Title: Number of episodes in bipolar disorder: The case for more thoughtful conceptualisation and measurement

Running title: Number of episodes in bipolar disorder

Authors: Hailey Tremain*, Kathryn Fletcher¹ and Greg Murray¹

Author details
¹Centre for Mental Health, Faculty of Health Arts and Design, Swinburne University, Melbourne Australia

* Correspondence, Hailey Tremain htremain@swin.edu.au, c/o Greg Murray PO Box 218 John St Hawthorn VIC, 3122 Australia
Kathryn Fletcher kfletcher@swin.edu.au
Greg Murray gwmurray@swin.edu.au

Acknowledgements
HT is supported by an Australian Government Research Training Program Scholarship. GM receives funding from the National Health and Medical Research Council for a related project, grant number APP1102097. Neither funding body had input into the design or conduct of this study or the preparation of this manuscript.

Conflicts of Interest
This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/BDI.12872

This article is protected by copyright. All rights reserved
The authors do not have any conflicts of interest to report.

**Data Sharing**

Data sharing is not applicable to this article as no new data were created or analysed in this study.

**Abstract**

Objectives: Number of mood episodes (NoE) may be an important prognostic indicator in bipolar disorder, with implications for treatment. However, NoE has been conceptualised and measured inconsistently throughout the literature. This review examines the construct of NoE in bipolar disorder, with the aim of enhancing its conceptualisation and measurement.

Methods: A critical evaluation of literatures on important correlates of NoE, conceptually and phenomenologically overlapping features, and previous studies considering and measuring this construct was undertaken.

Results: The literature indicates that despite frequent use, NoE has been inconsistently defined and measured. Multiple studies have linked NoE with important clinical factors, including relapse, functioning, cognitive impairment, and the effectiveness of both pharmacological and psychosocial interventions, yet conclusions are limited by its inconsistent treatment. Additionally, it seems evident that that NoE may best be treated as a fuzzy construct (rather than precise figure), with yet to be defined overlaps with clinical variables such as age at onset and severity. Attempts to measure this construct have varied in comprehensiveness and structure.

Conclusions: The NoE construct may have important implications for individuals with bipolar disorders. However, more consistent and systematic definition and assessment of NoE is required to advance this literature and clarify its role. Recommendations aimed at advancing the conceptualisation and the measurement of NoE are provided.

Conceptualisation may be advanced by considering and exploring relationships between NoE and factors with which it overlaps, while measurement may best be improved with increased consistency and balancing accuracy with feasibility.

**Key words**

Bipolar
Bipolar Disorder/classification*
Bipolar Disorder/psychology

This article is protected by copyright. All rights reserved
The number of affective episodes an individual with bipolar disorder experiences is an important and under-recognised consideration in research and clinical practice. Accumulating mood episodes may have significant implications for individuals’ illness experience, prognosis and treatment. The aim of this critical review is to highlight the potential clinical relevance of the construct of ‘number of episodes’ (NoE) experienced by individuals with bipolar disorder (BD), and encourage more careful conceptualisation and measurement of this construct. This review will begin with a discussion of important correlates of NoE in BD. The following section highlights the relevance of the NoE construct to investigations of clinical stage and neuroprogression in BD. Next, the review focuses on conceptual issues surrounding NoE, followed by an outline of key issues relating to efforts to measure NoE. Finally, recommendations for improving both the conceptualisation and measurement of NoE in BD are offered.

**Correlates of number of episodes**

NoE may be an important prognostic indicator in BD. Multiple studies have demonstrated associations between NoE and a range of important outcomes amongst people with BD. This section will examine the key correlates of NoE in BD, including its relationship to clinical and functional outcomes, and to response to psychosocial interventions and pharmacotherapy. Important caveats to interpreting these data are examined in a later section; therefore, in this section, NoE will be treated as a unified, quantifiable construct, reflecting its treatment in the literature. Issues with this approach will be discussed thereafter.

**Longitudinal illness course.** Accumulating episodes may increase risk of relapse and recurrence in BD. For example, a narrative review concluded that across studies, NoE is a
reliable predictor of relapse in BD. More recently, within two longitudinal studies, NoE predicted risk of recurrence in the subsequent two- or four-year periods. Similarly, a large naturalistic study reported an increased risk of relapse leading to hospitalisation with each subsequent episode. These findings were confirmed in a large epidemiological study, wherein NoE predicted further hospitalisations.

**Illness features.** NoE may also be related to worsening symptoms and illness features. In the large Systematic Treatment Enhancement Program (STEP-BD) sample, higher NoE at baseline was associated with a range of clinical factors, including more chronic and severe symptoms, higher levels of disability, and lower quality of life. These differences remained after 12 months of evidence-based pharmacological and psychological interventions. Subsequent analyses of the STEP-BD sample showed that those who had experienced at least ten mood episodes were slower to recover from episodes and more likely to report symptoms of sadness, anhedonia, euphoria, irritability and anxiety between episodes. In an epidemiological study, NoE was associated with a higher number of current and lifetime psychiatric and medical comorbidities. Studies have also reported higher rates of suicidality and higher levels of perceived stigma for those with higher NoE.

**Functioning.** Individuals’ functioning also appears to worsen with accumulating mood episodes. For example, past total, manic and depressive NoE have been shown to predict global functioning in those with BD. As noted earlier, Magalhaes, et al. found that in the STEP-BD sample, having experienced more than ten episodes was a significant predictor of disability and reduced functioning. Similarly, the large European Mania in Bipolar Longitudinal Evaluation of Medication (EMBLEM) study demonstrated that significantly fewer individuals reporting multiple episodes achieved functional recovery than those who had experienced a single episode. Additionally, in the National Epidemiological Survey on Alcohol and Related Conditions (NESARC) study, NoE was associated with increased likelihood of cross-sectionally reporting permanent disability, as well as prospective functional decline.

Specific domains of functional impairment have been linked with NoE. For example, in one study comparing functioning between those with multiple episodes versus one prior episode, the former group had worse functioning across the domains of autonomy, work, interpersonal relationships and cognitive functioning, and these differences were consistent over 12 months. Similar domains of impairment were reported in the NESARC study; higher rates of unemployment and role impairment and poorer social functioning at baseline.
were associated with NoE. Within this study, prospective declines in these functional domains were predicted by NoE, across several years. In a small outpatient study, work and family role disability was predicted by number of manic episodes, and social role disability was predicted by number of depressive episodes. A further study demonstrated that for each manic episode experienced, participants were 1.4 times more likely to report poor work adjustment.

