Clinical Failure Rates with and without Empiric Atypical Bacterial Coverage in Hospitalized adults with Community-Acquired Pneumonia: A Systematic Review and Meta-analysis

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Background

- Both typical and atypical bacteria can cause community-acquired pneumonia (CAP); however, the need for empiric atypical coverage remains unclear.
- Prior meta-analyses of randomized controlled trials (RCTs) have not demonstrated the benefit of atypical coverage; but these studies included trials of antibiotics with discordant or substandard typical bacterial coverage.
- Two meta-analyses favoring atypical coverage were based mainly on observational studies.

Objectives

- To evaluate the impact of antibiotic regimens with atypical coverage to a regimen without atypical antibiotic coverage on:
  - rate of clinical failure (**primary endpoint**)
  - rate of mortality, bacteriologic failure, and adverse events

Methods

- The meta-analysis protocol was developed according to the PRISMA guidelines.
- We searched the PubMed, EMBASE, Cochrane Library, and ClinicalTrials.gov databases through 19 Sep, 2016.

Inclusion criteria:

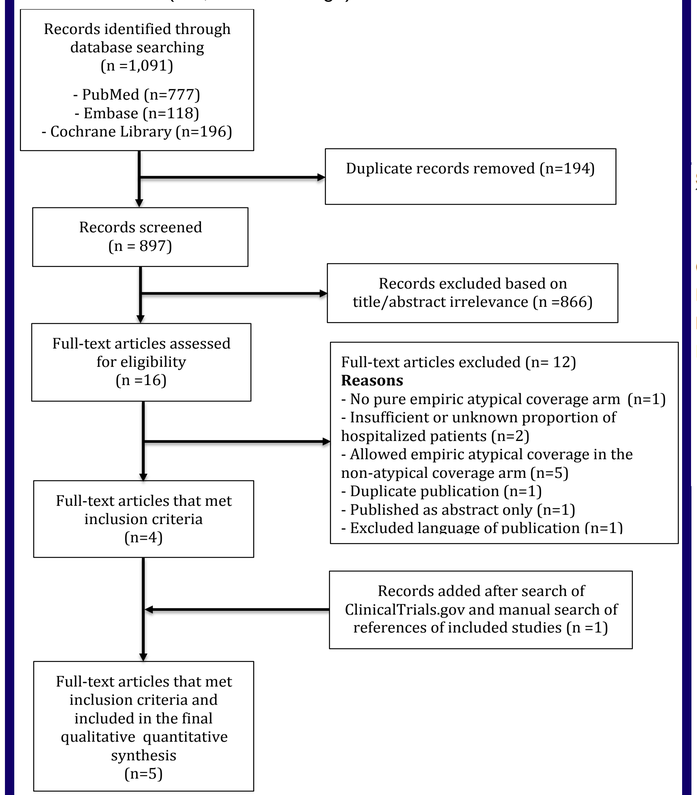
- RCTs of hospitalized adult patients with CAP
- Studies that compared empiric antibiotic regimens with atypical coverage (a respiratory fluoroquinolone or combination of a macrolide/doxycycline with a β-lactam) to a regimen without atypical antibiotic coverage (β-lactam monotherapy).

Exclusion criteria:

