Published in final edited form as:

Arch Intern Med. 2011 June 13; 171(11): . doi:10.1001/archinternmed.2011.221.

Depression and Type 2 Diabetes Mellitus: A Call to Explore the Common Cause Hypothesis

Briana Mezuk, PhD

Department of Epidemiology and Community Health, Virginia Commonwealth University School of Medicine, Richmond, VA (bmezuk@vcu.edu).

I read the recent article by Pan and colleagues¹ with great interest. Their findings using the Short-Form 36 Health Status Survey suggest that even mood disturbances that do not require clinical intervention are predictive of diabetes. This interpretation, combined with the counterintuitive finding that nonsevere depression was similarly, and potentially more strongly, associated with diabetes risk than severe depression reported in another recent article,² begs the question(s): What *is* it about depressed mood, regardless of severity, that predicts diabetes? Is there some omitted confounder that could explain this finding? The “Patient Perspective” that accompanied the recent article by Campayo and colleagues² hints at a potential candidate: stress. The woman described in this vignette experienced both a major life event—widowhood—and complicated bereavement prior to onset of diabetes. Stressful life events are a well-documented cause of depression.³ Recent work on the physiologic consequences of stress (canonized in concepts such as allostatic load) suggests stress can also increase the risk of physical health conditions in later life.⁴ If stress, rather than depression, is the true causal factor, this would explain the consistent finding from epidemiologic research that antidepressant use is not associated with lower risk of developing diabetes (and may, as reported by Pan et al¹ and others, be associated with an elevated risk of diabetes). Other depression treatment trials in the context of medical conditions have also failed to demonstrate reduced risk of medical conditions or complications, despite achieving psychopathologic improvements.⁵ If stress promotes development of both depression and diabetes,⁶ this suggests that treating depression without addressing the underlying sources of adversity and stress will not influence the risk of medical conditions subsequent to depression.

It is clear that we need to move beyond characterizations of comorbid depression-diabetes and begin testing etiologic models of how this phenomenon arises. These models must be flexible and creative to account for counterintuitive findings and acknowledge that the salience of various etiologic mechanisms may change over the lifespan.

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Correspondence: Dr Mezuk, Department of Epidemiology and Community Health, Virginia Commonwealth University School of Medicine, PO Box 980212, Richmond, VA 23298 (bmezuk@vcu.edu).

Financial Disclosure: None reported.

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