Findings are less straightforward in relation to the impact of NoE on cognitive functioning, partly due to methodological heterogeneity and study limitations. Multiple studies have linked NoE, especially manic episodes, with greater cognitive impairments, reporting differences across cognitive domains including executive function, psychomotor speed, cognitive flexibility, verbal processing and memory. However, in a cross-sectional study, Nehra and colleagues reported poorer cognitive performance in a first episode group, relative to a multiple episode group. A few explanations may illuminate this inconsistency. In the latter study, those with multiple episodes had experienced an average of fewer than two manic episodes, lower than that reported in other studies (as shown in a later section). Additionally, less time spent euthymic since their last episode and increased likelihood of psychotic symptoms in the first episode group may explain their poorer cognitive performance, given associations between these characteristics and cognitive functioning. A related finding is that individuals’ risk of developing dementia appears to increase with accumulating NoE in BD, with one study reporting that each episode incurs a 6 per cent increase in likelihood of developing dementia. Taken together, despite some inconsistencies, there appears to be an association between NoE and poorer cognitive functioning.

**Treatment response.** NoE has been linked with reduced treatment response, however the type of treatment appears important. For example, a meta-analysis of Olanzapine trials found that those with fewer NoE were consistently more likely to respond to Olanzapine when manic or depressed, and experienced improved relapse rates. Similarly, some studies have reported superior response to Lithium during mania in those with fewer NoE, and others have reported superior prophylaxis with fewer NoE. However, a comprehensive systematic review and subsequent meta-analysis failed to support these findings, suggesting that the weight of the evidence indicates that NoE has little role in the effectiveness of Lithium. Differences in findings may be attributable to differences in sample characteristics and outcome measures; for example, treatment adherence was not controlled,
and participant mood states and outcomes varied. Conclusions for antidepressant medications are also unclear, with some studies suggesting that NoE predicts response to antidepressants and others finding no differential effectiveness based on NoE. Again, these differences may reflect uncontrolled sample characteristics (polytherapy, NoE distribution and mood states). It appears that some medications may be more effective for those with fewer NoE, while differential effectiveness is not evident for others. NoE has also been associated with reduced medication adherence, further impacting treatment outcomes and research conclusions.

Turning to psychotherapy outcomes for BD, a more consistent pattern of findings in relation to NoE emerges, with a handful of studies comparing intervention outcomes based on NoE. For example, post hoc analyses of Scott et al.’s pragmatic effectiveness trial of cognitive behavioural therapy (CBT) suggested that only those with 11 or fewer episodes benefitted. Similarly, post hoc analyses of a group psychoeducation trial showed that, following psychoeducation, those with greater NoE reported less time to recurrence and more time spent in manic, hypomanic, mixed and depressive episodes. In another psychoeducation trial, individuals were classified into stages of illness and those considered to be within an earlier stage of illness (with lower NoE) experienced longer time to recurrence following caregiver psychoeducation, while no benefits were reported for those with higher NoE. Results from the STEP-BD trial of psychosocial interventions are consistent with these data. For example, those with lower NoE were more likely to (1) respond to psychotherapies (CBT, interpersonal and social rhythm therapy, family-focused therapy and collaborative care), and (2) achieve recovery and respond to all interventions more quickly. Additionally, those with fewer episodes responded similarly across interventions, while those with higher NoE had better results from more intensive interventions. Overall, study findings to date suggest that adjunctive psychotherapy may be less effective for those who have experienced greater NoE. However, it should be noted that there are issues with circularity when considering episode relapse and recurrence as evidence of intervention effectiveness in the context of NoE.

In sum, there is substantial (albeit not unequivocal) evidence for an association between greater NoE and important features of BD including relapse risk, illness course, clinical and functioning parameters, and treatment response. As suggested by Scott et al.’s highly cited CBT for BD outcome study (where post hoc analyses found a bifurcation in...
response at 12 episodes), the NoE construct clearly warrants more systematic attention in BD research and treatment.

**NoE: Theoretical importance**

The relationship between NoE and worsening clinical and functional outcomes has been explained by neuroprogression and clinical staging hypotheses. Because of this link, and in the absence of established markers of clinical staging in BD, many studies aim to employ NoE as a “proxy” of stage. This section will review the relevance of the NoE construct within the literature on neuroprogression and clinical staging.

**Staging and Neuroprogression** Staging and neuroprogression are linked, yet distinct, theoretical processes explaining illness progression in BD, and NoE may have an important role in both. Neuroprogression posits that accumulating episode recurrences lead to increased pathological processes and decreased protective processes within the brain; specifically, increased inflammation and sensitisation, decreased neurotrophins and cumulative alterations within the brain. As summarised by Post (2010), there is considerable support in the literature for chemical and structural brain changes linked with increasing NoE. Specifically, increased ventricle volumes and decreased volume of the hippocampus and corpus callosum, as well as reduction in grey matter volume in several regions have been associated with accumulating NoE.

Biochemical evidence, while scarce, broadly concords with structural data. For example, Grande, et al. clustered individuals based on NoE, functioning, duration of illness, and age at onset. The resultant two clusters could be differentiated by levels of the cytokine IL-6. However, these results are yet to be replicated. A further implicated process is that of oxidative stress, wherein an imbalance of oxidants and antioxidants leads to epigenetic changes. An association between NoE and oxidative stress has been demonstrated in BD, with individuals with higher NoE demonstrating elevated antioxidant enzymes, pointing to altered oxidative processes. Therefore, biochemistry may change with increasing NoE in BD, but insufficient data exists to demonstrate how this is linked with episode recurrences.

