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Classifying episodes in schizophrenia and bipolar disorder: Criteria for relapse and remission applied to recent-onset samples

Keith H. Nuechterlein [a,*], David J. Miklowitz [b], Joseph Ventura [a], Michael J. Gitlin [a], Mitchell Stoddard [a], David Lukoff [c]

[a] *UCLA Department of Psychiatry and Biobehavioral Sciences, 300 UCLA Medical Plaza, Room 2251, Los Angeles, CA 90095-6968, United States*
[b] *Department of Psychology, University of Colorado, Boulder, United States*
[c] *Saybrook Graduate School, San Francisco, CA, United States*

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Abstract

Research on predicting and preventing episodes of schizophrenia and mood disorder lacks consistent, specific definitions of episodes. We present an operational system for identifying relapse, exacerbation, and remission of schizophrenia and bipolar disorder within longitudinal studies that involve repeated symptom assessments. Three major classes of episodic outcome are defined: relapse or significant exacerbation, nonrelapse, and stable, severe persisting symptoms. These major classes are further subdivided to distinguish nine categories of episodic outcome. To examine ease of use, interrater reliability, and validity, the classification system was applied to recent-onset samples of schizophrenia patients ($N=77$) and bipolar mood disorder patients ($N=23$) followed on medication for 9- to 12-month periods. A range of episodic outcomes were distinguished with high interrater reliability. Despite being prescribed continuous medication, 21% of the recent-onset schizophrenia patients and 61% of bipolar patients met criteria for relapse or significant exacerbation during this follow-up period. Predictive relationships support the validity of this system for classifying episodes. A computer program is available to facilitate its use. Use of these explicit definitions of episodes may help to clarify the relationship between episodic outcome and other fundamental domains of illness outcome, particularly other symptom dimensions, work functioning, and social functioning.

Keywords: Outcome; Psychosis; Mania; Brief Psychiatric Rating Scale; First episode

Several key dimensions of outcome have been delineated in schizophrenia and mood disorders, including episodic symptoms, negative or deficit symptoms, functional outcome, and subjective experience (Strauss and Carpenter, 1972, 1978; Andreasen, 1982; Carpenter et al., 1988; Harrow et al., 1990; Brekke and Long, 2000). Reliable, standardized, and widely accepted systems for classifying different aspects of outcome are unfortunately not available, making it difficult to compare results across studies. Although all dimensions of outcome in these disorders could benefit from further measurement developments, we focus in this article on a new system for classifying episodic outcomes.

Many studies of schizophrenia have emphasized the episodic nature of psychotic symptoms (Strauss and Carpenter, 1972; Zubin and Spring, 1977; Strauss and Carpenter, 1978; Shepherd et al., 1989), and an episodic course has long been considered characteristic of

* Corresponding author. Tel.: +1 310 825 0036; fax: +1 310 206 3651.
E-mail address: keithn@ucla.edu (K.H. Nuechterlein).

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mood disorders (Coryell and Winokur, 1982; Frank et al., 1991). In longitudinal studies of illness course and in treatment studies, the occurrence of relapses has been the most common index of symptomatic outcome, yet few clinicians or researchers use the same operational definition (Falloon, 1984; Frank et al., 1991; Lader, 1991; Gilbert et al., 1995). This situation greatly impedes identifying commonalities across studies in the contributors to episodes of psychiatric disorders.

Falloon (1984) highlighted the conceptual and methodological disarray concerning the term "relapse" in schizophrenia. After surveying 15 treatment outcome studies from the 1970s, Falloon found that no two studies used the same relapse criteria. Furthermore, the designation of relapse was tied to a host of different variables: "Admission to a psychiatric hospital unit, increase of medication, worsening of florid symptoms of schizophrenia, worsening of any psychiatric symptoms, and threatened clinical exacerbations..." (Falloon, 1984, p. 295). Although many of these early studies included symptom ratings, the relapse definition was almost always a global clinical one rather than one tied to specific changes on rating scales. Critical psychometric considerations (e.g., interrater reliability) were also not addressed for the relapse definitions in these studies.

The situation has improved somewhat since Falloon's (1984) review, but diverse and relatively subjective definitions continue to be widely used. Gilbert et al. (1995), for example, found that one-third of the studies that they reviewed regarding neuroleptic discontinuation among schizophrenic patients provided no definition of relapse, while another one-sixth of the studies simply used resumption of active medication as the definition. Although the more recent studies sometimes included specific symptom rating criteria for relapse or significant exacerbation, the rating instruments and the criteria varied markedly.

Prien et al. (1991) and Frank et al. (1991), representing a task force of the MacArthur Foundation Research Network on the Psychobiology of Depression, noted that the literature on mood disorders is characterized by a parallel lack of consistent use of terms such as relapse, remission, recovery, and recurrence. They proposed several quantitative, operational definitions of these terms for depressive disorders. Similarly, in the NIMH Collaborative Study on the Psychobiology of Depression, the return of a full manic or depressive syndrome by Research Diagnostic Criteria (RDC) was used as the relapse criterion for bipolar disorder (Keller et al., 1993; Winokur et al., 1994). However, the implementation of these recommendations in other studies of mood disorder has been inconsistent. As shown in Table 1, examples of criteria drawn from studies of the short-term outcome of schizophrenia help to illustrate the variety of ways in which the terms "relapse" and "psychotic exacerbation" have been used. Investigators have increasingly incorporated specific symptomatic criteria but have often then combined operational criteria for symptom changes with global clinical judgments.

For example, Vaughn et al. (1984) used a combination of the Psychiatric Assessment Scale (PAS; Krawiecka et al., 1977), the Present State Examination (PSE; Wing et al., 1974), and other clinical data to divide outpatient outcomes into relapse, exacerbation, improved, remission, and unchanged high persisting symptoms categories. Final judgments regarding outcome classification, however, involved consideration of qualitative clinical information as well as the PAS and PSE ratings. Final judgments regarding outcome classification, however, involved consideration of qualitative clinical information as well as the PAS and PSE ratings. Similar mixtures of operational rating scale criteria and clinical judgment criteria have been used by Hogarty et al. (1988, 1991) and Marder et al. (1987). The combination of objective and subjective procedures may lead to low reliability of outcome classifications and disagreement in findings across studies.

A few investigators have used relapse definitions that were wholly based on specific symptomatic ratings. Kane et al. (1983), like Marder and Hogarty and their associates, used the Brief Psychiatric Rating Scale (BPRS, Overall and Gorham, 1962) to define psychotic relapse, but with a different specific cutoff. Lieberman et al. (1987) used a combination of increases on individual symptom items, increases in the sum of these items, and duration of symptom change to define relapse, focusing on items from the Schedule for Affective Disorders and Schizophrenia-Psychosis and Disorganization (SADS-PD; Spitzer et al., 1978) rather than the BPRS.

Thus, despite movement to incorporate symptom rating criteria into definitions of exacerbation and relapse, most researchers have continued to use clinical judgments as the final and decisive step in classifying episodic outcomes. While clinical judgment clearly has an essential place in clinical treatment decisions, use of more explicit operational criteria for research purposes would aid professional communication and comparison of results. Furthermore, available criteria do not make explicit distinctions among the symptom patterns of patients who do not show significant symptom exacerbations or relapses. Symptom patterns that involve full remission, improvement in psychotic or affective symptoms over time, subsyndromal exacerbations, or stable low levels of persisting symptoms are usually not ex-