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The bipolar–depressive continuum in the National Epidemiologic Survey on Alcohol and Related Conditions

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To the Editor:

We thank Dr. Weinstock and colleagues for noting our recent article on differences in depressive episodes in major depressive disorder (MDD), bipolar I disorder (BD-I), and bipolar II disorder (BD-II) analyzing data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) (1). In our study we documented the existence of a linear trend in the severity of major depressive episodes: highest for BD-I, followed by BD-II, and lastly by MDD. As Dr. Weinstock and colleagues point out, our conclusions converge with those of their studies (2, 3) and with those from other groups whose work also draws on NESARC data (4).

It is reassuring that the conclusions of our studies converge despite addressing two complementary but rather different questions. Dr. Weinstock's analyses focused on the differences in probability of DSM-IV depression symptom endorsement after adjusting for disorder severity across unipolar and bipolar depressive disorders (2, 3). By contrast, because we were interested in the nosological question of whether different mood disorders arrayed along a dimension, we decided to move beyond symptoms and examined the existence of linear trends in BD-I, BD-II, or MDD across a broad range of variables, including sociodemographic characteristics, clinical characteristics, and lifetime treatment

patterns. Our results, which remained significant when stratifying the analyses by gender and by race/ethnicity, strongly supported the existence of a spectrum of severity.

Our analyses were also complementary regarding sampling selection. Dr. Weinstock's group included individuals based on endorsement of lifetime depressed mood and/or anhedonia regardless of whether they met DSM-IV criteria for MDD, BD-I, or BD-II. Consistent with the focus of our analyses, we used DSM-IV diagnoses as inclusion criteria, as we were interested in contributing data to the discussion of the DSM-5 mood disorders classification. Despite these differences in sampling selection, our conclusions pointed in the same direction.

The adjustment for other covariates was also complementary in the analyses conducted by the two groups. To adjust for the severity of depressive symptomatology when comparing symptom differences between bipolar and unipolar depression, Dr. Weinstock's group relied on item response theory methods. As our focus was broader, we were concerned about the effect of other potential confounders beyond severity of depression, including unmeasured confounders. Therefore, in addition to adjusting for number of symptoms of depression, we adjusted for the Short Form Health Survey–12, a global reliable and valid impairment measure in population surveys that takes into account the severity of depression as well as the impact of other disorders (5).

Finally, our analyses were complementary in the statistical approach to multiple comparisons. Dr. Weinstock and colleagues used the Benjamini–Hochberg correction. They raise the concern that, because we did not apply a similar correction to our analyses, our analyses run the risk of inflating type I error. Because we conducted 290 comparisons at an $\alpha = 0.05$, we could expect $290 \times 0.05 = 14.5$ to be significant simply by chance. We found that 192 were. A test of binomial proportions indicates that the probability of having at least 192 significant tests out of 290 is approximately 1 in 10000000. Therefore, our pattern of results is highly unlikely to be due to chance.

We believe that, overall, the findings of these groups of studies consistently suggest the existence of a continuum of depressive clinical syndromes that would be better characterized by dimensional approaches. In this regard, severity is being considered for inclusion as a specifier in upcoming diagnostic classifications (6). We eagerly await studies with epidemiological, clinical or biological data that may contribute to clarify the structure of mood disorders.

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