Clinical staging in psychiatry presumes that, for a proportion of individuals, mental illnesses follow a predictable, progressive trajectory. Specific staging models have been proposed for BD and, while these are yet to be adequately validated, are widely considered to be of heuristic value. NoE has been described as both a feature and an explanatory factor for this process.
in clinical staging of BD. NoE may be causally related to the functional and clinical sequelae of advancing illness stages. Mood episodes have been associated with systemic toxicity, and in addition to the potential neurological impacts, may lead to functional and clinical changes associated with progression through clinical stages. This appears to have face validity with consumers; for example, individuals with higher NoE are more likely to perceive that they have experienced ‘illness progression’ further. Further, as predicted by sensitisation and kindling models, initial episodes are likely to be precipitated by environmental triggers and stressors, while later episodes may occur without exogenous precipitants, implying sensitisation of mood regulatory structures via structural, chemical and functional changes.

While the literature regarding clinical staging and neuroprogression in BD is still maturing, NoE is frequently employed as a marker or proxy of stage and therefore optimising the assessment of NoE may in turn advance this literature.

The construct of NoE: Conceptual issues

The consideration of NoE is complicated by the complex and heterogeneous presentations of BD, and by factors which overlap conceptually and phenomenologically with NoE. For example, related illness features such as rapid cycling, predominant polarity and duration of illness complicate the exploration of NoE. In addition, definitional issues contribute further to heterogeneity; including definition of episodes, onset and offset, recurrence and relapse. Conceptual issues related to the construct of NoE, as illustrated in Figure 1, are introduced in this section.

By definition, individuals with rapid cycling BD experience higher NoE than non-rapid cyclers; around seven times as many manic and twice to three times as many depressive episodes, adding to the overall burden. Rapid cycling is also linked with poorer outcomes, and it is difficult to disentangle impacts associated with accumulating NoE alone from those related to episodic frequency. Further, rapid cycling is typically a transitory phenomenon, adding to attribution difficulties. Despite this complexity, research exploring the impact of NoE has demonstrated that these effects cannot be wholly accounted for by rapid cycling; for example differences in Lithium responsiveness based on NoE were independent of rapid cycling status. Therefore, rapid cycling status may be a related, yet separable, construct to NoE, with the precise contribution of each as yet difficult to ascertain. Similarly, an individual’s total illness duration, their duration of untreated illness, and the age
at which they experienced their initial mood episode have each been linked with poorer outcomes in BD, and each interacts with NoE. Research is yet to untangle the relative contributions of each with relation to NoE, and this will be an important direction for future research.

Further, it appears likely that manic, hypomanic and depressive episodes may have different impacts, and therefore that the proportion of each (an individual’s ‘predominant polarity’) is relevant to the role of NoE. Some studies have found episodes of one pole to be more strongly associated with specific outcomes. For example, several studies have reported that manic episodes, but not depressive episodes, are associated with poorer cognitive function. In addition, work and familial functioning were related to manic NoE, while social functioning was related to depressive NoE in one study. However, the relative impacts of episodes of different types is still largely unknown.

Careful assessment and documentation of these overlapping constructs, as illustrated in Figure 2, will contribute to illuminating their interrelationships and advancing the understanding of the role of NoE. However, regardless of whether future research in this area indicates that NoE imparts unique impact over and above the role of illness factors such as those described above, NoE may nonetheless represent a useful proxy for illness progression.

Additionally, across various studies, differing definitions of NoE and of episode-related constructs have been used. For example, hypomania has been variously defined as periods of at least 2 days to at least 7 days, while others fail to report whether mixed or hypomanic episodes have been included when reporting NoE, with such differences potentially influencing conclusions. Changes within major diagnostic classification systems also have the potential to influence episode classification and counts. For example, mixed episodes are typically classified as manic or elevated episodes, however the latest Diagnostic and Statistical Manual (DSM-5) introduced a ‘with mixed features’ specifier which can apply to manic or depressive episodes, rather than a separate episode type.

The construct of NoE: Measurement issues

Given its potential importance, with NoE being increasingly discussed in the literature, establishing methods to maximise the reliability of measurement while balancing feasibility is required. This section summarises measurement issues associated with NoE, drawing from published research and existing measurement tools.
Assessment methods. A number of methods have been employed to date to gather information relevant to NoE, and these are summarised in Table 1. Many studies considering NoE fail to define or disclose their definition or method of assessment of NoE. When methods of assessment are disclosed, these range widely in degree of structure, burden on participants, and comprehensiveness.

For example, some studies have collated episode histories from various sources, such as clinical case histories, hospital records and family members. When an extensive clinical history is available and its use is practical, benefits can include improved accuracy. However, for both research and clinical purposes this is often unfeasible, and as such, measures which balance pragmatics with maximising precision may be preferable.

In the absence of medical history documents, participants are often asked to recall their lifetime mood episodes with varying prompts, and existing instruments have been used or tailored for this purpose. Specifically, the current editions of the Mini International Neuropsychiatric Interview (MINI) (version 7.0.2) and the Structured Clinical Interview for the DSM (SCID-5-RV), each contain a question regarding depressive NoE (see Appendix A), but not specifically manic nor hypomanic NoE. Several studies report using or adapting these instruments to quantify NoE, and others have used a combination of these and the previously described methods.

The Affective Disorders Evaluation (ADE) is another tool used for gathering data about NoE, created and implemented by the STEP-BD group. The ADE includes a question per episode type, aided by prior questions elucidating interviewees’ symptoms. Further, the NIMH Life Chart Method (NIMH-LCM) involves graphing mood shifts including episodes above (hypo/mania) and below (depression) a dateline, with manualised prompts. The NIMH-LCM has been used in several studies, however, while it was developed for both retrospective and prospective use, it has only been validated prospectively, limiting its applicability for retrospective recall.

Retrospective assessment issues. Retrospective recall is inherently problematic and subject to heuristic biases, particularly for emotionally salient psychological phenomena. In addition, a key issue with retrospective assessment methods is that many individuals with BD experience autobiographical memory difficulties, most commonly overgeneral autobiographical memory. These difficulties are compounded by greater numbers of previous episodes, and cognitive and memory impairments are most prominent during episodes, impacting the recall thereof. Martino, et al. compared subjective recall of...
episodes with clinician rated episodes over periods of 2 to 6 years, finding less than 20 per cent concordance. In most cases, episodes were underreported by individuals with BD, averaging 2.74 episodes (58%) over the study period. This may reflect a broader underestimation of NoE based on self-report methods, resulting in a systematic underestimation of NoE. Table 2 compares data from a number of studies reporting on the NoE construct.

