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Strategies for improving treatment of bipolar disorder: integration of measurement and management

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Objective: Bipolar disorder is a common and complex condition associated with high rates of disability and high health care costs. The aim of this article is to provide an overview of the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD).
Method: The Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) was conceived in response to an NIMH request for proposals to study the effectiveness of treatments for Bipolar Disorder. Aspects of this program have been adapted and enriched for presentation in this paper.
Result: Designed for implementation in routine practice across a variety of settings, STEP-BD offers a disease management program in which standardized assessments are linked to critical decision points in clinical management pathways.
Conclusion: This paper describes strategies used in STEP-BD to improve the treatment of Bipolar disorder: a simple conceptual model, which integrates assessments and management, and several specialized elements, used in the STEP-BD assessment package.

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Key words: bipolar disorder, clinical management; assessment; treatment; clinical outcomes

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Introduction

Bipolar disorder is a complex chronic condition, recognized as a leading cause of disability (1) and is associated with high health care costs (2–4). Even the prevalence of bipolar disorder is a matter of considerable debate (5). Recent professional and popular literature includes reports indicating high rates of delayed diagnosis and misdiagnosis (6–8) and responsible voices raising concerns about over diagnosis (9–11). Partisans in this debate may agree about little, but share an understandable quest for greater diagnostic confidence. Without proper diagnosis, patients cannot experience the benefit of treatments shown to reduce the increased mortality associated with untreated bipolar disorder (12).

Despite the broadly consistent recommendations across the various treatment guidelines and algorithms for bipolar disorder published over the last 10 years, great variations in practice persist (13–16). Variation in the depth and breadth of assessment may account for a substantial percentage of this variance.

The Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) was conceived in response to an NIMH request for proposals to study the effectiveness of treatments for Bipolar Disorder. In order to ensure that patients received high quality care and to reduce variance between practitioners in diverse treatment centers, STEP-BD centers agreed to adopt a common disease management program based on 'model practice' procedures.

In each of the past 5 years, tabulated needs assessment responses from STEP-BD investigator meetings and staff training programs consistently identified improving clinical assessment as one of the top three clinical needs. Of particular interest are the results indicating clinical needs collected from 223 clinicians attending training sessions who were not affiliated with a STEP-BD network site. Among these 62.7% ranked diagnostic assessment as the number one

obstacle to improved clinical outcome for bipolar disorder.

Aims of the study

This paper describes strategies used in STEP-BD to improve the treatment of Bipolar disorder: a simple conceptual model, which integrates assessments and management, and several specialized elements used in the STEP-BD assessment package.

Material and methods

Material pertinent to the development and implementation of the STEP-BD program has been reviewed and adapted for this paper. The literature has been enriched where relevant by reference to articles retrieved via MEDLINE and EMBASE searches using relevant terms.

Results

Fundamentals of collaborative disease management: conceptual model

Bipolar disorder challenges even the most experienced clinician. Inherent variability of symptoms, high rates of substance abuse, anxiety disorders, medical comorbidity, a substantial risk of suicide and other potentially severe adverse outcomes are among the characteristics that complicate clinical management of patients with bipolar disorder. The need to manage patients despite this apparent chaos fuels a desire for guidance, which has spawned many laudable scholarly efforts to construct treatment algorithms and guidelines. The utility of these decision-support materials in clinical practice is often limited, because the time-intensive process required to write comprehensive scholarly consensus guidelines tends to produce unwieldy documents that become rapidly outdated by the flow of new data and the emergence of new therapies.

Can any method over come these limitations and order the complexity and lack of predictability typically encountered over the course of bipolar disorder? Ideally a treatment would be selected, because its mechanism of action corrects the pathophysiology underlying a disease state. Not only are there no truly patholytic treatments available, the pathophysiology underlying bipolar disorder remains unknown. STEP-BD offers treatment pathways that organize a sequence of critical decision points into standard care treatment pathways for commonly encountered conditions such as depression, mania, rapid cycling, and prophylaxis and encourages treating psychiatrists to participate as guideline makers for their patients. The success of this approach does not depend on the practitioner referencing or memorizing the critical decision points or even the specific recommendation written into the clinician's handbook. Instead STEP-BD training focuses on a simple conceptual model that integrates measurement into management and aims to facilitate the clinician's ability to deliver individualized evidence-based treatment.

The Collaborative Care Disease Management schema outlined here is intended as a dynamic set of principles for clinician self-guidance rather then imperative paperbound directives. It recognizes the ability of clinical users to appreciate critical decision points as they arise, weigh treatment options and apply a disciplined approach to the assessment and intervention process. The utility of this approach requires that the clinician be mindful of a concise conceptual schema, maintain a critical awareness of the evidence pertinent to the decision-making process, and possess sufficient skills to establish a collaborative relationship with patients and their supports.

