Clostridium difficile infections following systemic antibiotic administration in randomized controlled trials: a meta-analysis

Konstantinos Z. Vardakas,1,2 Kyriakos K. Trigkidis,1 Eleni Boukouvala,3 Matthew E. Falagas,1,2,4
1. Alfa Institute of Biomedical Sciences, Athens, Greece, 2. Department of Internal Medicine-Infectious Diseases, Iaso General Hospital, Athens, Greece, 3. Department of Applied Mathematics and Physics, National Technical University of Athens, Athens, Greece, 4. Department of Medicine, Tufts University School of Medicine, Boston, Massachusetts, USA

OBJECTIVE
Antibiotics have been among the most important risk factors for Clostridium difficile infection (CDI). However, only data from non-randomized studies have been reviewed. We sought to evaluate the risk for development of CDI associated with the major antibiotic classes by analyzing data from randomized controlled trials (RCTs).

METHODS
- We searched Cochrane Library, Scopus and PubMed databases
- Only randomized controlled trials (RCTs) were eligible for inclusion
- Studies were excluded if:
  - one antibiotic was compared with a pre-specified combination of antibiotics from the beginning of the study
  - antibiotics were not administered systemically
  - antibiotics were not administered for bacterial infections
  - if additional antibiotics were administered in a subset of the enrolled patients that were equally distributed in the two arms of the study
  - if the study evaluated combination of antibiotics in both arms and the second antibiotic (or more) was the same or from the same class in both arms, the study was included in the analysis

RESULTS
- Seventy nine RCTs were included (32042 patients).
- Cephalosporins were associated with more CDI episodes than penicillins (Figure 1A) and fluoroquinolones (Figure 1B) alone.
- Carbapenems were associated with more CDI episodes than fluoroquinolones (Figure 2A) and cephalosporins (Figure 2B) alone, but not penicillins (Figure 2C).
- There was no difference in CDI frequency between fluoroquinolones and penicillins (Figure 3).
- Clindamycin was associated with more CDI episodes than all comparator antibiotics (Figure 4).
- Neither linezolid (RR 0.99, 95% CI 0.44-2.26) nor vancomycin (RR 1.16, 95% CI 0.45-2.99) was associated with more CDI episodes.

CONCLUSION
Data from RCTs showed that clindamycin and carbapenems were associated with more CDIs than other antibiotics.