Short- versus long-duration antimicrobial treatment for exacerbations of chronic bronchitis: a meta-analysis
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CRD summary
This review concluded that short-duration treatment (five days) with antimicrobials appeared as effective as and safer than long-duration treatment (seven to ten days) of patients with acute exacerbations of chronic bronchitis. The authors' conclusions appear likely to be reliable despite a relatively limited search and some potential for selection bias.

Authors' objectives
To evaluate the effectiveness and safety of short (five days) versus long (seven to ten days) duration of antimicrobial treatment of patients with acute exacerbations of chronic bronchitis.

Searching
PubMed and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched up to October 2007. Search terms were reported. References of identified studies were checked. Studies published as abstracts only were excluded.

Study selection
Randomised controlled trials (RCTs) that compared the efficacy and safety of the same antimicrobial agent for short versus long duration in patients with acute exacerbation of chronic bronchitis were eligible for inclusion. The antimicrobial was required to be given at the same dose and administered by the same route in each treatment arm. Both chronic bronchitis and acute exacerbations of chronic bronchitis were defined in the review.

The primary outcomes assessed were treatment success (defined as total cure or partial improvement of symptoms such that no further antimicrobial treatment was required) and drug-related adverse events in both the intention-to-treat and clinically evaluable populations. Secondary outcomes were all-cause mortality, long-term disease-related outcomes, withdrawals, incidence of diarrhoea, treatment success in microbiologically evaluable patients and pathogen eradication.

All included trials assessed oral antibiotics. The antimicrobials assessed were cefixime 400mg/daily, grepafloxacin 400 mg/daily, moxifloxacin 400mg/daily, levofloxacin 500 mg/daily, gatifloxacin 400mg/daily and clarithromycin 1000mg/daily. None of the trials allowed additional antibiotics

Two reviewers independently assessed the studies for inclusion in the review.

Assessment of study quality
Two reviewers independently assessed the trials for validity using a modified version of the Jadad scale. This awarded up to 5 points for the criteria of randomisation, blinding and treatment of withdrawals and drop-outs. Trials with a score of 2 or more points were considered to be good quality.

Data extraction
Two reviewers independently extracted data to permit the calculation of relative risks (RR) with 95% confidence intervals (CI). Where data were reported for multiple time points, the longest post-treatment time was selected for microbiological outcomes.

Methods of synthesis
Pooled relative risks with 95% confidence intervals were calculated using a Mantel-Haenszel fixed-effect meta-analysis unless there was statistically significant heterogeneity, in which case a DerSimonian and Laird random-effects model analysis was used. Heterogeneity was assessed using $I^2$.

Sensitivity analyses were used to explore the effects of excluding trials assessing quinolones subsequently withdrawn for

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safety reasons, a trial with a Jadad score of 2 and a trial assessing different formulations as well as durations of clarithromycin.

A subgroup analysis evaluated trials which enrolled only patients with Anthonisen classification type I or II acute exacerbations of chronic bronchitis.

**Results of the review**

Seven RCTs (n=3,083 patients) were included in the review. The mean sample size was 440 patients (range 217 to 614). All trials were multi-centre and were double-blinded. Jadad scores ranged from 2 to 5 points.

Treatment success in the intention-to-treat population did not differ significantly between the short and long duration treatments (RR 0.99, 95% CI 0.95 to 1.03, 4 RCTs). The clinically evaluable (7 RCTs) and microbiologically evaluable populations (7 RCTs) also showed no statistically significant differences between the groups.

There were statistically significantly fewer adverse events in the short duration treatment groups compared to the long duration groups (RR 0.84, 95% CI 0.72 to 0.97; five RCTs), although there were no differences in the number of withdrawals due to adverse events (four RCTs) or the number with treatment-related diarrhoea (five RCTs). There were also no differences in mortality (four RCTs) or eradication of any of the three bacteria assessed (five RCTs).

Sensitivity and subgroup analyses results did not differ significantly from those of the main analyses.

**Authors' conclusions**

Short-duration treatment with antimicrobials appeared as effective as, and safer than, long-duration treatment of patients with acute exacerbations of chronic bronchitis.

**CRD commentary**

The review question and inclusion criteria were clear. Two relevant databases were searched but the decision to limit the review to trials published in full may have led to the omission of relevant studies and the possible introduction of selection bias. The authors reported using methods designed to reduce reviewer bias and error at all stages of the review process. Trial quality was assessed and the results of the assessment used to inform the synthesis, which appeared appropriate.

The authors' conclusions reflected the results of the review and, despite a relatively limited search, appear likely to be reliable.

**Implications of the review for practice and research**

**Practice**: The authors stated that the recommendations of the guidelines of the European Respiratory Society, in collaboration with the European Society for Clinical Microbiology and Infectious Diseases, that patients with acute exacerbations of chronic bronchitis should be treated with seven to ten days of antimicrobials, may be excessive.

**Research**: The authors stated that there was a need for further research on the long-term outcomes (i.e. the exacerbation-free interval) of short-duration versus long-duration antimicrobial treatment of acute exacerbations of chronic bronchitis.

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