A collaborative model for iterative measurement/management

Overview

An iterative process by which clinical activity flows from a critical decision point to an intervention and is regulated by the feedback of measured outcomes is illustrated in Figure 1. This model starts with the recognition of a critical decision point (e.g. a new episode of acute depression). Appropriate treatment recommendations are then formulated by constructing an individualized 'menu of reasonable choices' which reflects the clinician's knowledge of the available evidence regarding treatment efficacy, tolerability, and individual patient-related factors (e.g. prior treatment response). The menu of reasonable choices presents what the care provider regards as 'equipoise options' and encourages the patient to review the profile of each option and exercise their preference. Proper involvement of patients and their supports as collaborators requires education and negotiation. Inclusion of systematic measurement in routine follow-up determines outcome, which brings the collaboration to the next decision point.

Recognition of critical decision points

Accurate diagnostic assessment of the current mood state is crucial to choosing an effective

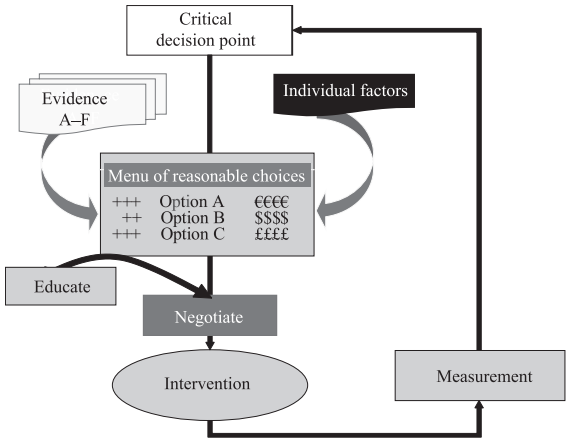

Fig. 1. Collaborative care disease management.

intervention. STEP-BD attempts to strengthen the link between measurement and management by establishing the patient's current 'Clinical Status' at each visit. These eight operationally defined clinical states are defined below and differ only slightly from familiar DSM-IV diagnostic categories. Clinical status definitions were designed with a focus on the week previous to the assessment in order to facilitate the intuitive linkage between assessment and intervention that can be obscured by technicalities in the current DSM-IV nomenclature.

Menu of reasonable choices: Offering evidence based management options

At each decision point, clinicians can usually provide ambulatory patients with opportunities to collaborate in the treatment planning by offering a choice among the options they consider to be reasonable choices. Construction of a 'menu of reasonable choices' reflects the clinician's knowledge of the pertinent scientific evidence and knowledge about factors individual to the patient and their current circumstances.

Generally the process of constructing a menu of reasonable choices starts with the list of treatments that could be considered 'first line' based on the best available clinical trial data, and is winnowed down to include only those that the clinician believes are appropriate given a patient's prior treatment response, family history, and the current therapeutic objectives. The menu selections should include the intervention the clinician regards as the very best option as well as any other as yet untried treatments with proven efficacy that are available to the patient and expected to be well tolerated.

Pathways for acute manic and mixed episodes, bipolar depression, rapid cycling, suicide prevention and maintenance treatment have been published (17) and cannot be reproduced here due to space limitations. General principles for the selection of strategies and treatments can be applied to construct a 'menu of reasonable choices' at each of the critical decision points across all pathways.

1. Use proven treatments first, begin with treatments having category A evidence (see below).
2. Choose a strategy of Sequential Care or Urgent Care.
3. Avoid the use of mood-elevating treatments (e.g. antidepressants, stimulants) unless balanced by treatments with proven acute or prophylactic antimanic efficacy.
4. Use a multiphase treatment strategy that targets the treatment plan to specific objectives as patients progress through phases of acute, continuation and maintenance treatment.
5. Offer an optimal trial for assessment of Benefit : Burden.

Weighing unequal evidence

The principle of using proven treatments first requires an up-to-date knowledge of the available peer-reviewed evidence and a process of critical evaluation to weigh the evidence. It is worth noting that for many decisions, pertinent high-quality evidence might be totally lacking. None the less, a good clinical manager will want to offer treatments based on the best available evidence and will want to assign weight to such forms of evidence as are available. Grading systems frequently employed in the construction of evidence-based guidelines can be cumbersome, but are easily adapted to inform the critical analysis needed to rank treatments in routine practice.

