

parisons should merely be considered exploratory or hypothesis-generating [6].

Moreover, because of the incompleteness of data, especially regarding potential confounding variables, logistic regression analyses to adjust for baseline imbalances cannot be adequately performed. Therefore, unraveling the relative contribution of intrinsic TB susceptibility, other immunosuppressive medication, comorbidities, and the TNF- α antagonists to the development of TB and the other events is impossible with data from the FDA-AERS database. Because of the major inconsistencies in Wallis et al. [1], and the limitations inherent to data in the FDA-AERS database, the conclusions of the article are not supportable.

Acknowledgment

Conflict of interest. T.F.S. is an employee of Centocor, an operating company of Johnson & Johnson. Centocor is the manufacturer of Remicade (infliximab).

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Reply to Schaible

SIR—Schaible [1] is correct that our original analysis [2] improperly included cases arising outside of the United States. The Adverse Events Reporting System (AERS) data that we obtained under the Freedom of Information Act came from the US Food and Drug Administration essentially without guidance or instruction. We hope that other investigators using this invaluable resource will benefit from our error and avoid this mistake in their research. A revised analysis of these data appears elsewhere in this issue of *Clinical Infectious Diseases* [3]. As it indicates, the difference between infliximab and etanercept persists for tuberculosis (TB) and several other granulomatous infections after the removal of data for foreign cases. Furthermore, this difference is amplified when one focuses on the initial 90 days of anti-TNF therapy. Accelerated onset of TB is closely linked to increased overall TB risk for other immunosuppressive conditions, such as AIDS. Time from initiation of anti-TNF therapy to onset of TB is a robust parameter that is unlikely to be compromised by the uncertainties that are inherent in other aspects of the AERS database. We therefore believe that our conclusion—that the risk of reactivation of TB is greater with infliximab than with etanercept—is correct.

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Conflict of interest. R.S.W. has served as a consultant for Amgen and is the recipient of a research grant from Wyeth. M.B. and J.W. are former employees of Zynx Health, a subsidiary of the Cerner Corporation. Zynx Health provides consulting services to biotechnology and pharmaceutical companies, including Amgen, which provided grant support for the original study [1]. D.B.: No conflict.

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Tuberculosis Cases Associated with Infliximab and Etanercept

SIR—We write with regard to the article “Granulomatous Infectious Diseases Associated with Tumor Necrosis Factor Antagonists” by Wallis et al. [1]. This article makes important contributions to the scientific literature about the infectious complications, particularly tuberculosis (TB), associated with these effective biologic agents. The US Centers for Disease Control and Prevention (CDC; Atlanta, GA) anticipates that this issue will have emerging public health importance as these agents are employed more widely. Wallis and colleagues have reviewed the US Food and Drug Administration (FDA) adverse events database and have shown that, on a rate basis, more TB cases are associated with infliximab than with etanercept. Furthermore, they found that the onset of TB in these cases occurs sooner after drug administration with infliximab than with