

Issues in Estimating the Course of Rapid-Cycling Bipolar Disorder

TO THE EDITOR: We found the article by Christopher D. Schneck, M.D. et al. (1), published in the March 2008 issue of the *Journal*, to be very informative and useful. The authors presented an excellent real-world naturalistic study, which is difficult to design with regard to methodology. However, we would like to present several inquiries regarding the method and interpretation of the study.

First, we noted that among those patients who completed 1 year of treatment (N=1,191), only 5% (N=58) had four or more episodes at the 1-year follow-up. However, the significant number of dropouts (N=551) may raise concerns, since most of the patients who discontinue therapy are rapid-cycling patients and it is possible that the actual number of these individuals in the study might have been greater than what was observed. It is also possible that the initially enrolled patients and informants could have displayed a recall bias (2), which is reflected by the initial high percentage of rapid-cycling patients. Therefore, at the end of 1 year, the reduction in the percentage of rapid-cycling patients might possibly have been overestimated as a result of these influences.

Second, we would like to suggest that there may have been an influence of comorbidities, such as substance abuse or general medical conditions, which can affect the course of bipolar disorder, including rapid cycling (3).

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Dr. Schneck Replies

TO THE EDITOR: We appreciate the comments by Dr. Bhattacharyya et al. They raise a number of important questions regarding the methodology and statistical analysis used in our study, notably the possibility that we underestimated the prevalence of rapid cycling at the end of the study by including only those patients who completed 1 year of treatment.

To address this issue, we conducted a separate analysis that included all patients who were either stable for 1 year or who

had at least one episode prior to dropping out of the study and compared these results with our original results (Table 1). Patients who were stable when they discontinued the study were not included. Using this method, the relative percentages of patients assigned to the “frequent cycling” category (i.e., two to three episodes per year) decreased from 27% to 22%, and the percentage of patients in the rapid-cycling category (four or more episodes per year) decreased from 5% to 4%. Therefore, it appears that those patients who experienced more mood episodes were not more likely to drop out relative to those patients who experienced fewer episodes.

We agree with Dr. Bhattacharyya et al. that recall bias may have led to the large percentage of reported rapid-cycling patients at the study entry, which we highlighted in our discussion. However, patients’ recall of prior episodes is commonly used in studies of rapid cycling in order to estimate prevalence rates (1, 2) and is consistent with everyday clinical practice. Moreover, it is usually not feasible to independently verify the number of prior episodes. In our study, patient reports of rapid cycling were adequate to predict future cycling and to predict increased cycle frequency while undergoing antidepressant treatment. Thus, the mood instability described by patients retrospectively as rapid cycling appears to be consequential. Additionally, our use of strict DSM-IV criteria to demarcate prospectively observed mood episodes, as well as the model practice procedures employed by the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) psychiatrists, also likely contributed to the decline in cycling rates.

What contribution, if any, did comorbidities play in the development of rapid cycling? The large number of patients enrolled in our study limited the number of variables that could be reliably captured. However, studies examining the role of medical comorbidities (particularly hypothyroidism and gonadal steroid effects) and their relationship to rapid cycling have yielded either negative or equivocal results (3, 4). Studies of substance abuse and its association with rapid cycling have also yielded mixed results. For example, in our earlier study (5), rates of substance abuse among rapid cycling bipolar I and II disorder patients were equivalent (36%), although Kupka et al. (6) found an association between rapid cycling and substance abuse in patients with bipolar I disorder.

The comments by Dr. Bhattacharyya et al. highlight the complexities in studying the course of bipolar disorder in general and in rapid cycling in particular. We hope that future studies using the STEP-BD data set may provide a better understanding of rapid cycling patients over the course of their 4 years in the STEP-BD study.

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TABLE 1. Mood Episodes of Patients

Study	Group									
	Stable		One Episode Per Year		Two to Three Episodes Per Year		Four or More Episodes Per Year		Dropped Out	
	N	%	N	%	N	%	N	%	N	%
Published analysis ^a	409	34	402	34	322	27	58	5	551	32
Separate analysis ^b	409	23	653	38	386	22	67	4	227	13

^a Cycling categories include patients who met criteria and who completed 1 year of treatment.

^b Cycling categories include patients who met cycling criteria at any time, regardless of drop-out status.

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Suicidal Behavior: The Need for Its Documentation in Multiaxial DSM-V Diagnoses

TO THE EDITOR: The recent editorial by Maria A. Oquendo, M.D. et al. (1), published in the November 2008 issue of the *Journal*, calls attention to the fact that the current DSM formulations do not allow suicide risk to be documented as part of a multiaxial diagnosis. Thus, as a result of this absence, suicidal behavior fails to have the prominence that it requires in light of its association with increased risk for future completed suicides and suicide attempts. I am in full agreement with the need to address this important problem, since my previous attempt (2), approximately 25 years ago, to sensitize the scientific community to the same concern in conjunction with the then upcoming revision of DSM-III appears to have had no impact. However, in contrast to the recommendation by Dr. Oquendo et al. to consider suicidal behavior as a separate diagnosis with documentation in a distinct sixth axis, I proposed that “consideration be given to the possibility of including a sixth digit that would call attention to whether axis I or II diagnoses are associated with the presence of suicidal behavior” (2). In retrospect, this approach should also be extended to suicidal behavior associated solely with general medical conditions or axis III diagnoses. I also emphasized the need “to denote single and multiple episodes and to indi-

cate whether the behavior was life-threatening” (2). Nevertheless, the differences between the respective recommendations should not detract from the main focus of efforts toward systematic documentation of suicidal behavior in the DSM-multiaxial system, and hopefully the discussion to determine the best solution will remain open.

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Dr. Oquendo Replies

TO THE EDITOR: We thank Dr. Pomara for the comments on our article. We wholeheartedly agree with the importance of documenting the frequency and lethality of suicidal behavior. For each past suicide attempt, the risk of future suicidal behavior increases (1). Although low lethality attempts do not guarantee that future attempts will be of low lethality, medically dangerous attempts are an ominous indication. The notion of a sixth digit linking a diagnosis to suicidal behavior is intriguing but is perhaps less essential to the key issue, which is the systematic documentation of suicidal behavior in a clinically prominent part of a patient's medical record such that information is not lost.

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