

Spatio-temporal distribution of antibiotic resistance genes in *Escherichia coli* in the US, 2000-2023.

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Antibiotic resistance is recognized as one of the leading public health concerns in the 21st century. Among the various microbes that have developed antibiotic resistance, *Escherichia coli* is of particular concern due to its ubiquity and its role as a significant reservoir for resistance genes. To date, no study has provided a comprehensive examination of the geographic patterns in *E. coli* resistance to various classes of antibiotics across the US utilizing a OneHealth perspective. This study utilizes *E. coli* samples from the National Database of Antibiotic Resistant Organisms (NDARO) and the resistance genes detected by AMRFinderPlus to understand the spatial-temporal dynamics of genotypic resistance among *E. coli* populations in the US. We chose to focus on six classes of antibiotics, including 3rd generation cephalosporins, carbapenems, trimethoprim, sulfonamides, fluoroquinolones, and tetracyclines, based on their significance in human and veterinary health. Among 30528 *E. coli* samples between 2000 and 2023, the overall rates of resistance are 18.5% for cephalosporins, 1.5% for carbapenems, 32.0% for trimethoprim, 19.9% for sulfonamides, 4.9% for fluoroquinolones, and 38.7% for tetracyclines. Our results reveal generally increasing resistance rates against all examined antibiotics in humans and companion animals, but also significant geographic disparities and variations in resistance genotypes between different hosts, indicating potential transmission barriers or selective pressure. Finally, certain resistance genes are significantly correlated, likely due to co-selection or mobile genetic elements that facilitate the horizontal transfer of multiple resistance genes.

Primary authors: TANG, Zhuo 'Austin' (University of Iowa); CARREL, Margaret (University of Iowa)

Presenter: TANG, Zhuo 'Austin' (University of Iowa)

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