Table 2 about here

**Burden on individuals with BD.** Being asked to recall details of often traumatic and disruptive mood episodes is likely to be distressing for many individuals with BD. Lengthy and overly intrusive assessment may impact individual’s motivation to engage with assessment and provide accurate information. Structured assessment methods may result in more accurate recall and reduced burden.

Assessing the NoE an individual with BD has experienced is therefore likely to have significant implications for treatment and research. While various methods have been employed for this purpose, assessment largely appears to be perfunctory, with far less attention paid than to other important clinical factors, such as symptom severity. The definition and measurement of episodes varies between studies, with differences in researchers’ definitions and operationalisations of episodes themselves, onset and offset, recurrence and relapse. As a result, comparisons between studies are imprecise, rendering conclusions about the specific role of NoE tenuous. This implies a need for more reliable and precise measurement of NoE. On the other hand, given evidence that individuals’ self-reported NoE is linked with important clinical and functional outcomes (e.g. 6), the burden associated with collating medical histories and informant reports and the distress which may result from such examinations, efforts may be better spent enhancing self-reported recall methods, balancing feasibility with precision. Without transparent and replicable assessment methods, the relationship between NoE and clinical and prognostic factors will remain slippery.

**Where to from here?**

In order to progress the understanding of the role of NoE in the experiences and treatment of individuals with BD, more rigorous consideration of this construct is necessary. Several tools exist which can be used to gather information about NoE, but these are inconsistent in their definition of episodes and the methods used to aid the recall of this
information. Our aim here is to support future research by offering provisional guidance towards consistent, feasible and accurate measurement of NoE, derived from a review of the literature. Accordingly, a discussion of key recommendations follows and these are summarised in Box 1.

Towards an improved understanding of NoE

Explicit operationalisation. At a minimum, studies considering NoE ought to disclose their definition and the process used to gather this information. Standard definition of episodes by type (manic, hypomanic, mixed and depressive), and of related constructs including recurrence, relapse and remission are required for consistency across studies. Appropriate definitions are provided in an International Society of Bipolar Disorders report⁹⁰, and compatible working group report⁹¹, and are best supported by internationally recognised diagnostic criteria, as in the Diagnostic and Statistical Manual of Mental Disorders⁷⁶ or the International Classification of Diseases. These are summarised in Table 3. Further, there is preliminary support for the possibility that episodes of different types may have different impacts, and so separate reporting of total, manic, hypomanic, mixed and depressive episodes is recommended in order to advance this understanding.

Documentation of overlapping phenomena. Future research will benefit from assessing and reporting the various course of illness variables which overlap with NoE. As shown in Figure 2, the various phenomena related to both NoE and important outcomes in BD, such as duration of illness, age of onset, and rapid cycling, complicate the understanding of the role of NoE. The first step towards improving our understanding of such relationships is the consistent assessment and reporting of these phenomena. Subsequently, further clarification may be offered by carefully designed studies which aim to untangle the role of these factors.

NoE and staging. Despite NoE likely representing an oversimplification of clinical staging phenomena, with episodic parameters speculative, NoE is currently the best candidate for the operationalisation of clinical staging in BD⁶,⁹². Additionally, this operationalisation has clinical relevance and face validity, and is (theoretically) relatively simple to assess. However, there are issues associated with its use in this context. In addition to the assessment issues already described, if assessment of NoE is employed as a proxy of stage within research contexts, ideally, it should be considered within the context of the individual, with additional factors which contribute to the assessment of ‘stage of illness’ (such as functional
and neurocognitive decline), and factors which may confound it (such as rapid cycling, age of onset and duration of illness) informing such assessments and addressing issues of reductionism and circularity.

**Research agenda.** This review has illuminated some key areas for future research. Firstly, while a range of tools are currently available to assess the construct of NoE, none has been extensively validated or compared for this purpose and as such, further research is required to evaluate existing tools and/or develop a new measure for the assessment of NoE. Research designs which would advance this issue would directly compare the psychometric properties and predictive validity of multiple (available or newly-designed) measures of NoE. In addition, more research assessing the relationship between episodes of different types and i) important clinical outcomes and ii) overlapping phenomena is needed. For example, employing measures which gather data about different episode types and modelling their relationships with important clinical outcomes to assess the contribution and differential impacts of each would constitute a valuable next step. Similarly, as noted, studies assessing overlapping constructs alongside NoE (as in Figure 2) and controlling for these or evaluating their relative predictive validity for key outcomes or prognostic indicators may contribute to untangling the relationships between, and relative clinical utility of, these phenomena.

**Towards improved measurement of NoE**

**Consistent measurement.** Assessment supported by collateral history has benefits, however self-reported NoE has been linked with various clinical and functional correlates. Neither has been utilised and documented consistently in the literature. Therefore, establishing and documenting consistent methods for assessing this construct are necessary. Ultimately, replicable, standardised assessment methods will vastly improve the heterogeneity present in the literature and the understanding of the implications of NoE.

**Balancing feasibility and accuracy.** As highlighted in this review, methods of assessment for NoE vary widely, and many of these, such as collating medical and case histories, appear unfeasible for use in the contexts in which NoE is likely to be of most use (such as clinical practice). In addition, prolonged and detailed recollection of episodes is likely to be distressing for individuals with BD, and there is no evidence to suggest that this leads to more accurate episode recall. It appears likely that individuals systematically underestimate their NoE and that those with greater NoE may count with even less accuracy. In sum, we propose that NoE may best be treated as a fuzzy concept, rather than a precise datum and therefore efforts to achieve a reliable, feasibly attained ‘estimate’ of NoE may be
more important than efforts to derive a precise figure. Therefore, we suggest that future assessment attempts should pay more attention to minimising burden and achieving increased consistency, rather than greater precision.

**Structured assessment methods.** Self-report assessment methods adopted to assess NoE vary in their degree of structure and the types of prompts offered (see Table 1). Structured assessment methods are frequently employed in psychological assessment to aid recall and contribute to standardisation of clinical assessments, with well-documented heuristic biases (such as mood-congruence) less impactful in structured formats\(^93\). In addition, structured assessment methods may reduce burden on participants. Therefore, developing structured methods to support the recall of NoE is likely to improve the reliability of assessment while reducing burden on individuals.

