**Projecting the impact of carbapenem restriction on antibiotic resistance in *Pseudomonas aeruginosa* bacteremia**

Jeffrey P. Townsend, Yiziying Chen, Amber Tang, Abhishek Pandey, Eric Foster, Dilip Nathwani, Eric Sarpong, Vimalanand Prabhu, Sanjay Merchant, Shikha Surati, Meagan C. Fitzpatrick, Alison P. Galvani

**Background:** Rising levels of carbapenem resistance (CR) are a pressing public health concern in the United States. Therapeutic alternatives to carbapenems are limited. Implementation of antimicrobial stewardship programs (AMSP) can help reduce inappropriate antibiotic use and thereby minimize selection pressure for resistance. Formulary restriction is one strategy used by AMSP. In this study, we evaluate the impact that timely restriction of carbapenem use would have among bacteremia patients infected with *Pseudomonas aeruginosa* in the US.

**Materials/methods:** We developed a Malthusian population-genetic model of selection for CR. Increases in CR were modeled as a consequence of inappropriate prescription from a retrospective cohort study of the inappropriate empiric treatment (Zilberberg et al. 2017) and projections were based on historical resistance frequencies and yearly carbapenem consumption associated with *P. aeruginosa* bacteremia. We then projected peak *P. aeruginosa* CR frequencies and cumulative CR cases from 2020–2040. We compared scenarios without any carbapenem restriction to those in which carbapenem usage was decreased linearly to 51.7% of levels at implementation, as achieved in previous AMSP (Van Hollebeke et al. 2016), with 5-year rollouts starting in 2020 (early) or 2030 (late).

**Results:** Early implementation of carbapenem restriction mitigates CR frequencies that ascend as high as 28—45% in 2020, compared with late implementation that would allow peak CR frequencies as high as 59—75%. A late implementation of carbapenem restriction yields a greater decrease in the number of resistant cases per year compared to early implementation, but the higher yield does not compensate for the increase in early cases nor the higher final CR frequency. By 2040, early carbapenem restriction could prevent 30,000 CR cases of *P. aeruginosa* bacteremia, compared to 15,800 prevented by late implementation.

**Conclusions:** We demonstrate that timely restriction of carbapenem consumption could markedly reduce future CR frequencies in bacteremia patients infected by *P. aeruginosa*. High CR frequencies are likely to evolve in *P. aeruginosa* even under restriction. However, implementing early carbapenem restriction should be expected to result in a lower ultimate frequency of CR and a lower number of cumulative cases of resistant infections decreasing the overall burden of CR cases that will be encountered in the future.

Keywords: Antibiotic resistance, mathematical model, antibiotic stewardship

Presentation Type – Poster Presentation Preferred