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## Analysis of Mortality in Mental Disorders-Reply

**Elizabeth Reisinger Walker, PhD, MPH, MAT,**

Department of Health Policy and Management, Rollins School of Public Health, Emory University,  
1518 Clifton Road NE, Atlanta, GA 30322

**Robin E. McGee, MPH, and**

Department of Behavioral Sciences and Health Education, Rollins School of Public Health, Emory  
University

**Benjamin G. Druss, MD, MPH**

Department of Health Policy and Management, Rollins School of Public Health, Emory University

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Dr. Raven highlights the importance of developing accurate population-based estimates of excess mortality among people with mental disorders. She raises several methodological issues that are relevant to developing estimates of disease burden in general and to understanding excess mortality in individuals with mental disorders in particular.

The letter notes concerns about generalizing from meta-analytic findings of elevated relative risk of mortality to population-based estimates of excess mortality. This potential issue applies to all studies that seek to develop population estimates from observational data.<sup>1</sup> While narrowing inclusion criteria may reduce heterogeneity, it may also introduce other biases into estimates. For instance, many community-based mortality studies do not include individuals with the most severe disorders or institutionalized and marginalized populations; thus including only these studies could result in underestimation of excess mortality. To address the issue of sample heterogeneity, we chose to use broad inclusion criteria, and then present aggregate estimates of mortality risk alongside estimates stratified by key parameters including psychiatric diagnosis. This is an established approach that has been used in public health studies that have employed meta-analysis to estimate the impact of a wide range of risk factors on excess mortality.<sup>2</sup>

Dr. Raven also takes issue with using models with minimal adjustment (e.g. age, sex) rather than fully adjusted estimates among studies that reported risk ratios. Studies of excess mortality seek to address the counterfactual question: how many fewer deaths would occur in the absence of mental illness? In this relationship, factors such as chronic physical disorders, smoking, and low socioeconomic status are not confounders; rather, they represent likely steps in the pathway between mental illness and early mortality. Also, while Dr. Raven proposes that treated individuals may be at elevated risk of mortality because they are sicker,

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**Corresponding Author:** Elizabeth Reisinger Walker, Telephone: 404-712-8527, Fax: 404-727-9198, ereisin@emory.edu.

**Co-authors:** Robin E. McGee; robin.mcgee@emory.edu

Benjamin G. Druss; bdruss@emory.edu

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it is equally likely that effective mental health or medical care is an important factor mitigating excess mortality burden. We believe that more research is needed to test how clinical, behavioral, and social factors mediate excess mortality,<sup>3</sup> as well as the potential impact of treatment on reducing that burden.

Our study's findings are consistent with other recent reviews of excess mortality related to mental disorders.<sup>4</sup> Notably, updated estimates for the 2010 Global Burden of Disease study using natural history models have highlighted that the population-based mortality burden of mental disorders is far greater than had previously been calculated using cause-specific methodologies.<sup>5</sup> We recognize that all of these estimates must be interpreted in light of the limitations discussed above. We would argue, however, that it is both appropriate and necessary to use the existing literature to provide comprehensive estimates of excess mortality due to mental disorders. These estimates provide a first step towards addressing this public health crisis.

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