Meta-analysis of Randomized Control Trials Evaluating New Beta-Lactamase Combination Antibiotics

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Background

- Ceftolozane/ Tazobactam (C/T), Ceftazidime/ Avibactam (C/A), Meropenem/ Vaborbactam (M/V) and Imipenem/ Relebactam (I/R) are new combination beta-lactam/ beta-lactamase inhibitor antibiotics primarily used to treat multidrug-resistant (MDR) Gram-negative infections.
- This study synthesized outcomes of comparative observational studies and randomized control trials (RCTs) that evaluated clinical success of these antibiotics compared to other therapies.

Methods

- PubMed, EMBASE, and Google Scholar were searched from January 1st, 2013 through September 2nd, 2020 for comparative observational studies and RCTs of C/T, C/A, M/V and I/R.
- Study and patient demographics were collected along with clinical success rates.
- Meta-analysis was used to determine the pooled clinical success rates of C/T, C/A, M/V, and I/R.
  - Clinical success was defined as the resolution of all signs and symptoms of infection such that no further intervention was needed.
- Heterogeneity and publication bias were assessed via I^2 values and funnel plots, respectively.

Results

Table1: Demographics of Included Articles

Variable Name	Randomized Control Trials (n=17)	Observational Studies (n=8)
Duration of Study (mos)	23.0	49.6
Sample Size	8,238	828
Location	Global=16 Asia=1	USA=5 Spain=2 Italy=1
Number of Sites	84.5	8
Antibiotic under Investigation	C/A=8 C/T=3 I/R=3 M/V=2	C/A=4 C/T=4

Figure 1: Diagram of Search Results

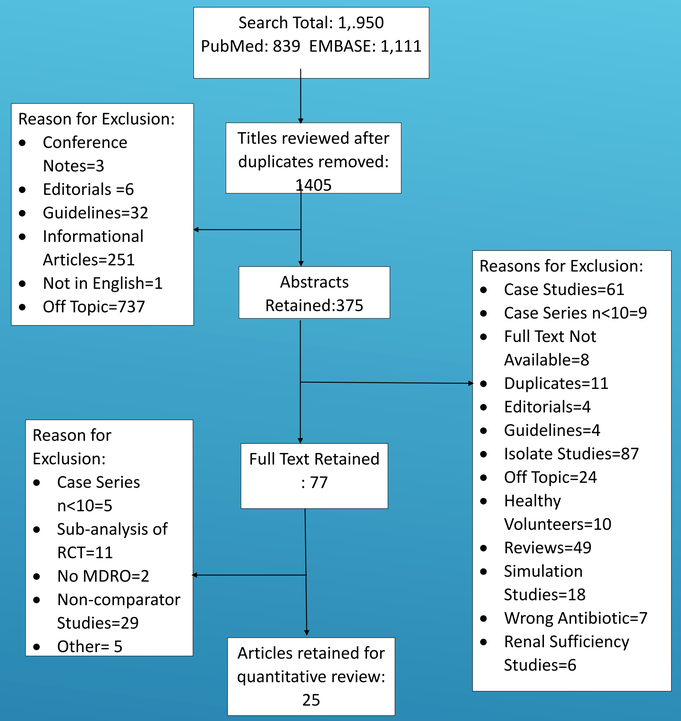


Figure 2: Pooled Results of Observational Studies

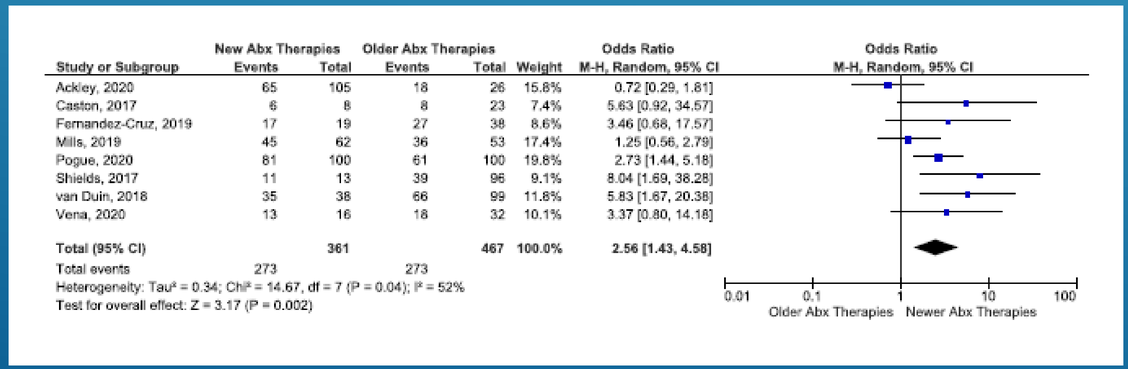
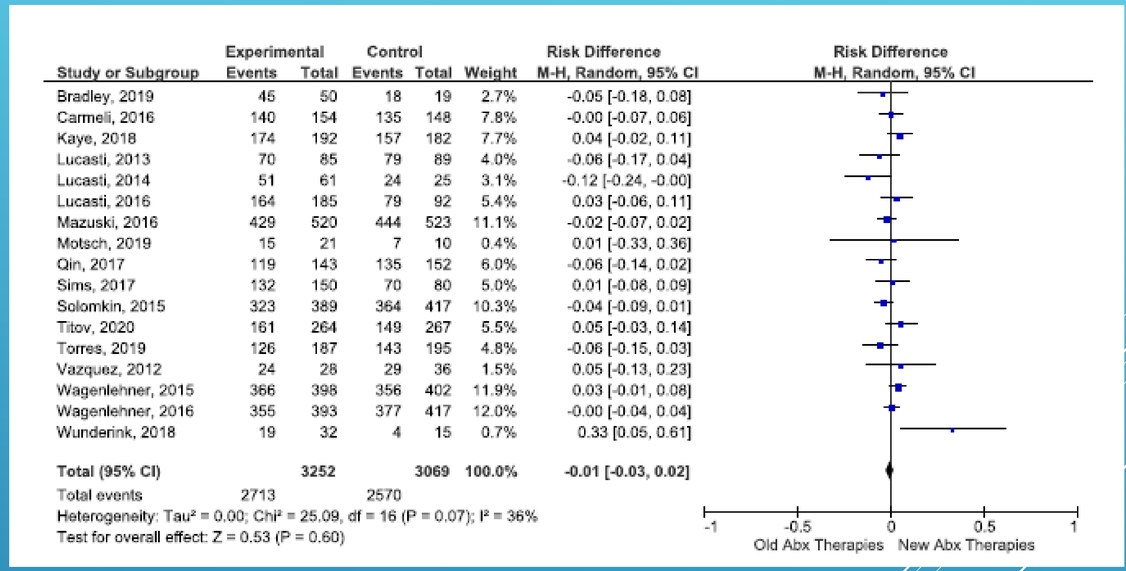


Figure 3: Pooled Results of Randomized Control Trials



Conclusion

- Among RCT's the novel antibiotics were non-inferior to the older antibiotic therapies
- In the observational studies there was a strong association between the newer antibiotics and odds of clinical recovery from infection.
- The 2020 IDSA CRE guidelines recommend the use of C/A, M/V, and I/R for the treatment of Carbapenem-resistant Enterobacteriaceae infections
- The guidelines also recommend the use of C/T, M/V, and I/R for the treatment of multi-drug resistant Pseudomonas aeruginosa infections.
- Additional studies are needed to further evaluate these drugs' effectiveness for treatment of MDR infections.

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