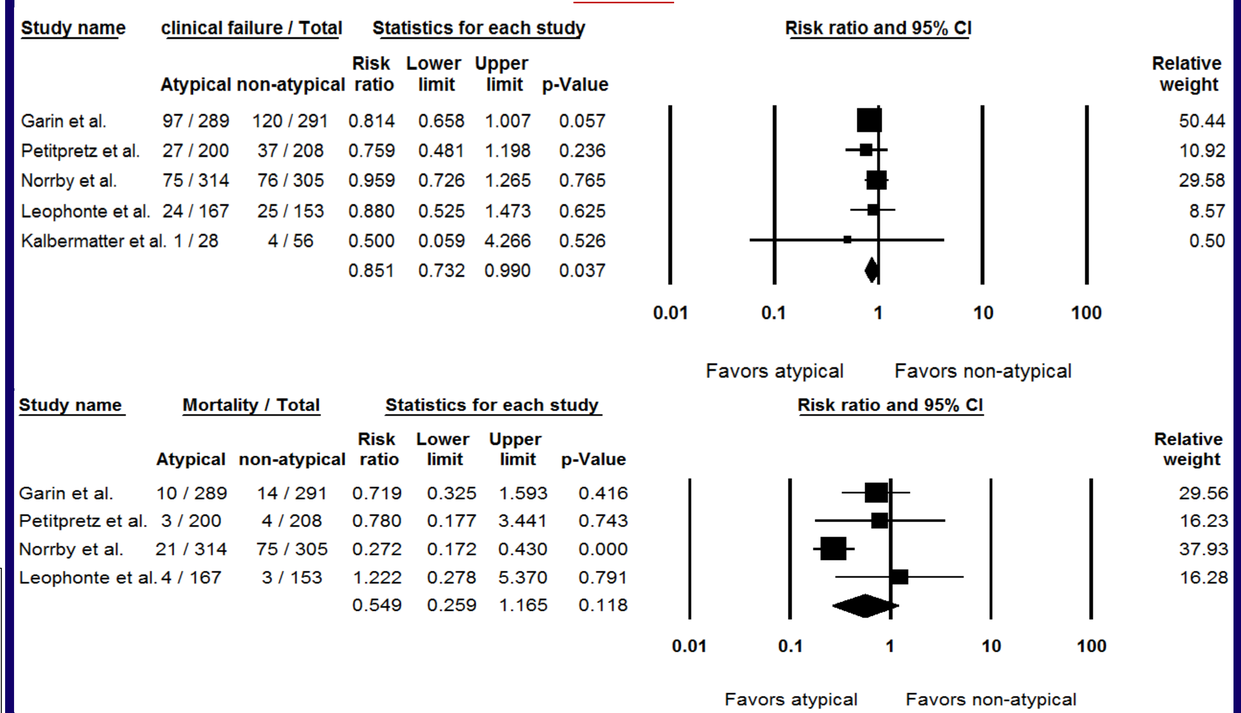
- Studies published as abstracts only
- Studies that deviated from the assigned empiric β-lactam monotherapy (permitted adding empiric atypical bacterial coverage)
- Studies including >25% outpatients and/or >10% of patients with nosocomial pneumonia
- Having conditions other than CAP without reporting separate outcomes for the CAP group.

Data Synthesis and Analysis

- Outcome rates assessed early during treatment or end of treatment were preferred over assessments at follow up post therapy.
- The results from the intention-to-treat analysis was used.
- The RRs with 95% CIs was assessed using fixed-effect models.
- The random-effects model was used when a P-value between studies is less than 0.1 in the Chi² test for heterogeneity).
- We assessed the quality of studies by using the Cochrane risk of bias tool for RCTs (low, unclear or high).



Results



- There were no statistically significant differences between the two groups in rates of bacteriologic failure (RR=0.816, 95% CI 0.523-1.272, *P*=0.369), total adverse events (RR=0.982, 95% CI 0.697-1.383, *P*=0.918), diarrhea (RR=0.746, 95% CI 0.311-1.79, *P*=0.512), and adverse events requiring antibiotic discontinuation (RR=0.83, 95% CI 0.542-1.27, *P*=0.39.

Conclusions

- Our meta-analysis of RCTs is the first to confirm the benefit of empiric atypical bacteria coverage in hospitalized adult patients with CAP (clinical failure rate reduced by ~15%). This supports the current major guideline recommendations.
- The strengths of this meta-analysis relies on the stringent criteria for study inclusion, which makes it very innovative, increases its clinical relevance, and addresses antibiotic regimens recommended in major CAP guidelines.
- However, some of the difference noted may be due to differences in typical coverage between treatment arms.
- We recommend including empiric atypical coverage for hospitalized (sicker) patients with CAP and then use modern diagnostic testing to exclude atypical pathogens and allow streamlining of therapy.