The best quality of evidence comes from placebo-controlled double-blind trials in which treatment assignment is made by randomization. This level of evidence merits an 'A' rating when the trial has included an appropriate sample sufficiently large to have at least an 80% chance of detecting a difference (statistical power) and provide confidence that the results are not due to chance alone. A detailed review of statistical considerations is beyond the scope of this paper, but two points are important to note here. First, generally accepted statistical conventions allow the interpretation of results as significantly different, when the probability that the observed difference is attributable to chance alone is 5% or less. Second, studies reporting differences insufficient to meet this standard merely fail to allow rejection of the null hypothesis and do not indicate that the

conditions are the same. In order words, failure to detect a statistically significant difference does not mean treatment conditions are equivalent.

For purposes of weighing evidence, simply remembering the criteria above for category 'A' provides a readily remembered standard sufficient to judge the quality of many published reports. A somewhat more refined approach might reserve an 'A+' for those instances where less than 40 studies have been reported and more than one double-blind placebo controlled study supports a positive finding. An 'A–' could indicate positive outcomes on some but not all relevant measures. Double-blind controlled trials without placebo or not completely satisfying the requirements above, would be category 'B'. Open trials can be very valuable when controlled and are most informative when the treatments being compared are assigned by randomization. Such trials will be categorized as 'C' and 'C+', respectively. Uncontrolled observations are frequently problematic but case series and even single case reports can provide a rationale for selecting treatment and can be categorized 'D' and 'D–', respectively. In the absence of published studies treatments could be rated 'E+' or 'E–' depending on whether or not clear category 'A' evidence supported a class effect treatment.

This rough guide to ranking treatments (see Table 1) can help establish the evidence basis for grouping medications in the roughly equivalent ranks referred to below as 'equipoise options' and used to create a menu of reasonable choices for patients. Note: Lacking high-quality head to head comparison studies, ranking within a grouping (e.g. treatments with Category A) cannot be well justified.

Table I. Quality of evidence for widely used psychotropics

	Prophylaxis (mood stabilizer)	Acute mania/mixed	Acute bipolar depression	Rapid cycling
Lithium	A +	A +	B	C –
Divalproex	A –	A +	D	D
Carbamazepine	D	A +	D	D
Lamotrigine	A +	F	A	A
Gabapentin	E-	F	D	D
Topiramate	E-	D	D	D
Oxcarbazepine	E-	D	E –	D
Aripiprazole	A	A +	D	D
Clozapine	D	D	E	D
Haloperidol	D	A	E –	E –
Olanzapine	B	A +	A	D
Risperidone	E +	A +	D	D
Quetiapine	E +	A +	A	D
Ziprasidone	E +	A	E –	E –
Omega 3	D	E –	F	F

The Quality of evidence

Category A: double blind placebo controlled trials with adequate samples
Category B: double blind comparator studies with adequate samples
Category C: open trials with adequate samples
Category D: uncontrolled observation or controlled study with ambiguous result
Category E: no published evidence, ± clear evidence of a class effect
Category F: available evidence negative

The term 'mood stabilizer' is problematic in any discussion of evidence-based treatment. Nearly all guidelines use the term 'mood stabilizer' in reference to a class of treatments for bipolar patients, but this widely used term has no consensus scientific definition and no therapeutic agent has been approved as a 'mood stabilizer'. Worse still, its usage by medical professionals can produce misunderstanding. In 1999 focus groups conducted prior to initiation of STEP-BD asked patients, family members and clinicians about their perception of 'mood stabilizer'. For clinicians 'mood stabilizer' is most frequently understood as a shorthand reference to lithium, carbamazepine, and valproate. For patients, the meaning of mood stabilizer ranges from an appealing means of achieving affective balance to a threatening modality offering only to anchor mood to perpetual dysphoria. Some bipolar patients, when offered a mood stabilizer for treatment of an acute episode of depression, reported feeling suspicious that their suffering was not being taken seriously.

The tendency to refer to interventions with anticonvulsant or putative antimanic properties as 'mood stabilizers' even in the absence of any data specific to their use in bipolar disorder reflects the imprecision of the term and serves no public health interest. While there is no basis for an evidence-based claim to be a mood stablizer, many of the commonly used agents above do have category A evidence that demonstrates their efficacy for one or more bipolar-related indication. Instead of continuing the use of an imprecise term, it may be preferable for clarity of communication to refer to treatments in terms that convey their range of proven acute and/or prophylactic (anti-cycling) efficacy for bipolar disorder.

The term 'mood stabilizer' need not be expunged from our discourse, but should be limited to only those instances where alternatives with less common usage might detract from the meaning intended.

Choose a sequential care or urgent care strategy

A wide range of potentially appropriate treatments might be sequenced and dosed very differently for

individuals at the same decision point. The collaborative care approach begins by determining whether priority should be given to tolerability or efficacy, based on the patient's current diagnosis, symptom profile and past history. Treatment tactics are then organized in accordance with the strategy that best serves the current priority.

