

Reply to Azithromycin: Short Course with Long Duration

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We appreciate the interest in our review of antibiotic duration in hospitalized patients. Drs. Sikkens and van Agtmael comment that drug pharmacokinetics can alter true treatment duration.^{1,2} Specifically, azithromycin has a long half-life in tissues.³ We did not consider pharmacokinetics in our prespecified protocol for study inclusion, nor require that studies compare the same drug between treatment groups. This is consistent with a systematic review of antibiotic duration in community-acquired pneumonia, which included 3 of the 4 studies comparing short-course azithromycin to a longer course of another antibiotic.⁴ Similarly, in a recent pilot study of antibiotic duration in bloodstream infections, only treatment duration was prespecified.⁵ We agree that the differing pharmacokinetics between drugs is a limitation to our findings.

To assess whether the inclusion of studies using short-course azithromycin biased our conclusions, we performed an additional meta-analysis for clinical efficacy excluding the 4 studies that compared azithromycin with another drug. This subgroup

included 9 trials comprising 1270 patients. The overall risk difference was 0.3% (95% CI -2.7%, 3.3%), consistent with the primary findings that short-course antibiotic treatment is non-inferior to long-course antibiotic treatment. None of these 4 studies examined mortality; thus, the meta-analyses for short-term and long-term mortality are unaffected.

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