At a minimum, studies considering NoE ought to disclose their definition and the process used to gather this information. Standard definition of episodes by type (manic, hypomanic, mixed and depressive), and of related constructs including recurrence, relapse and remission are required for consistency across studies. Appropriate definitions and operationalisations are provided in an International Society of Bipolar Disorders report\(^90\), and compatible working group report\(^91\), and are best supported by internationally recognised diagnostic criteria, as in the Diagnostic and Statistical Manual of Mental Disorders\(^76\) or the International Classification of Diseases. These are summarised in Table 3. Further, there is preliminary support for the possibility that episodes of different types may have different impacts, and so separate reporting of total, manic, hypomanic, mixed and depressive episodes is recommended in order to advance this understanding.

[Table 3 about here]

**Balancing feasibility and accuracy.** As highlighted in this review, methods of assessment for NoE vary widely, and many of these, such as collating medical and case histories, appear unfeasible for use in the contexts in which NoE is likely to be of most use (such as clinical practice). In addition, prolonged and detailed recollection of episodes is likely to be distressing for individuals with BD, and there is no evidence to suggest that this leads to more accurate episode recall. It appears likely that individuals systematically underestimate their NoE and that those with greater NoE may count with even less accuracy. In sum, we propose that NoE may best be treated as a fuzzy concept, rather than a precise datum and therefore efforts to achieve a reliable, feasibly attained ‘estimate’ of NoE may be
more important than efforts to derive a precise figure. Therefore, we suggest that future assessment attempts should pay more attention to minimising burden and achieving increased consistency, rather than greater precision.

**Structured assessment methods.** Self-report assessment methods adopted to assess NoE vary in their degree of structure and the types of prompts offered (see Table 1). Structured assessment methods are frequently employed in psychological assessment to aid recall and contribute to standardisation of clinical assessments, with well-documented heuristic biases (such as mood-congruence) less impactful in structured formats. In addition, structured assessment methods may reduce burden on participants. Therefore, developing structured methods to support the recall of NoE is likely to improve the reliability of assessment while reducing burden on individuals.

To advance the assessment of NoE, it is useful to draw parallels with other phenomena that rely upon memory of distal past events and may induce discomfort. For example, we know that asking about specific types of traumatic events generates more reliable recall than asking omnibus questions about ever having experienced trauma across one’s lifetime, and the same may hold true for the assessment of NoE. In addition to a structured approach, providing a simple definition of each type of episode being assessed and prompts to assist with recall are suggested. Examples of potential questions and prompts for each type of episode are provided in Appendix B. For example, some respondents may focus only on those episodes which led to hospitalisation, and timeline-based prompts may assist with recalling other episodes. These examples are based on the methods employed in two recent RCTs for which NoE was an inclusion criterion, however they have not been validated. In addition, given the potential for distress associated with the recall of mood episodes, advising respondents about this potential and ways to manage this (such as ceasing the assessment), while monitoring the impacts of the assessment is recommended (see Appendix B). Finally, to assist with comparability across measures and studies, number of episodes per type and in total should be recorded as a continuous (rather than categorical) metric.

[Box 1 about here]
Conclusion

NoE is a prognostic indicator in BD. Additionally, NoE has the potential to shape interventions and assist clinicians to tailor interventions to increase their effectiveness and reduce delays to accessing optimally effective interventions. NoE also informs clinical staging models in BD, offering an initial step towards operationalising the complex staging phenomenon, which is yet to be adequately translated into applied research with validated assessment tools. Therefore, efforts to improve its assessment have the potential to offer substantial benefits. Despite this, measurement of NoE to date has been inconsistent, with varying definitions and methods utilised and reporting sporadic. The various methods for assessing NoE employed have relative strengths and limitations. Self-reported NoE supported by consistent prompts appears to be a promising and feasible method; in future this could be supported by a standard structured interview. In addition, recommendations drawn from this review include consistent, evidence-based and transparent operationalisation and due consideration of factors which may interact with or confound NoE, in particular duration of illness, number of hospitalisations, rapid cycling, and predominant polarity.
References


This article is protected by copyright. All rights reserved


This article is protected by copyright. All rights reserved


This article is protected by copyright. All rights reserved


Table 1

<table>
<thead>
<tr>
<th>Method</th>
<th>Benefits</th>
<th>Limitations</th>
<th>Published examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission history/Case records</td>
<td>• Potential for increased reliability</td>
<td>• Admission doesn’t equate to episodes</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>• Doesn’t rely on recall</td>
<td>• Time-consuming to attain and use</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Privacy</td>
<td></td>
</tr>
<tr>
<td>Informants</td>
<td>• May assist with recall</td>
<td>• Reliant on cooperation</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>• Doesn’t rely on (individuals’ recall)</td>
<td>• Differing reliability, dependant on individual</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Not standardised</td>
<td></td>
</tr>
<tr>
<td>Existing clinical tools/interview</td>
<td>• Convenient, tools already being used for diagnosis (SCID, MINI)</td>
<td>• Relies heavily on self-report, memory</td>
<td>9,10,16,20</td>
</tr>
<tr>
<td></td>
<td>• Structured</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Potential for standardisation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unprompted self-report</td>
<td>• Brief</td>
<td>• Likely to be impacted by memory issues</td>
<td>42</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Likely to become less reliable with increasing</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>NoE</td>
<td></td>
</tr>
<tr>
<td>Prompted self-report</td>
<td>• Structured Well-designed prompts likely to aid recall (world or significant life)</td>
<td>• Can be time consuming</td>
<td>3,5,6,8,71,73,80</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Currently not used consistently (e.g. different prompts)</td>
<td></td>
</tr>
</tbody>
</table>
Table 2