The **sequential care strategy** gives highest priority given to tolerability.

The **urgent care strategy** gives highest priority to immediate efficacy.

Just as with other medical conditions such as hypertension, risk assessment drives the priority of treatment. A mildly hypertensive patient might be offered diet and exercise, and should that prove ineffective then a diuretic and then a beta-blocker. In this sequential care scenario, the most benign untried option available is offered at each decision point. Dosing typically starts with monotherapy at a low dose and progresses gradually until the desired effect is achieved. An urgent care approach might be offered to patients suffering from malignant hypertension. Urgent care options might sacrifice tolerability for the potential life-saving benefit of intravenous antihypertensive treatment. Urgent care dosing typically starts with combination therapy and progresses with aggressive titration to reach effective therapeutic levels as quickly as possible.

This general approach enables the clinician to choose an appropriate specific strategy for the patient's circumstances. The strategy selected provides the organizing principle for assembling treatments in a sequence most desirable for individual patients within each treatment pathway.

Optimally, treatment trials are carried out until: clinical objectives are met; the trial is declared ineffective (due to lack of response at maximal tolerated dose); or adverse effects force a change in treatment. Changing treatments before reaching one of these three endpoints can lead to a series of uninterpretable suboptimal trials.

Education

A menu of reasonable choices can be presented to all but the most acutely ill patient for discussion of the potential interventions that the clinician views as roughly equivalent: so-called 'equipoise options'. The degree to which discussions provide meaningful basis for negotiating a treatment plan tends to reflect the degree to which the patient has been educated about the illness and the options available. Therefore education is an essential part of the treatment process. Practical information concerning the expectable benefits, tolerability, adverse effects and costs of each option relative to the others should be presented forthrightly. The use of enduring materials allows much of the psychoeducation to take place under circumstance more favorable to retention than can typically be accomplished in an office visit, particularly when patients are acutely ill. To improve the impact of office-based education, STEP-BD provides a workbook and educational video and encourages viewing with family members.

Written materials such as the practical medication tables used in STEP-BD, which allow the patient to make side-by-side comparisons of the interventions offered, can be very helpful in this process (available at http://www.manicdepressive.org). These tables are reviewed with patients and copies of the selected intervention can be distributed to the patient and their supports.

Negotiation

Unfortunately medical schools offer little training in negotiation. The iterative collaborative process starts by giving highest priority to patient preference in the selection of a treatment from the group of equipoise options. This establishes a process of negotiation in which patient and care provider can establish criteria to judge the results of each intervention and make contingency plans in advance of anticipated problems. As the next decision point is reached, the menu of reasonable choices for that patient will be modified by the outcome of the prior intervention and another round of negotiation will lead to selection of the next reasonable intervention based on patient preference.

The overarching aim of the iterative cycles of negotiation and measurement is to increase the concordance between the treatment recommendations offered by the clinician as the best option and that accepted by the patient. In most cases, the lessons of repeated measured experience brings all partners to modify their positions and achieves better outcomes over time.

Measurement

The value of feedback of measurement upon management may seem so obvious as a means to increase the probability of a positive outcome over time as to not need explicit statement. Clinical records, however, often lack any specific measure of treatment outcome. Measures need not be long formal scales or intrusive, but do need to be used routinely to serve this purpose. Patients can usually

be enlisted in extending the collaboration beyond selection of treatment to include participation in the disciplined record keeping necessary to track outcomes and obtain the benefit of this iterative process.

Enhanced assessment for bipolar disorder

The process of careful systematic assessment extends from the initial evaluation to every follow-up visit and includes active listening, probes for specific diagnostic information including suicidality, substance use, and general medical conditions. Complete assessment requires utilization of collateral information (information from family, friends, medical records and other care providers).

The major goal of assessment is identification of clinical decision points in the course of illness. Care providers, patients and family members share an interest in making the process, by which assessments are translated into making intervention strategies as accurate and time-efficient as possible.

An unstructured, largely narrative, record and treatment plan is problematic for systematic disease management. A completely structured system could overwhelm users with a vast array of rarely used options and assessments. The STEP-BD provides standardized assessment instruments for the initial clinical assessment and routine follow-up. Space limitations here permit only discussion of a few features of the instruments used to enhance assessment in STEP-BD. Full versions of the instruments and their user's guides are available at http://www.manicdepressive.org.

