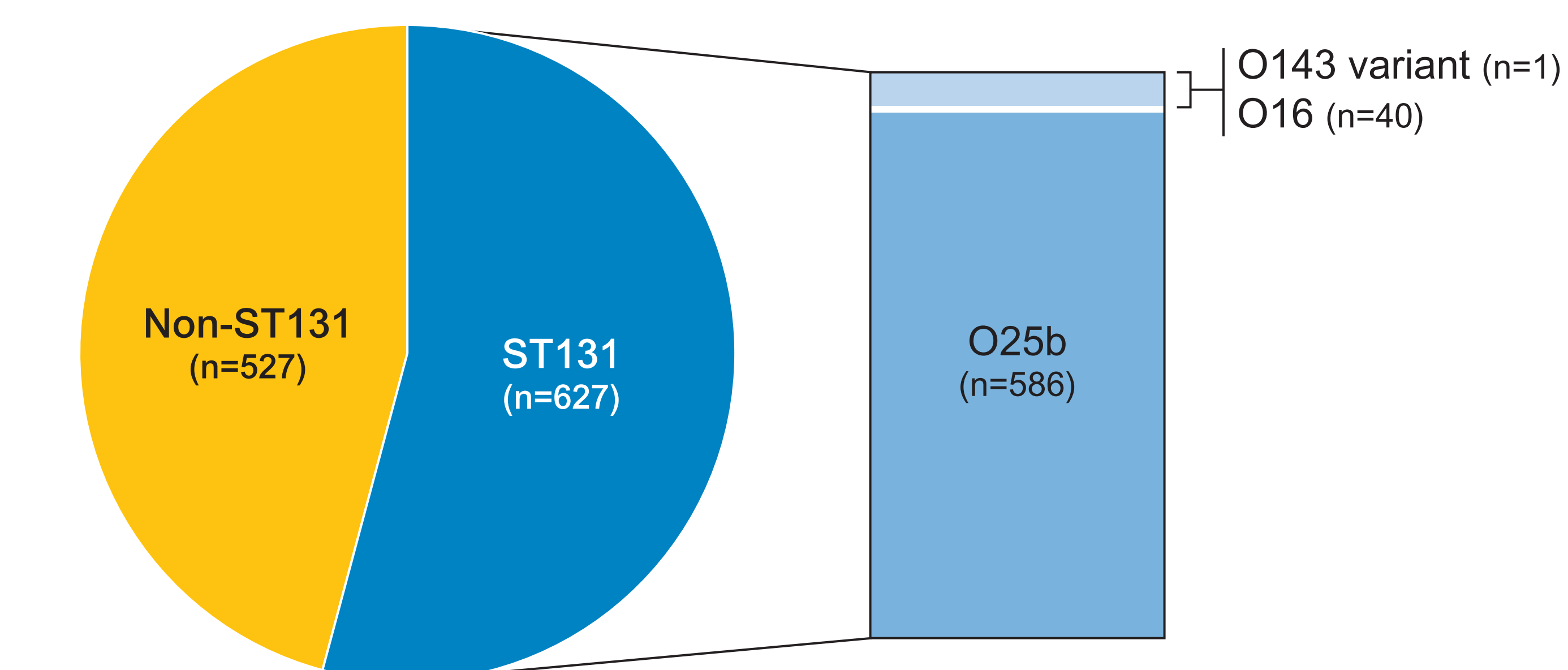


Figure 2. Distribution of ST131 *Escherichia coli* isolates across the US Census Divisions

