note that 38.7% of patients in this group received an additional agent during their hospital stay that provided atypical coverage for an average of 4.5 days. The addition of a macrolide, a fluoroquinolone, or doxycycline was accepted as strategy-compliant if the agent was added for medical reasons. Since the study assessed empirical antibiotics only, atypical coverage could be added after the first day of the hospital stay without deviating from the protocol, even in the subgroup referred to as “antibiotic-adherent.” The benefit of beta-lactam monotherapy versus other guideline-recommended regimens has historically centered on the question of whether atypical coverage is beneficial. It would therefore be useful to know the difference in mortality between those in the beta-lactam monotherapy group who did not receive additional antibiotics against atypical pathogens and those who received beta-lactam–macrolide or fluoroquinolone.

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No potential conflict of interest relevant to this letter was reported.


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TO THE EDITOR: In this study, the noninferiority margin was 3 percentage points and the expected mortality was 5%. No clinical rationale for the large noninferiority margin was given. The study ran from February 2011 to September 2013. An article detailing the rationale for the study, but not the noninferiority margin, was published in April 2014, after the study was completed. The original protocol, dated May 20, 2010, had specified a noninferiority margin of 2 percentage points at 28 days, and a final protocol, dated September 21, 2011, which was 7 months after the study had started, amended the margin to 3 percentage points at 90 days. The large noninferiority margin reported in the study is not clinically justified, the statistical rationale was published only after the trial had been completed, and the noninferiority margin and primary end point were changed once the study was under way. This study should be therefore interpreted with caution.

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THE AUTHORS REPLY: Van der Eerden and Piszczek and Partlow mention that 38.7% of patients assigned to the beta-lactam strategy also received non–beta-lactam antibiotics at some time during the beta-lactam–strategy period. The protocol al-