Initial clinical evaluation

The Affective Disorder Evaluation (ADE) is a standardized tool for initial clinical assessment used in STEP-BD. Its main objective is to provide a time-efficient means by which a reliable current and lifetime diagnosis can be made and initial treatment recommendations can be formulated. The ADE form collects a wide array of clinical data, including 284 fields coded for harvest into a research database. In outline the ADE (see Table 2) consists of modules, which correspond to those found on most psychiatric evaluation forms. What features make the ADE a specialized tool for evaluation of mood disorders? To enhance the reliability of diagnosis, the ADE uses an adaptation of the mood disorder modules from the Structured Clinical Interview for DSM-IV (18) (SCID). These modules assess current mood episode and lifetime mood disorder diagnosis and flow in an orderly sequence designed to reflect the DSM-IV mood disorder classification (see

Table 2. Outline of affective disorder evaluation

History of present illness
Narrative
Current medications
Mood episode screening questions
Current depression module
Current mood elevation module
Episode onset
Course over past 2 years
Longest well period
Dysthymia
Cyclothymia
Current clinical status
Lifetime mood disorder diagnosis:
Abnormal mood elevation
Most extreme primary mood elevation
Associated features of hypomania/mania
Number of episodes
Age at once set of earliest episode
Major depression
Most extreme primary depression
Associated features of hypomania/mania
Number of episodes
Age at once set of earliest episode
Pattern of mood symptoms
Episode sequence
Seasonality
Rapid cycling
Perimenstrual symptoms
Postpartum episodes
Treatment emergent affective switch
Psychotic symptoms (current and past)
Childhood history
Other psychiatric history
Social and academic history
Family history
Psychoactive substance use
Prior treatment and response
Medical history
Laboratory assessments
Mental status
Physical exam
Multiaxial diagnoses
Treatment recommendations

Figure 2) The ADE uses a set of standardized notation and recording conventions that make it time efficient. These techniques are carried over to the Clinical Monitoring Form used at follow-up and will be described below. Two features of the ADE are highlighted here which specifically aim to improve diagnostic confidence by ensuring documentation of the most extreme episode of mood elevation and assessing bipolarity as a continuous dimensional characteristic.

Improving diagnostic confidence

The occurrence of clear-cut episodes of mood elevation (e.g. mania, hypomania, mixed) is the cardinal feature by which the DSM-IV distingui-

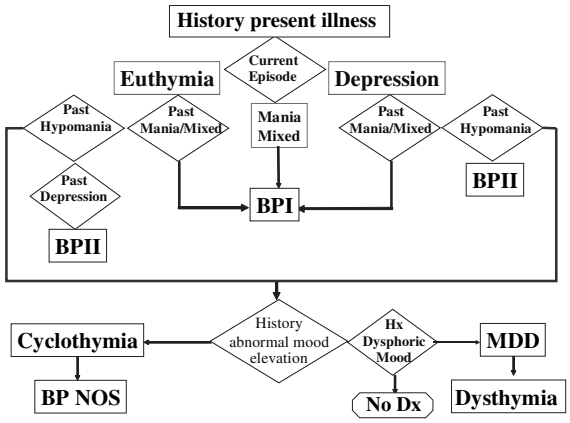

Fig. 2. Diagnostic evaluation of mood disorders.

shes bipolar disorder, from unipolar disorder. Unfortunately, even patients with histories including several dramatic manic episodes sometimes endure multiple changes in their diagnosis, because the record does not include adequate documentation of even a single clear cut episode.

Merely recording a diagnosis of bipolar disorder without a well-documented episode does little to prevent needless diagnostic revision and misguided treatment. A record detailing the most extreme episode of mood elevation including a narrative and systematic symptom ratings often provides the decisive evidence needed to prevent the revision of a well-established diagnosis when poor memory and/or perceptual distortion, which accompany abnormal mood episodes, renders the patient's self report insensitive to prior episodes of mood elevation. Therefore, the ADE is structured with an emphasis on identification and documentation of the most extreme episode of mood elevation.

At the end of an evaluation, the goal of producing a DSM-IV diagnosis usually drives the assessment toward consideration of bipolarity as a categorical assessment. Rarely, however, does every feature of an individual's history consistently typify bipolar disorder or consistently point away from a bipolar diagnosis. Hence, a continuous bipolarity score could be a useful alternative to categorizing bipolarity as present or absent and can improve diagnostic confidence.

Rationale for a bipolar Index

Confidence in mood disorder diagnosis is limited under the DSM classification by reliance on clinical features defining syndromal mood episodes. Kraepelin noted the unreliability of symptomatic assessments and used age of onset and course of illness to distinguish what he termed manic-depressive insanity from many conditions with overlapping cross-sectional phenomenology (19). Leonhard's proposed bipolar and monopolar subtypes (20) were validated primarily by family history studies conducted by Angst, Parris, and Winokur (21) and support the DSM-IV classification of Unipolar and Bipolar Mood Disorders. Response to treatment has also been used to distinguish illness subtypes.