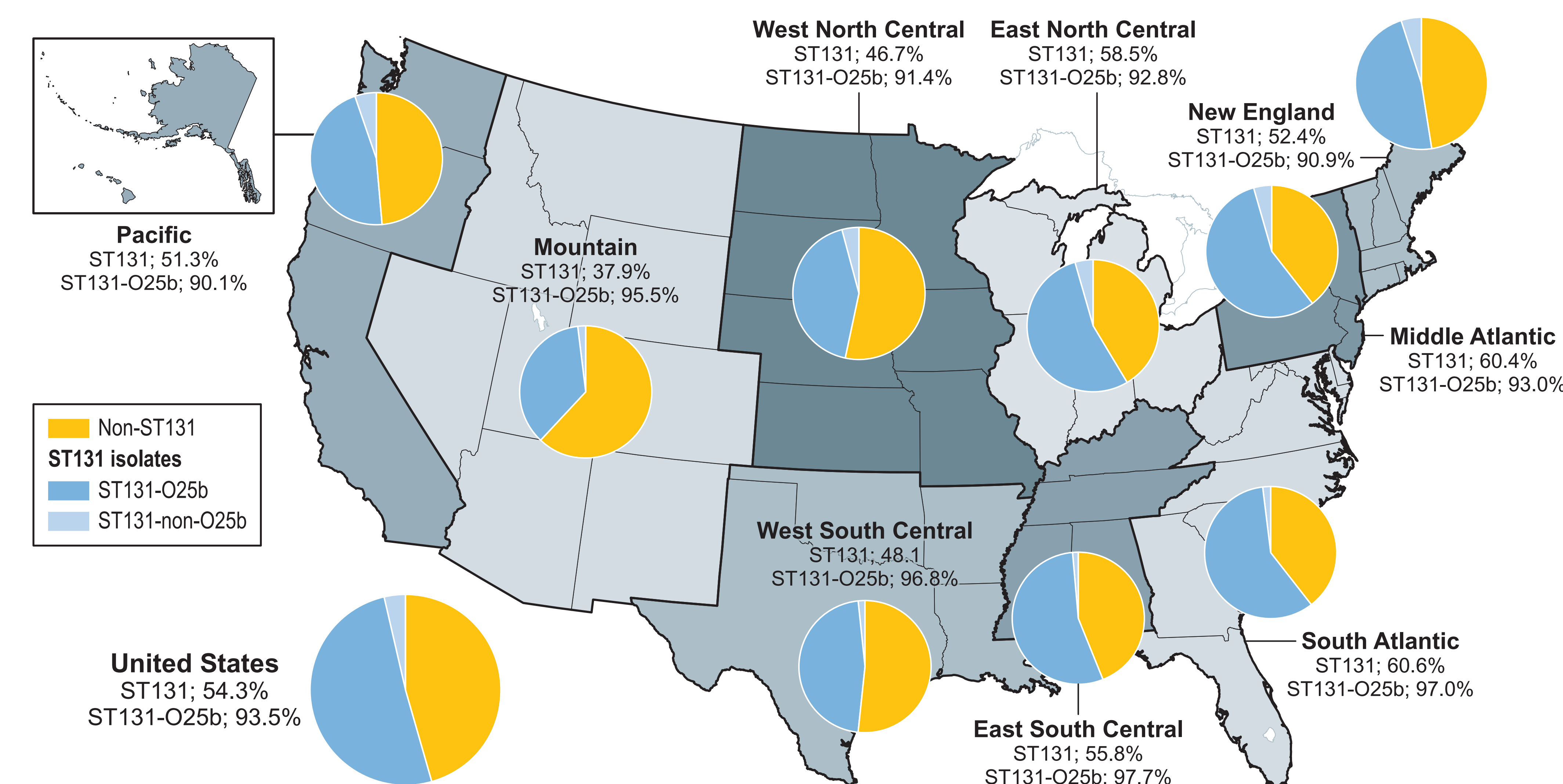


Figure 3. Activity of antimicrobial agents tested against ST131 *Escherichia coli* isolates collected from US hospitals during 2017 and 2018

