Uncomplicated depression is normal sadness, not depressive disorder: further evidence from the NESARC

We write to update the results of our recent paper (1) suggesting that uncomplicated depressive episodes are not in fact disorders and should be excluded from the diagnosis of major depressive disorder (MDD). We also address some concerns expressed about our claims.

The concept of “uncomplicated depression” is essentially a generalization to all stressors of the “bereavement exclusion” that appeared in DSM-IV (and was eliminated in DSM-5). Uncomplicated depression is defined as a response to a stressor that satisfies current DSM-5 five-symptoms-for-two-weeks criteria for MDD but is better explainable as a normal distress response, as evidenced by the fact that it lasts no longer than six months and does not include any of the following pathosuggestive symptoms: marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, and psychomotor retardation. Uncomplicated episodes thus contain only depressive symptoms common in general distress reactions (e.g., sadness, moderate withdrawal or role impairment, decreased interest in usual activities, insomnia, decreased appetite, difficulty concentrating, fatigue).

THE INITIAL STUDY AND ITS REPLICATION

In our recent paper (1), using longitudinal data from the Epidemiological Catchment Area (ECA) study (2), we found that in those with lifetime uncomplicated MDD at baseline, the one-year recurrence rate (3.4%) was not significantly different from the background MDD incidence rate in those who never previously had MDD (1.7%), but both were dramatically lower than recurrence rates in other (“complicated”) MDD (14.6%). Thus, in terms of recurrence risk, uncomplicated MDD is different from other MDD but indistinguishable from no-MDD-history. We concluded that “consideration should be given to eliminating uncomplicated episodes as a class from MDD diagnosis”.

However, that study had several limitations. We (3) therefore replicated and broadened the analysis using an entirely different, more recently collected longitudinal community data set – the National Epidemiological Survey on Alcohol and Related Conditions (NESARC, 4) – that allowed a more clinically meaningful 3-year follow-up window and use of an expanded set of three clinically important validators (depression recurrence, suicide attempt, generalized anxiety disorder (GAD)), as well as other advantages in measuring impairment and clinical significance. Due to data-set

limitations, only single-episode uncomplicated cases could be evaluated in this study.

The results were that people with single-episode uncomplicated major depression had rates during follow-up of MDD recurrence (6.9%), GAD (4.3%), and suicide attempt (0.1%) that were not significantly different from background rates for those who never had MDD (6.1%, 2.7%, and 0.3%, respectively), but were dramatically and significantly lower than rates for both single-episode complicated cases (19.5%, 7.8%, and 0.8%, respectively) and multiple-episode cases (27.1%, 11.2%, and 1.7%, respectively) (3). The results were not explainable by group differences in severity or treatment rates. Given the replication’s success, we concluded that uncomplicated MDD is a benign condition that is typologically distinct from the rest of MDD, thus supporting our earlier thesis that uncomplicated MDD is in fact a form of normal sadness.

However, in a commentary on the replication, Maj (5) expressed some concerns about the evidence provided by our study. These previously unaddressed concerns are now considered.

CONCERN 1: QUALITY OF REMISSION WAS NOT EVALUATED

In MDD, the quality of remission, and especially the number of residual depressive symptoms, is important both because subthreshold depression is harmful in itself and such symptoms predict recurrence and may indicate a latent pathology. Yet, Maj notes, our studies did not report the residual symptom levels among those not experiencing MDD during the follow-up. To address this concern, we analyzed the average number of MDD symptom groups experienced during follow-up by individuals in each of our baseline MDD groups who did not have recurrences during the follow-up period.

In each of the four baseline wave 1 lifetime MDD history groups, the mean number of residual symptom groups experienced by those who had no wave 2 recurrences during the 3-year follow-up period was: 0.37 (95% CI: 0.35-0.39) for the no lifetime MDD history group (N=25,514); 0.49 (95% CI: 0.34-0.65) for the lifetime uncomplicated single episode group (N=379); 0.75 (95% CI: 0.65-0.85) for the lifetime complicated single episode group (N=1,756); and 1.00 (95% CI: 0.91-1.10) for the lifetime multiple episodes group (N=1,876).