Integrating information gathered in the evaluation across the five dimensions that have been used to validate psychiatric disorders, STEP-BD computes bipolarity index scores by rating the patient's profile relative to the traits thought most characteristic of Bipolar I disorder. The Bipolarity Index provided in Table 3 was developed by a consenus committee of experienced bipolar investigators (Sachs G, Baldassano C, Ghaemi SN, Demopoulos C) who assigned common clinical features along each of these five dimensions a 0–20 score, where 20 points represents the presence of traits considered most characteristics of Bipolar I disorder (see Table 4). A theoretical case with the traits most convincing for bipolar disorder on every dimension would score 100 points, most Bipolar I patients score above 60.

Incorporation of this rating system into the initial clinical assessment provides an index of the confidence by considering bipolarity as a continuous dimensional construct and helps to focus the evaluation process. See Table 3 for Bipolarity Index with full scoring criteria.

Diagnosis: five dimensions
I Episode Characteristics
II Age of Onset (1st affective episode)
III Course of Illness/Associated Features
IV Response to Treatment
V Family History

For each dimension

20 = Most convincing characteristic of bipolar disorder
15 = Convincing characteristic of bipolar disorder
10 = Known associated feature of bipolar disorder
5 = Non-specific feature suggestive of bipolar disorder
2 = Feature with possible relationship to bipolar disorder
0 = No evidence of bipolar disorder

Focus initial neuropsychiatric assessment to establish current and lifetime diagnosis

Accurate determination of lifetime mood disorder diagnosis and current episode is critical because

Table 3. Bipolarity index

For each of the items below circle the item characteristic of the patient:	
Most convincing characteristic = 20	Convincing characteristic of Bipolar Disorder = 15
Known associated feature of Bipolar Disorder = 10	Non-specific feature suggestive of Bipolar Disorder = 5
Feature with possible relationship to Bipolar Disorder = 2	No evidence of Bipolar Disorder = 0
I Episode characteristics	**Score** = /20
20	Documented acute mania or mixed episode with prominent euphoria, grandiosity or expansiveness and no significant general medical or known secondary etiology
15	Clear-cut acute mixed episode or dysphoric, or irritable mania with no significant general medical or known secondary etiology
10	Clear-cut hypomania with no significant general medical or known secondary etiology Clear-cut cyclothymia with no significant general medical or known secondary etiology Clear cut mania secondary to antidepressant use
5	Clear cut hypomania secondary to antidepressant use Episodes with characteristics sxs of hypomania but symptoms, duration or intensity are subthreshold for hypomania or cyclothymia A single major depressive episode with psychotic or atypical features (Atypical = 2 of 3: hypersomnia, hyperphagia, leaden paralysis of limbs Any postpartum depression
2	Any recurrent typical unipolar major depressive disorder History of any kind of psychotic episode(i.e. presence of delusions, hallucinations, ideas of reference, or magical thinking)
0	No history of significant mood elevation, recurrent depression, or psychosis
II Age of onset (1st affective episode/syndrome)	**Score** = /20
20	Age 15–19 years
15	Age < 15 or 20–30
10	First episode age 30–45
5	First episode > 45
0	No history of affective illness (no episodes, cyclothymia, dysthymia or BP NOS)
III Course of illness/associated features	**Score** = /20
20	Recurrent distinct manic episodes separated by periods of full recovery
15	Recurrent distinct manic episodes with incomplete interepisode recovery Recurrent distinct hypomanic episodes with full interepisode recovery
10	Comorbid substance abuse Psychotic features only during acute mood episodes –ncarceration or repeated legal offences related to manic behaviour (e.g. shoplifting, reckless driving, bankruptcy)
5	Recurrent unipolar MDD with three or more major depressive episodes Recurrent distinct hypomanic episodes without full interepisode recovery Recurrent medication non-compliance Comorbid borderline personality Comorbid anxiety or eating disorders (e.g. OCD, panic disorder, bulimia) History of ADHD in childhood and periods of above average scholastic or social function Gambling, risky investment, overspending, or sexual indiscretions have (or would if not concealed) pose a problem for patient, friends, or family Behavioral evidence of perimenstrual exacerbation of mood symptoms
2	Baseline hyperthymic personality (when not manic or depressed) Married three or more times (including remarriage to same individual) In two or more years has started a new job and changed jobs after less than year Has more than two advanced degrees
10	None of the above
IV Response to treatment	**Score** = /20
20	Full recovery within 4 weeks of therapeutic treatment with mood stabilizing medication
15	Full recovery within 12 weeks of therapeutic treatment with mood stabilizing medication or relapse within 12 weeks of discontinuing treatment Affective switch to mania (pure or mixed) within 12 weeks of starting a new antidepressant or increasing dose
10	Worsening dysphoria or mixed symptoms during antidepressant treatment subthreshold for mania Partial response to one or two mood stabilizers within 12 weeks of therapeutic treatment Antidepressant-induced new or worsening rapid-cycling course
5	Treatment resistance: lack of response to complete trials of three or more antidepressants Affective switch to mania or hypomania with antidepressant withdrawal

