randomization); because agitation may not always coincide with a research assessment, it is likely that even more than 37% had hyperactive delirium. Thus, "dangerous or distressing symptoms of delirium" were common. We agree that the results of the MIND-USA Study do not preclude the possibility that other antipsychotics have beneficial effects in this population, and we continue to view antipsychotics as one of several options when managing agitated delirium, especially in a patient who would be adversely affected by more heavily sedating medications. Nevertheless, because antipsychotic therapy initiated in the ICU is continued at discharge in 25% of cases,[3] we would not routinely use antipsychotics to treat critically ill patients with agitated delirium unless their use is supported by findings from adequately powered randomized trials.

We refer Ishiki et al. to the point above — 37% of the participants in the MIND-USA Study had hyperactive delirium during the trial. Thus, the prevalence of mixed delirium (i.e., hyperactive alternating with hypoactive delirium) in our trial was similar to that observed in the meta-analysis by Krewulak et al.,[4] which showed that the prevalence of delirium in mechanically ventilated ICU patients was 62% (as compared with 48% in the MIND-USA Study, which was conducted in ICUs that used the ABCDEF bundle). Furthermore, the authors found that 11% of ventilated delirious patients had hyperactive, 32% had mixed, and 56% had hypoactive delirium, findings similar to our results. We agree that the sedatives and analgesics used to treat critically ill patients may interact with the effects of haloperidol and ziprasidone. Because of this possibility, potential treatments for delirium should be studied in the context of large randomized, controlled trials, during which differences in outcomes can be confidently attributed to receipt of the trial drug.

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Since publication of their article, the authors report no further potential conflict of interest.

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Prednisone for Prevention of Paradoxical Tuberculosis-Associated IRIS

TO THE EDITOR: The article by Meintjes and colleagues (Nov. 15 issue)[1] on the use of prednisone for the prevention of paradoxical tuberculosis-associated immune reconstitution inflammatory syndrome (IRIS) provides evidence to improve the treatment of persons who are coinfected with tuberculosis and the human immunodeficiency virus. Nevertheless, I have concerns about the inclusion in the trial of patients with a clinical diagnosis of tuberculosis and those with positive findings on smear microscopy. Many nontuberculous mycobacteria have morphologic and structural characteristics[2] that are similar to those of *Mycobacterium tuberculosis* and cause a cavitary tuberculosis-like disease[3] that is similar to tuberculosis. A diagnosis of tuberculosis that is based on smear microscopy methods or clinical manifestations could therefore be a misdiagnosis.

In addition, although antituberculosis medications are usually not effective against nontuberculous mycobacteria, they may be an effective treatment in some patients.[4] As such, the investigators'

approach of enrolling patients with a clinical diagnosis of tuberculosis who had a response to antituberculosis treatment, as a way of ensuring that patients with potentially misdiagnosed tuberculosis were excluded, may not be the best. Future studies should be restricted to patients who have positive findings on culture or molecular tests, since these provide a definitive diagnosis of tuberculosis. This could improve the validity of the trial results.

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

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THE AUTHORS REPLY: In our article, we acknowledged that the inclusion of patients with clinically diagnosed tuberculosis was a limitation, but we noted that a response to therapy was required, which strengthened the likelihood that these patients had tuberculosis. Although we agree with Jones that infection with nontuberculous mycobacteria can mimic tuberculosis and sometimes has a response to antituberculosis therapy, disease due to nontuberculous mycobacteria is uncommon in southern Africa[1,2] except in high-risk groups such as gold miners.[3]

Sputum specimens for mycobacterial testing were obtained at three visits from patients who were able to produce sputum. Of 475 sputum cultures of specimens obtained from 194 patients, nontuberculous mycobacteria were cultured in 6 specimens. However, we considered the nontuberculous mycobacteria in all 6 specimens to be contaminants, since *M. tuberculosis* was also cultured in specimens obtained from 4 of the patients, and the nontuberculous mycobacteria were cultured on a single visit.

In a post hoc subgroup analysis involving patients with a clinical diagnosis of tuberculosis (performed in line with World Health Organization guidance[4]), tuberculosis-associated IRIS developed in 13 of 31 patients in the placebo group and in 6 of 34 patients in the prednisone group (42% vs. 18%; relative risk, 0.42; 95% confidence interval, 0.18 to 0.97). This suggests that the benefit of prednisone extended to patients with a clinical diagnosis of tuberculosis.

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Since publication of their article, the authors report no further potential conflict of interest.

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- **A letter can be signed by no more than three authors.**