Thus, there is not a significant difference in the number of symptoms during follow-up between the no-MDD-history group and the uncomplicated single episode MDD group. There is no “residual symptom” problem indicating implicit pathology or risk of recurrence among the uncomplicated group above the non-MDD baseline. In contrast, the complicated single episode and multiple episode groups both experienced significantly higher residual symptom levels than the no-history and uncomplicated single episode groups. In sum, recovery in uncomplicated depression generally returns to population baseline levels of depressive symptoms, which is unlike the recoveries of those with other MDD.

CONCERN 2: THE LENGTH OF THE FOLLOW-UP PERIOD WAS TOO SHORT

Maj (5) also argued that the 3-year follow-up may have been too short to detect recurrences in uncomplicated cases because recurrence after recovery can occur after longer intervals. He noted, for instance, that in the National Institute of Mental Health (NIMH) Collaborative Depression Study, the median time to first recurrence of MDD in people who had fully recovered from their index episode was over 4 years (6).

However, the baseline NESARC data used in our study were lifetime MDD data at interview 1. Thus, the duration of the follow-up was not just three years. In fact, many of the individuals classified with lifetime MDD at wave 1 had not had their last MDD episode for some years prior to the wave 1 interview, so the average time interval since recovery was potentially much greater than three years. Thus, to address Maj’s concern, we calculated for each of our MDD groups the average time from the end of the last episode to the wave 1 interview to obtain a more accurate approximation of the time intervals from the last episode to the outcome reported for wave 2.

The mean years of remission prior to wave 1 assessment for each group were: 9.1 (95% CI: 7.9-10.3) for the lifetime uncomplicated single episode group (N=417); 9.1 (95% CI: 8.6-9.6) for the lifetime complicated single episode group (N=2128); and 3.9 (95% CI: 3.6-4.2) for the lifetime multiple episodes group (N=2501).

Thus, the average time from the end of the last episode to the beginning of the wave 2 follow-up period was lengthy, about nine years for both uncomplicated and complicated single-episode cases and about four years for multiple episode cases. This substantial time interval is more than enough for elevated recurrence rates to emerge during the examined 3-year window, and such elevated rates did occur for the single-episode complicated cases but not for the uncomplicated cases at the same 9-year average time since the baseline episode.

CONCLUSIONS

Our recent replication and extension (3) of our earlier results (1) supports the predictive validity of the uncomplicated versus complicated depression distinction across stressors, supplementing a previous study supporting concurrent validity (7). A course with elevated recurrence relative to population baselines is generally considered the single most salient identifying feature of depressive disorder versus normal sadness (8) and a primary rationale for inferring underlying dysfunction (9), yet no such elevation occurs for uncomplicated depression.

The evidence thus supports two conclusions. First, uncomplicated depression is not similar to, and is typologically distinct from, major depressive disorder. Second, given the lack of differences between uncomplicated depression and no history of MDD in crucial negative sequelae including recurrence, suicide attempt, and GAD, uncomplicated depression is best interpreted as an intense normal emotional episode. The additional analyses presented here in response to Maj’s (5) concerns regarding quality of recovery and duration of follow-up substantially strengthen the support for these conclusions.

Jerome C. Wakefield¹⁻³, Mark F. Schmitz⁴

¹Department of Psychiatry, School of Medicine, New York University, 550 First Avenue, New York, NY, USA;

²Silver School of Social Work, New York, NY, USA;

³InSPIRES (Institute for Social and Psychiatric Initiatives – Research, Education and Services), Bellevue Hospital/New York University, New York, NY, USA;

⁴School of Social Work, Temple University, Philadelphia, PA, USA

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