Table 3. Continued

2	Immediate near complete response to antidepressants (in 1 week or less)
0	None of the above or no treatment
V Family history	**Score** = /20
20	At least one first-degree relative with documented bipolar illness
0	First-degree relative with documented recurrent unipolar MDD or schizoaffective disorder Any relative with documented bipolar illness Any relative with documented recurrent unipolar MDD and behavioural evidence suggesting bipolar illness
5	First-degree relative with documented substance abuse, or any relative with possible bipolar illness
2	First degree relative with possible recurrent unipolar MDD First degree relative with diagnosed related illness: anxiety disorders, eating disorders, ADD
0	None of the above or no family psychiatric illness
	Total Score /100

Table 4. Characteristics most convincing for bipolar disorder across five diagnostic dimensions

Episode characteristics:	20 = Documented acute mania or mixed episode with prominent euphoria, grandiosity or expansiveness and no significant general medical or known secondary etiology
Age of onset:	20 = Age 15–19 year
Course of illness:	20 = Recurrent distinct manic episodes separated by periods of full recovery
Response to treatment:	20 = Full recovery within 4 weeks of therapeutic treatment with mood stabilizing medication
Family history:	20 = At least one first degree relative with documented bipolar illness

these assessments provide the basis for selecting and staging treatment modalities.

A complete evaluation includes the psychiatric and medical history, directed physical examination and indicated laboratories. Routine baseline evaluation should include complete blood count, serum chemistries and thyroid functions. Electroencephalogram, imaging studies, toxicology, and erythrocyte sedimentation rate are also reasonable at least once in order to screen for potential secondary causes of mood episodes.

Bipolar illness is relatively easy to diagnose when the patient presents with a current manic or mixed episode. Failure to diagnosis bipolar illness in a depressed patient is a common occurrence and frequently associated with antidepressant treatment emergent mania. The potential for this bad outcome can be reduced by including systematic screening for episodes of abnormal mood elevation in the evaluation of all mood disorder patients.

By identifying and characterizing the most extreme period of mood elevation, it is possible to rapidly determine whether a patient meets criteria for Bipolar I, Bipolar II, Cyclothymia or Bipolar NOS (Figure 2). A template for the standardized ADE used in STEP-BD can be found on http://www.manicdepressive.org.

Avoid reliance on self-report alone

Mood often colours perception! Since the psychiatrist's direct observation of the patient is usually limited to brief interviews, assessment of bipolar patients can be improved by augmenting the patient's clinical report with reports from significant others. Whenever possible, clinicians should endeavour to establish and maintain a positive therapeutic alliance with the patient, the patient's family and any systems important in caring for the patient. With the consent of the patient, establishing a policy of open communication gives the psychiatrist access to old records and the important observations of those who know the patient well. Since a central feature of bipolar illness is episodic distortion in self-assessment, this offers the patient some protection against the risk of relying solely on their self-observation to guide treatment decisions. As the recipient of multiple inputs, the psychiatrist must weigh the conflicting descriptions of the patient's symptoms. The sensitivity and specificity of clinical examination is greatly influenced by the illness and the perspective of the reporter. In general, patient self-report is most sensitive and least specific for symptoms of depression. In contrast, friends and family tend to be most sensitive and least specific for symptoms of mood elevation.

Follow-up assessment: linking clinical status and intervention at every visit

The 'Clinical Monitoring Form' (CMF) is a 1-page standardized record-keeping form designed for use as a routine progress note and can be used in conjunction with a Waiting Room Self-Monitoring Form (forms and users guides available http://

www.manicdepressive.org). The CMF records all the data required to determine the clinical status and over 100 other clinically important variables. Simple recording conventions are used to score symptoms (see Table 5), record medication dose, rate adverse effect, track substance use and mental status. The CMF provides several summary ratings such as the clinical global impression of severity (CGI-S) and the global assessment of function (GAF) along with a clinical status. Each clinical status links to a treatment pathway (e.g. acute depression, relapse prevention, rapid cycling) consisting of a series of critical decision points along with the recommended interventions.

