

Dr Lurie and Colleagues Reply

**To the Editor:** We thank Dr Ishii and colleagues for their comments. Although chronic infections might be associated with psychiatric disorders (eg, depression with tuberculosis<sup>1</sup> and HIV<sup>2</sup>), our analysis focused on antibiotic exposure more than 1 year before psychiatric diagnosis. Our results were persistent even for last prescriptions 5–10 years prior to the index date. Thus, use of a lag period in this way is expected to minimize any association with current active infections or current exposure to cytokines. This analysis was performed in order to reduce reverse causality, in which patients with an undiagnosed underlying psychiatric condition might have higher risk for infectious conditions (as suggested by Seminog and Goldacre<sup>3</sup>). Of note, our analysis was adjusted for the number of infectious events, further reducing possible bias due to recurrent exposure to high levels of proinflammatory cytokines. The increased risk for depression and anxiety with increasing antibiotic prescriptions (even below 5 prescriptions) further supports the possibility of a primary antibiotic effect rather than the effect of the infectious event.

In addition, cytokines were reported to be involved not only in anxiety and depression, but also in psychosis and schizophrenia.<sup>4</sup> This association was not found in our analysis, which adds to the evidence of differential role of antibiotics, rather than to the role of cytokines.

There is no doubt that prescribing antibiotics for the right indications saves lives and prevents significant morbidities. However, both physicians and patients should better understand the possible risks and benefits of antibiotic use, taking into account mental health implications.

REFERENCES

1. Yen YF, Chung MS, Hu HY, et al. Association of pulmonary tuberculosis and ethambutol with incident depressive disorder: a nationwide, population-

- based cohort study. *J Clin Psychiatry*. 2015;76(4):e505–e511.
2. Ciesla JA, Roberts JE. Meta-analysis of the relationship between HIV infection and risk for depressive disorders. *Am J Psychiatry*. 2001;158(5):725–730.
3. Seminog OO, Goldacre MJ. Risk of pneumonia and pneumococcal disease in people with severe mental illness: English record linkage studies. *Thorax*. 2013;68(2):171–176.
4. Miller BJ, Buckley P, Seabolt W, et al. Meta-analysis of cytokine alterations in schizophrenia: clinical status and antipsychotic effects. *Biol Psychiatry*. 2011;70(7):663–671.

Ido Lurie, MD<sup>a,b</sup>  
ido.lurie@gmail.com  
Yu-Xiao Yang, MD, MSCE<sup>c,d,e</sup>  
Kevin Haynes, PharmD, MSCE<sup>d,e</sup>  
Ronac Mamtani, MD, MSCE<sup>d,e,f</sup>  
Ben Boursi, MD<sup>a,c,d,e,g</sup>

<sup>a</sup>Tel-Aviv University, Tel-Aviv, Israel

<sup>b</sup>Shalvata Mental Health Center, Hod Hasharon, Israel

<sup>c</sup>Division of Gastroenterology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia

<sup>d</sup>Center for Clinical Epidemiology and Biostatistics, Perelman School of Medicine at the University of Pennsylvania, Philadelphia

<sup>e</sup>Department of Biostatistics and Epidemiology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia

<sup>f</sup>Division of Hematology/Oncology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia

<sup>g</sup>The Integrated Cancer Prevention Center, Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel

**Potential conflicts of interest:** Dr Haynes is an employee of Anthem Healthcare. Drs Lurie, Yang, Mamtani, and Boursi have no relevant conflict of interest to declare.

**Funding/support:** The work was supported by the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health (NIH), through grant UL1TR000003. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

*J Clin Psychiatry* 2016;77(12):e1654  
dx.doi.org/10.4088/JCP.16lr11074a

© Copyright 2016 Physicians Postgraduate Press, Inc.

It is illegal to post this copyrighted PDF on any website.