

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

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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
 - the antibiotics were not administered systemically
 - antibiotics were compared with non-antibiotics
 - 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 the study was eligible for inclusion.
- 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.

Figure 1A. Forest plot depicting the risk ratios of CDI with cephalosporins compared to penicillins

Figure 1B. Forest plot depicting the risk ratios of CDI with cephalosporins compared to fluoroquinolones.

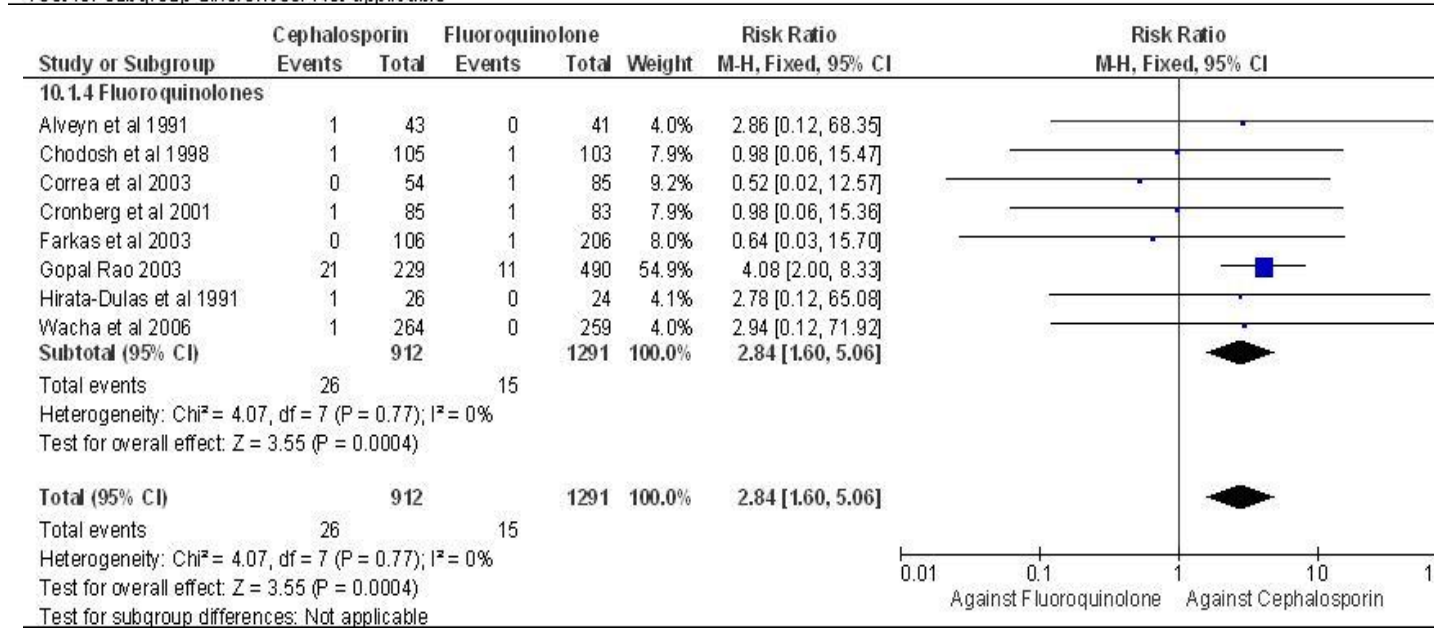
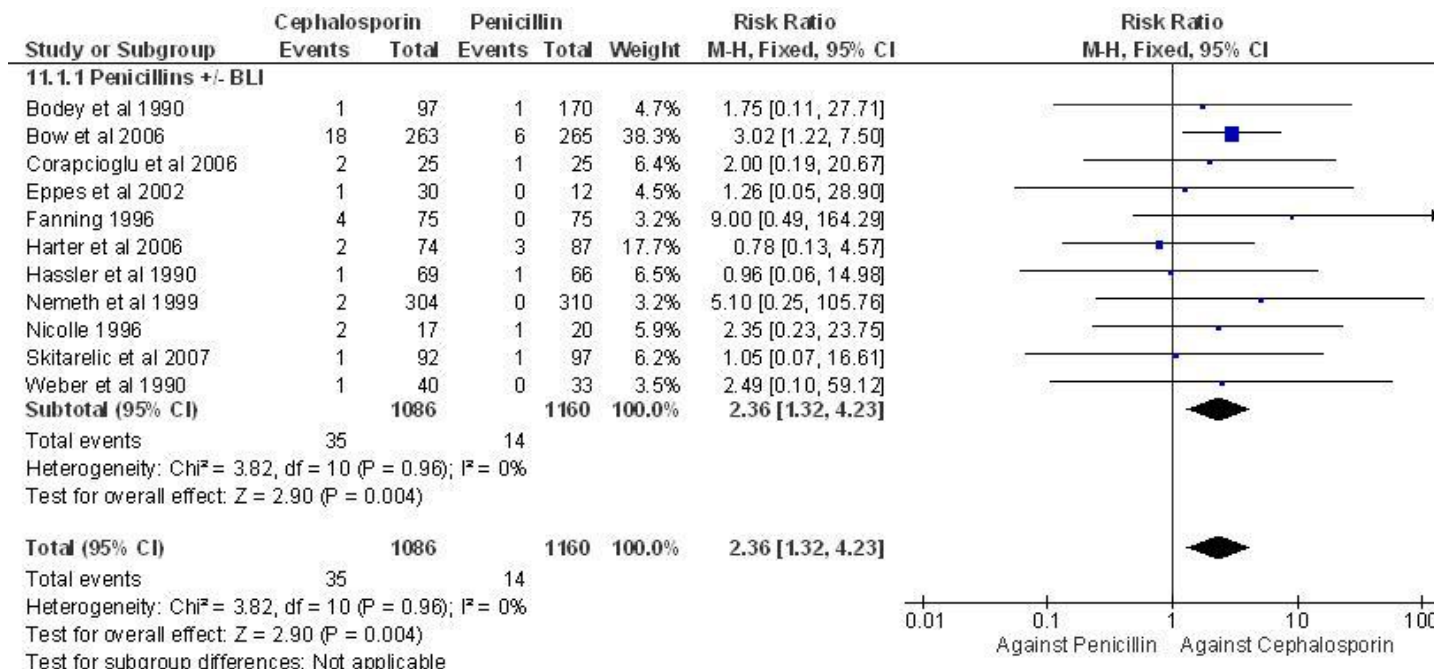