Using the patient self-report form as a starting point, clinicians can usually elicit the information needed for a comprehensive progress note, such as the CMF, within 10 min. Very ill patients or those unwilling to collaborate require additional time, but even in these circumstances a systematic assessment adds efficiency.

Many clinical interactions are lengthy due to inefficient communication. Substantial time expenditure may be required to elicit even simple information like number of hours slept, or an appointment may be extended when, in the closing minute of an appointment, important information is revealed unexpectedly. Furthermore, after leaving their appointment, patients often experience dismay at having forgotten to tell their care provider something very important. These common frustrations can be reduced by encouraging patients to bring in information recorded outside of appointment time. Patients can participate in their own assessment by completing a waiting-room self report form and a daily mood chart (for downloadable versions see http://www.manicdepressive.org). Active patient collaboration with the assessment routine yields substantial rewards because time efficiency produces more time for unstructured communication with their clinician. In addition, information recorded contemporaneously by the patient at home or in the waiting room improves rapport by providing a time-labelled source of patient subjective experience. This record can be a powerful counterweight when patients' recollection are coloured by nihilism ('I've never been well'), or euphoric recall ('I never had a problem').

With minimal time investment, new patients usually become sufficiently informed to begin contributing as meaningful collaborators to the assessment process within the first few visits and are usually willing and able to leverage their contact time by completing simple self-report forms.

Table 5 CMF recording conventions for associated symptoms of depression and mania

0 = None or usual		
Decreased	from normal, euthymic state	Increased
−1/4	Questionable, slight or rare symptom (occurred once or twice) but not clinically significant	+ 1/4
−1/2	Clearly present symptom but subthreshold for DSM-IV Mild Moderate	+ 1/2
−1	Clearly present and fulfills DSM-IV criteria	+ 1
−1.5	Marked	+ 1.5
−2	Severe	+ 2

Determination of clinical status

At every follow-up visit, the assessment determines the presence of one of the eight mutually exclusive clinical states listed in Table 6. Practioners accustomed to using the DSM-IV will immediately recognize that seven of the eight correspond with familiar terms. The concept of clinical status builds on this familiar nomenclature to improve the linkage between the current assessment and a management decision point in one of the clinical pathways.

Over the course of bipolar illness, patients may present with acute symptoms diagnosable under DSM-IV criteria as fully syndromal episodes of major depression, mania, hypomania, or mixed episodes and a recovered state, which requires 8 weeks with minimal symptomatology. These easily link with pathways described in subsequent chapters, but do not suffice to guide treatment over the course of bipolar disorder.

Table 6 Definitions for assignment of clinical status

	DSM IV	Clinical status
Fully syndromal	Depression Mania Hypomania Mixed	Depression Mania Hypomania Mixed
Subsyndromal	**Partial recovery** Symptoms substhreshold for full episode or less than 8 weeks with minimal symptoms	**Continued symptomatic** ≥ 3 moderate symptoms
		Recovering < 2 moderate symptoms
Well	Recovered	**Recovered** > 8 weeks with < 2 moderate symptoms
New subsyndromal		**Roughening** ≥ 3 moderate symptoms following after meeting criteria for 'Recovered'

Under DSM-IV the designation 'partial recovery' is given to two very different groups: patients who remain ill, but whose current symptoms are subthreshold for a full episode; and euthymic patients whose well state has a duration of less than 8 weeks. STEP-BD avoids this management problem by using the separate clinical status designations 'continued symptomatic' and 'recovering'. Therefore, by merely giving separate names to what DSM-IV has already dichotomized, the clinical status can provide a clear link to management recommendations. 'Continued symptomatic' patients have fluctuating symptoms that are just below the criteria for a full episode and should continue acute phase management, while newly well 'recovering' patients can be managed in accordance with continuation phase treatment guidelines.

An eighth term, 'roughening' is used to describe the occurrence of new subsyndromal symptoms after the patient has met the 'recovered' criteria. Roughening indicates an increased likelihood of a new episode (22,23).

Conclusion

This paper describes techniques designed to improve treatment outcome in STEP-BD and can be implemented in routine clinical management. The iterative model presented seeks to increase the linkage of measurement with management. Use of this model requires recognition of 'critical decision points', working knowledge of evidence-base treatments, and understanding of individual factors. The collaborative approach recommended requires that practitioners the skill to negotiation and have the capacity to enlist the patient and their supports as collaborators. Systematic assessment techniques can improve diagnostic confidence and provide outcome measures to gauge response to treatment.

Declaration of interest

Dr Sachs conducts no pharmaceutical industry funded research. He is on the advisory board of a number of companies and has been paid honoraria for lectures by many companies including Eli Lily & Co.

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