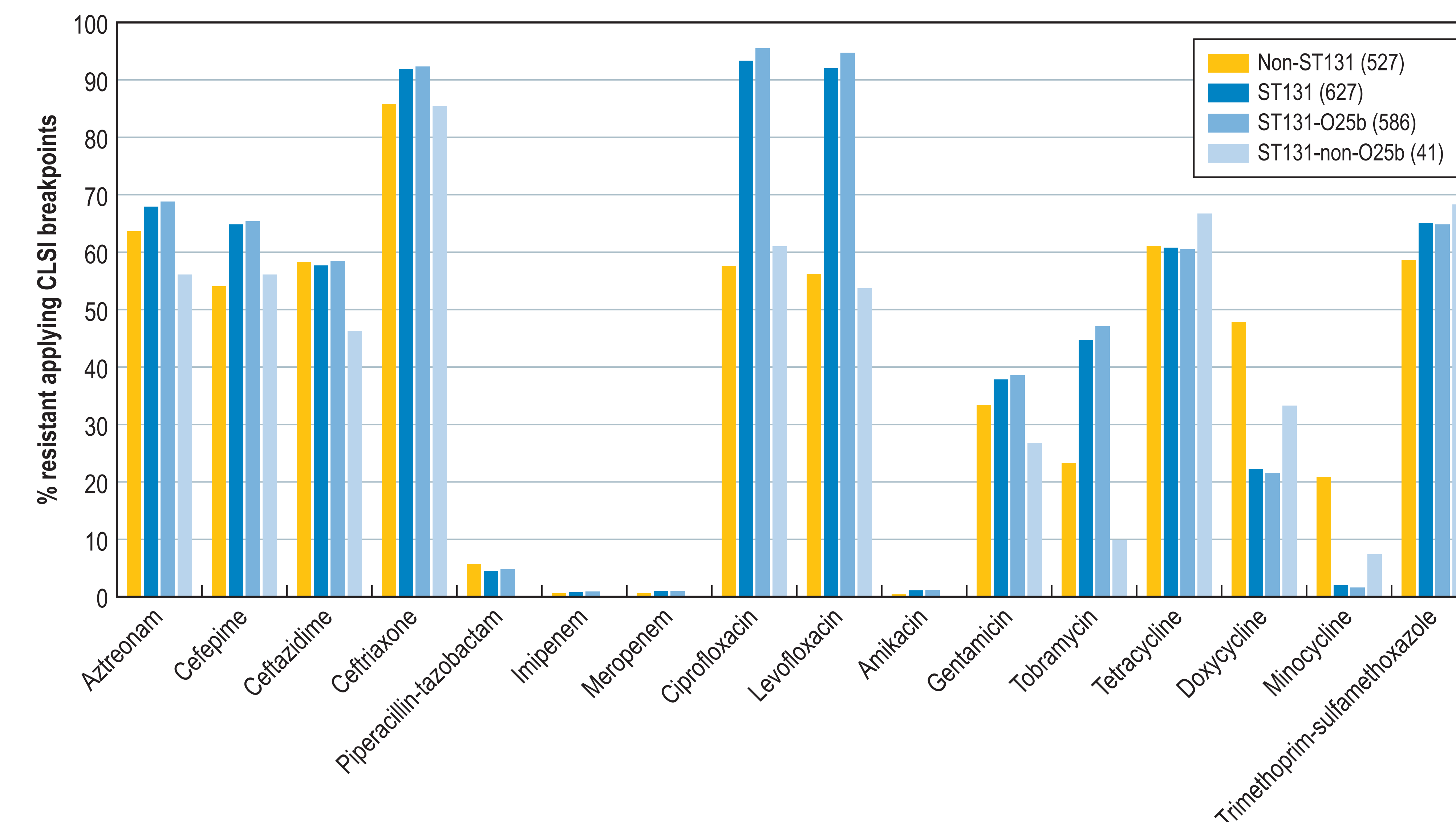
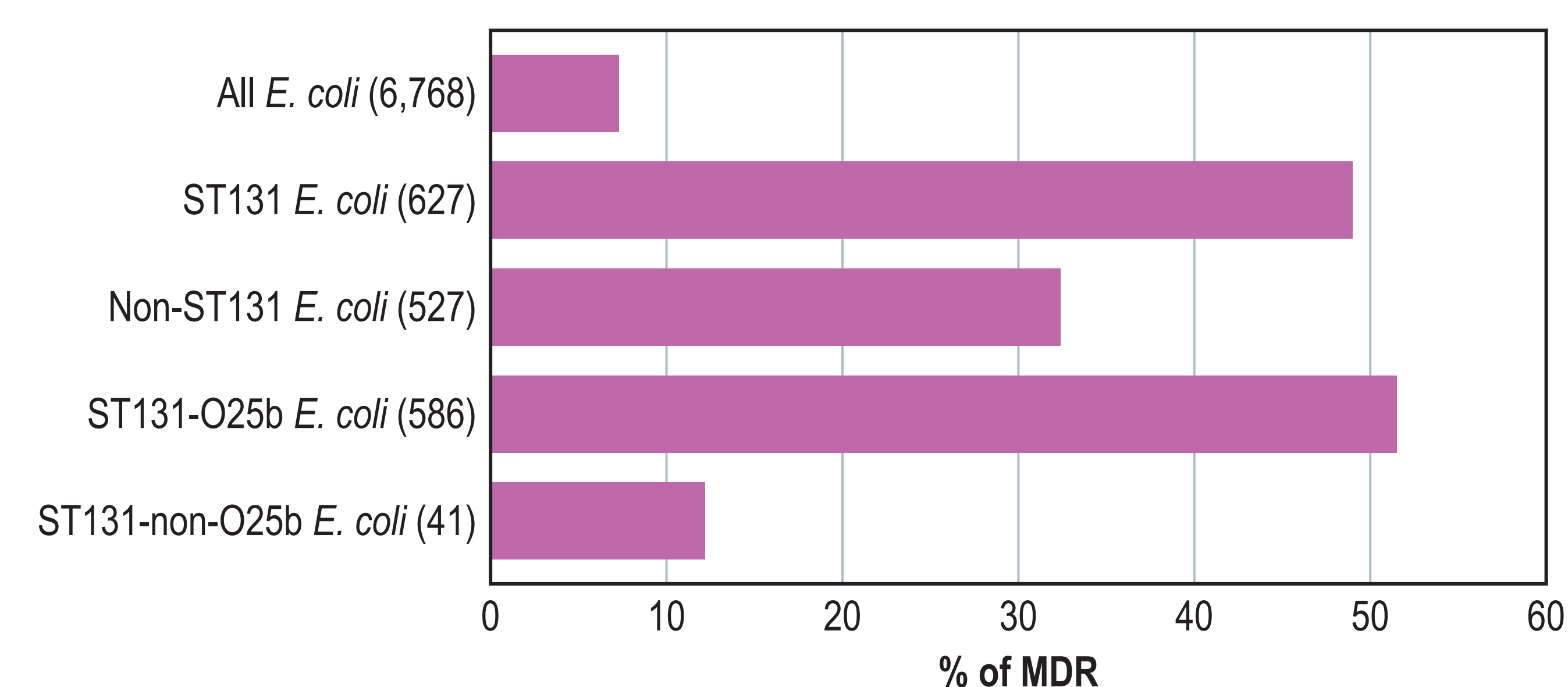


Figure 4. Comparison of the prevalence of MDR (resistant to ≥ 3 antimicrobial classes) isolates among analyzed *Escherichia coli* isolates



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