Figure 2A. Forest plot depicting the risk ratios of CDI with carbapenems compared to fluoroquinolones

Figure 2B. Forest plot depicting the risk ratios of CDI with carbapenems compared to cephalosporins

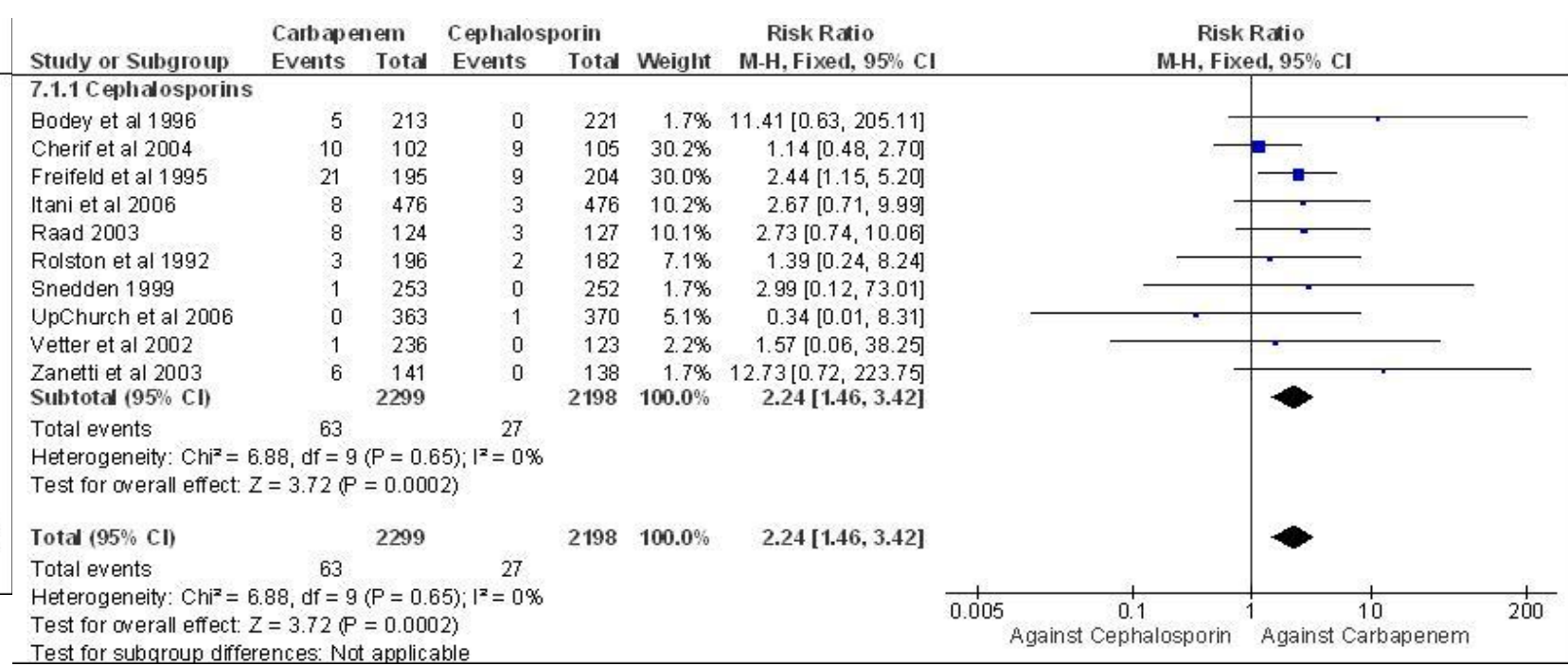
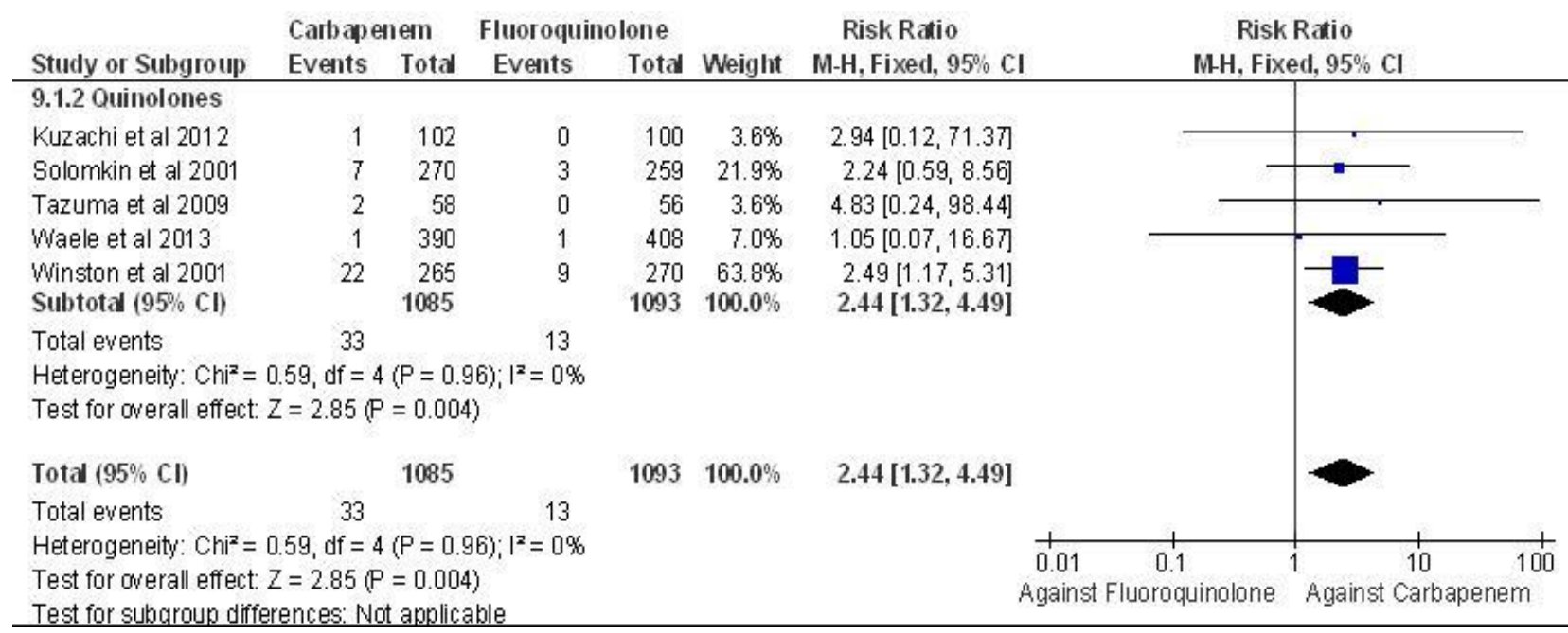
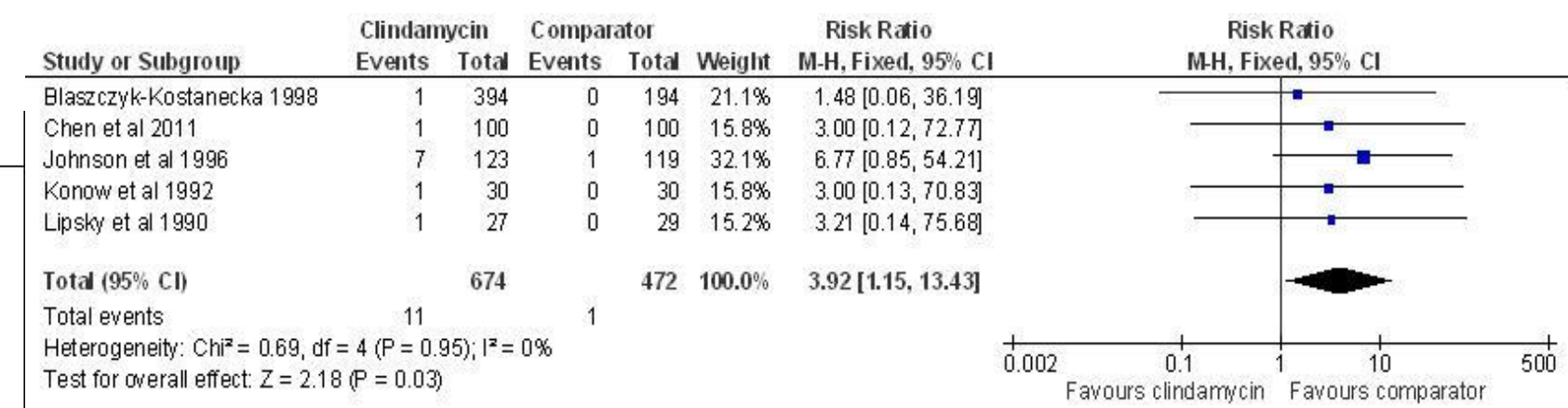


Figure 4. Forest plot depicting the risk ratios of CDI with clindamycin compared to other antibiotics



CONCLUSION

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

Figure 2C. Forest plot depicting the risk ratios of CDI with carbapenems compared to penicillins.

Figure 3. Forest plot depicting the risk ratios of CDI with fluoroquinolones compared to penicillins