Comparison of NoE Across Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Inclusion criteria</th>
<th>Method of assessing NoE</th>
<th>Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bonnin, et al. 16</td>
<td>(1) 18 - 65 years old. (2) BD I according to DSM-IV criteria (3) Euthymic for at least 6 months</td>
<td>Clinical interview including SCID for DSM-IV-TR</td>
<td>N = 85</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Grand mean NoE = 9.29</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Grand mean dep = 3.99</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Grand mean manic = 2.55</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Grand mean mixed = .52</td>
</tr>
<tr>
<td>Martino, et al. 72</td>
<td>(1) Age 18 – 60 (2) BD I or BD II (DSM-IV) (3) Euthymic for at least 8 weeks (4) 24-month follow-up available</td>
<td>SCID for DSM-IV-TR supported by clinical charts and direct patient interviews. When possible, attempts were made to verify these historical data with third-party reports (medical records, family interviews. Note that (hypo)manic episodes were defined as a period of at least one week with mild, moderate, or severe mania</td>
<td>N = 50</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mean NoE = 7.47</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mean dep = 4.16 (4.69)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mean hypo/manic = 3.31</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(3.84)</td>
</tr>
<tr>
<td>Rosa, et al. 75</td>
<td>(1) ≥ 18 years (2) Fulfillment of DSM-IV criteria for bipolar I or bipolar II disorder.</td>
<td>Episode definition/operationalisation not stated, SCID for DSM-IV-TR and examination of clinical records.</td>
<td>N = 131</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Grand mean NoE = 16.69</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Grand mean dep = 7.34</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Grand mean manic = 3.97</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Grand mean hypo = 4.56</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Grand mean mixed = 0.86</td>
</tr>
<tr>
<td>Colom, et al. 39, 93</td>
<td>(1) 18-65 (2) Diagnosis of bipolar disorder</td>
<td>Not explicitly specified – SCID for DSM-IV-TR was used to confirm diagnosis.</td>
<td>N = 120</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Grand mean NoE = 9.56</td>
</tr>
<tr>
<td>Study</td>
<td>Criteria</td>
<td>Methodology</td>
<td>Sample Size</td>
</tr>
<tr>
<td>-------</td>
<td>----------</td>
<td>-------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Jimenez, et al. 7</td>
<td>(1) ≥ 18 years</td>
<td>Semistructured interview based on the SCID for DSM-IV-TR which also considered data from medical records, to gather sociodemographic and clinical information.</td>
<td>N = 215</td>
</tr>
<tr>
<td>Martínez-Arán, et al. 17</td>
<td>(1) DSM-IV Bipolar I or II</td>
<td>SCID plus additional clinician/informant information as available</td>
<td>N = 108</td>
</tr>
<tr>
<td>MacQueen, et al. 11</td>
<td>(1) 18-65</td>
<td>SCID for DSM-III-R; medical chart records, further patient interviews, family members, treating clinicians and life charts, where available, were also consulted to determine the most accurate estimate of past number of episodes.</td>
<td>N = 64</td>
</tr>
<tr>
<td>Mansell, et al. 85</td>
<td>(1) BD I (DSM-IV)</td>
<td>Not explicitly disclosed, SCID used for diagnosis</td>
<td>N =19</td>
</tr>
<tr>
<td>Bourne, et al. 18</td>
<td>Individual patient data meta-analysis including: (1) 18-65 (2) Bipolar Disorder (not-defined)</td>
<td>Where possible, demographic and clinical variables were also collected for each primary data set including number of prior manic and depressed episodes.</td>
<td>Mean dep (n = 992) = 5.6 (10.7)</td>
</tr>
</tbody>
</table>
### Soni, et al. 10

1. **18-55**
2. Bipolar disorder according to ICD-10
3. Euthymic

Number of episodes was gathered during clinical interview including MINI

\[ N = 61 \]

- Grand mean NoE = 7.42
- Grand mean dep = 3.53
- Grand mean manic = 3.89

### Scott, et al. 38

1. \( \geq 18 \)
2. DSM–IV diagnosis of bipolar disorder I or II
3. History of two or more episodes one of which must have been within 12 months of recruitment; and
4. In contact with mental health services within the past 6 months.

Data collected before randomisation included diagnosis according to SCID (DSM–IV) and “diagnoses of past episodes of bipolar disorder according to DSM-IV criteria”.

\[ N=253 \text{ Categorical data only} \]

- Number of previous episodes, n (%)
  - 2-6: 74 (29%)
  - 7-11: 54 (21%)
  - 12-29: 59 (23%)
  - \( \geq 30 \): 66 (26%)

- Depressive episodes: median (IQR):
  - TAU: 5 (2-15)
  - CBT: 6 (3-20)

- Hypomanic/ manic/ mixed episodes: median (IQR):
  - TAU: 4 (2-9)
  - CBT: 4 (2-8)

### Peters, et al. 8

**STEP-BD**

1. \( \geq 18 \)
2. Individuals seeking outpatient treatment
3. Meeting DSM-IV diagnostic criteria for bipolar I disorder, bipolar II disorder, bipolar disorder, not otherwise specified (NOS), cyclothymia or schizoaffective disorder, bipolar type

Affective Disorders Evaluation (ADE) (Sachs et al., 2002) provided Information regarding number of previous episodes.

**Full STEP-BD sample (N=4361)**

- Depressive episodes:
  - 1-9: 1369 (39%)
  - 10-20: 642 (18%)
  - \( \geq 20 \): 1480 (42%)

- (Hypo) manic episodes:
  - 1-9: 1572 (45%)
  - 10-20: 604 (17%)
  - \( \geq 20 \): 1312 (37%)

(n and % of valid cases, no total episodes reported)

**RCT for bipolar depression subsample (N=205)**

- Depressive episodes:
  - 1-9: 68 (33%)
  - 10-20: 29 (14%)
Subsample, RCT for bipolar depression:

- ≥ 18
- DSM-IV criteria for bipolar I or II disorder
- Current acute episode of depression
- Be taking or willing to initiate treatment with a mood-stabilizing or atypical antipsychotic medication and willing to undergo psychotherapy

≥ 20: 108 (53%)
(Hypo)manic episodes:
- 1-9: 75 (37%)
- 10-20: 33 (16%)
- ≥ 20: 97 (47%)

<table>
<thead>
<tr>
<th>Swann, et al.</th>
<th>Step BD standard care pathways participants with sufficient data:</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) 18-65</td>
<td>The Schedule for Affective Disorders and Schizophrenia (SADS) and Research Diagnostic Criteria (RDC) were used to make diagnoses. Course of illness was examined in detail by using all available sources of information including medical records and collateral interviews where available.</td>
</tr>
<tr>
<td>(2) Meet RDC criteria for manic disorder</td>
<td></td>
</tr>
<tr>
<td>(3) Currently manic</td>
<td></td>
</tr>
</tbody>
</table>

Manic (n = 157): range 1-52, mode 8
Depressive (n= 130): range 1-36, mode 2

<table>
<thead>
<tr>
<th>Magalhaes, et al.</th>
<th>Affective Disorders Evaluation (ADE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 15</td>
<td>N = 3345</td>
</tr>
<tr>
<td>&lt; 5: 344 (10.3%)</td>
<td></td>
</tr>
<tr>
<td>5-10: 1275 (38.1%)</td>
<td></td>
</tr>
<tr>
<td>≥ 10: 1726 (51.6%)</td>
<td></td>
</tr>
<tr>
<td>Construct</td>
<td>Definition</td>
</tr>
<tr>
<td>----------------------</td>
<td>--------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Manic Episode</td>
<td>DSM-5 criteria(^{76}). If ICD-10 criteria are used, this should be noted.</td>
</tr>
<tr>
<td>Major Depressive</td>
<td>DSM-5 criteria(^{76}). If ICD-10 criteria are used, this should be noted.</td>
</tr>
<tr>
<td>Episode</td>
<td></td>
</tr>
<tr>
<td>Hypomanic Episode</td>
<td>DSM-5 criteria(^{76}). If ICD-10 criteria are used, this should be noted (in particular, duration criteria: see Hypomanic Episode, short duration below).</td>
</tr>
<tr>
<td>Hypomanic</td>
<td>The validity of the 4-day minimum duration of</td>
</tr>
<tr>
<td>Episode, short duration</td>
<td>symptoms for a hypomanic episode within the DSM-5 has been questioned(^{95,96}). Several authors have suggested that this does not reflect phenomenology and recommended a reduced duration of 2 to 3 days(^{95,97,98}). Should shorter duration episodes of 2 to 3 days be included, these should be recorded as a separate type and authors should consider excluding from aggregates.</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Mixed Features (previously Mixed Episode)</td>
<td>DSM-5 criteria(^{76}). If DSM-IV(^{99}) criteria are used (and therefore ‘Mixed episodes’ are recorded as a separate category), authors should note this and include these within total NoE and number of manic episodes when aggregating.</td>
</tr>
</tbody>
</table>
| Remission | The absence or minimal symptoms of both mania and depression for at least 1 week (at least eight weeks for ‘sustained remission’).\(^{91}\)  
**Depression:** Any present symptoms should not include DSM threshold sad mood or loss of pleasure (Criteria A1, A2)\(^{90}\).  
**Mania:** Any present symptoms should be mild, in particular criterion A. May therefore meet criteria for hypomania. | Consider rating each symptom on a severity scale such as the CGI (1-7).  
**Depression:** Fewer than 3 of the 7 remaining DSM A criteria, and those present rated \(\leq 3\)\(^{90}\).  
**Mania:** DSM A criterion for mania < 2, any B criteria rated \(\leq 3\) and no two B criteria rated = 3\(^{90}\).  
Rating scales:  
YMRS \(\leq 8\)  
MADRS \(\leq 10\) or HAMD \(\leq 7\)  
CGI-BP-S \(\leq 2\)\(^{91}\)  
BDRS \(\leq 8\)\(^{90}\). |
| Relapse | The return of symptoms satisfying the full syndrome criteria for an episode that occurs during the | Symptoms meeting DSM episode criteria, following at least 1, but less than 8 weeks of |
| Recurrence | Occurrence of a new syndromal episode meeting DSM criteria\cite{91}, during a period of sustained remission. | Symptoms meeting DSM episode criteria, following at least 8 weeks of remission. |

*Note: BDRS = Bipolar Depression Rating Scale\cite{100}, CGI = Clinical Global Impression\cite{101}, CGI-I-BP = CGI-Improvement scale for bipolar disorder\cite{102}, MADRS = Montgomery-Asberg Depression Rating Scale\cite{103}, HAM-D = Hamilton Rating Scale for Depression\cite{104}, YMRS = Young Mania Rating Scale\cite{105}. |
### Current Structured Tools Employed to Assess Number of Episodes

<table>
<thead>
<tr>
<th>Measure</th>
<th>Specific NoE question/s</th>
<th>Prompt type, example</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mini International Neuropsychiatric Interview 7.0.2</td>
<td>How many episodes of depression did you have in your lifetime?</td>
<td>Context of definition and assessment of episode</td>
<td>Manic/hypomanic NoE not asked by default (only asks whether more than once)</td>
</tr>
<tr>
<td></td>
<td>Did you have 2 more of these (manic) episodes lasting 7 days or more in your lifetime?</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Did you have 2 more of these (hypomanic) episodes lasting 4 days or more in your lifetime?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Structured Clinical Interview for the DSM-5 2</td>
<td>How many separate times in your life have you been (depressed/OWN WORDS) nearly every day for at least 2 weeks and had several of the symptoms that you described, like (SXS OF CURRENT MDE)?</td>
<td>Context of definition and assessment of episode</td>
<td>Manic/ hypomanic not asked by default, asked about age at onset instead</td>
</tr>
<tr>
<td>Affective Disorders Evaluation</td>
<td>The time we’ve been talking about is what we would call (hypo)mania.</td>
<td>Context of definition and assessment of episode</td>
<td>Response options are categorical (0, 1, 2, 3-4 5-9 10-20 20-50)</td>
</tr>
<tr>
<td></td>
<td>Using that time as a guide, how many times have you been like that for as long as 1 wk?</td>
<td></td>
<td>ADE is no longer available online</td>
</tr>
<tr>
<td></td>
<td>The time we’ve been talking about is what we’d call an episode of depression. Using that time as a guide, how many times have</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
you been like that for as long as 2 weeks?

| NIMH Life Chart (retrospective) | The time line in the middle of the chart (marking the months and years) is also called the baseline indicating a level or balanced mood state, i.e., you are not depressed or hypomanic or manic. Episodes of depression are drawn below the baseline (which is also the date line) and episodes of mania are drawn above the baseline | Prompts include list of major life events, medications changes, episode severity | Instructs users to ask friends and family about number of episodes |

References

Appendix B

Examples of Questions to Assess Episodes of Different Types

<table>
<thead>
<tr>
<th>Episode type</th>
<th>Definition</th>
<th>Question</th>
<th>Prompts and probes</th>
</tr>
</thead>
</table>
| Major Depressive Episode | “An episode of depression involves symptoms like:  
- sadness  
- less interest or pleasure in things you normally enjoy  
- low energy  
- changes to your sleep, appetite or concentration  
- feelings of hopelessness  
- thoughts of suicide  
To be considered an 'episode' of depression, several of these symptoms need to have been present for most of your lifetime.” | “How many episodes of depression have you experienced in your lifetime?” | “It may help you to start by remembering your first episode of depression. What age were you when you first experienced an episode of depression?”  
“Some people notice a pattern in their episodes, for example experiencing depression over the colder months followed by an elevated episode. Have you noticed any patterns in your own experience?”  
“What are some significant life events you’ve experienced (such as beginning or finishing...” |
the day, nearly every day for at least two weeks and you'd feel or behave noticeably different to how you normally would. These episodes of depression may have occurred before or after you were diagnosed with bipolar disorder.”

<table>
<thead>
<tr>
<th>Manic</th>
<th>“Elevated episodes involve elevated mood (feeling</th>
<th>“How many episodes</th>
<th>“It may help you to start by remembering</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>university, changing jobs, marriages, having children, moving home, or experiencing a loss)? Do you recall any episodes of depression around these times?”</td>
<td>“On average, how many episodes of depression do you experience per year?” Has this always been around this often, or more or less frequently in the past?”</td>
<td>“You talked about a period of depression which required you to spend some time in hospital, I’m wondering if there have been other episodes of depression that didn’t require hospitalisation, but that were still significant?”</td>
</tr>
<tr>
<td></td>
<td>“We know that thinking about difficult times in your past can sometimes be upsetting. While we’re talking about your past experiences, if you notice that this is the case for you, can you please let me know or ask to pause our discussion?”</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
high, elated, or very irritable), including symptoms like:
- having more energy or less need for sleep
- being more talkative or active
- racing thoughts
- making lots of plans or goals
- increased self-esteem
- pleasurable behaviours with negative consequences, like spending a lot of money

To be considered a 'manic episode', several of these symptoms will have occurred for at least a week and caused problems in areas like work, relationships, or friendships, or resulted in you being hospitalised. These episodes of mania may have occurred before or after you were diagnosed with bipolar disorder.

of mania have you experienced in your lifetime?

your first episode of mania. What age were you when you first experienced an episode of mania?

“What are some significant life events you’ve experienced (such as beginning or finishing university, changing jobs, marriages, having children, moving home, or experiencing a loss)? Do you recall any episodes of mania around these times?”

“On average, how many episodes of mania do you experience per year?” Has this always been around this often, or more or less frequently in the past?”

“You talked about an elevated period which required you to spend some time in hospital, I’m wondering if there have been other times that didn’t require hospitalisation, but involved elevated moods which impacted your functioning?”

“We know that thinking about difficult times in your past can sometimes be upsetting.
While we’re talking about your past experiences, if you notice that this is the case for you, can you please let me know or ask to pause our discussion?

| Hypomanic Episode | “Hypomania is similar to mania, except that the symptoms are usually less severe and don’t affect your functioning, but would be noticeable to someone who knows you. For example, you might have:  
- Needed less sleep  
- Been more talkative  
- Noticed your thoughts racing  
- Become more distractible  
- Made lots of plans or goals  
- Engaged in more pleasurable activities, even if these were risky  
'Hypomanic episodes' last four days or more. These episodes of hypomania may have occurred before or after you were diagnosed with bipolar disorder.” | “How many episodes of hypomania that lasted at least four days have you experienced in your lifetime? “ | “It may help you to start by remembering your first episode of hypomania. What age were you when you first experienced an episode of hypomania?” |
| | | | “What are some significant life events you’ve experienced (such as beginning or finishing university, changing jobs, marriages, having children, moving home, or experiencing a loss)? Do you recall any episodes of hypomania around these times?” |
| | | | “On average, how many episodes of hypomania do you experience per year?” Has this always been around this often, or more or less frequently in the past?” |
| | | | “We know that thinking about difficult times in your past can sometimes be upsetting. While we’re talking about your past |
| **Mixed Episode or Mixed features*** | Assessment based on whether DSM-IV-TR or DSM-5 criteria is used.  
DSM-IV-TR: “Mixed episodes involve these elevated symptoms at the same time as symptoms of depression for at least a week. These mixed episodes may have occurred before or after you were diagnosed with bipolar disorder.”  
DSM-5: “Mixed features means that, during any of the episodes of mania, hypomania or depression you’ve experienced, you also experienced some symptoms of the other type of episode at the same time”. | “How many episodes have you experienced in your lifetime which included some elevated and some depressed symptoms? Did you include any of these in the previous questions? “ | experiences, if you notice that this is the case for you, can you please let me know or ask to pause our discussion?” |

This article is protected by copyright. All rights reserved
Mixed episodes were replaced in the DSM-5 by a mixed features specifier, applied to Manic, Hypomanic or Major Depressive Episodes. The key difference is that full criteria for episodes of both types were required to be classified as a Mixed Episode (DSM-IV-TR), while a mixed features specifier is applied when full criteria are met for any type of episode, plus three or more criteria of an episode of another type (DSM-5). Therefore, these episodes would not appear as a separate ‘Mixed Episode’ but would be categorised and ‘counted’ under the relevant threshold episode (manic if full criteria for both are met).
Figure 1. NoE construct

NoE

Diagnosis

BD I, II, other

Episode type

Mixed states, rapid cycling (ultrapid, ultradian) atypical episodes, predominant polarity

Episode definition

Duration, relapse, recurrence, remission onset/offset

Symptoms

Severity, subthreshold symptoms between episodes

Manic

Elevated

Mixed

Depressed

DSM-5 criteria

Research derived
Figure 2. Summary of cognate clinical course factors with NoE

- Symptom severity
- Duration of illness
- Predominant polarity
- Rapid/ultradian cycling
- Hospitalisations

This article is protected by copyright. All rights reserved
Author/s:
Tremain, H; Fletcher, K; Murray, G

Title:
Number of episodes in bipolar disorder: The case for more thoughtful conceptualization and measurement

Date:
2019-12-15

Citation:

Persistent Link:
http://hdl.handle.net/11343/286745