Clinical Practice Guidelines for Bipolar Disorder From the Department of Veterans Affairs

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Background: For the last several years, the Department of Veterans Affairs (VA) has been involved in the development of practice guidelines for major medical, surgical, and mental disorders. This article describes the development and content of the VA-Clinical Practice Guidelines for Bipolar Disorder, which are available in their entirety on the *Journal* Web site (http://www.psychiatrist.com).

Method: A multidisciplinary work group composed of content experts in the field of bipolar disorder and practitioners in general clinical practice was convened by the VA's Office of Performance and Quality and the Mental Health Strategic Health Group. The work group was instructed in algorithm development and methods of evidence evaluation. Draft guidelines were developed over the course of 6 months of meetings and conference calls, and that draft was then sent to nationally prominent content experts for final critique.

Results: The Bipolar Guidelines are part of the family of the VA Clinical Guidelines for Management of Persons with Psychosis and consist of explicit algorithms supplemented by annotations that explain the specific decision points and their basis in the scientific literature. The guidelines are organized into 5 modules: a Core Module for diagnosis and assignment to mood state plus 4 treatment modules (Manic/Hypomanic/Mixed Episode, Bipolar Depressive Episode, Rapid Cycling, and Bipolar Disorder With Psychotic Features). The modules specify particular diagnostic and treatment tasks at each step, including both somatotherapeutic and psychotherapeutic interventions.

Conclusion: The VA Bipolar Guidelines are designed for easy clinical reference in decision making with individual patients, as well as for use as a scholarly reference tool. They also have utility in training activities and quality improvement programs.

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Although the Bipolar Guidelines were developed under the auspices of the Department of Veterans Affairs, the opinions expressed by the authors in this report are their own and do not necessarily reflect the official position of the VA.

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The complete text of the Clinical Practice Guidelines for Bipolar Disorder From the Department of Veterans Affairs *is available via the Internet (http://www.psychiatrist.com).*

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Clinical practice guidelines represent a profound paradigm shift as U.S. health care enters the 21st century. A generation ago, diagnoses and treatment decisions were made according to physician experience, tradition, and training. However, as economic limitations and consumer awareness have increased, better assessment of treatments and outcomes in general clinical practice has become necessary. Practice guidelines represent one type of effort to address this need by articulating parameters for optimal clinical practice based on available scientific evidence and generally accepted clinical opinion.

In medicine and surgery, the need for practice guidelines has been apparent for at least 15 years, when major unexplained variations in the rates of common surgical procedures were reported across neighboring cities.[1] The implementation of standardized guidelines has been one method used to reduce such variability.[2,3] By contrast, psychiatry has only recently begun to document and examine variability in clinical practice. One of the few studies on this issue was conducted by Fortney et al.[4] in the Department of Veterans Affairs (VA), who demonstrated a 4-fold variation in length of inpatient stay for depression

across VA medical centers. This variability could not be explained by either case mix or other patient-related factors. Thus, the VA is likely to provide an opportunity to study and standardize general clinical practice for common mental health problems.

The VA also provides an ideal, and important, system in which to develop and study the impact of mental health practice guidelines on general clinical practice. First, VA clinicians responsible for making psychiatric treatment decisions are trained in a broad spectrum of theoretical orientations, thus making it likely that many variations in practice patterns such as the above[4] are based on individual factors.

Second, the VA serves a large number of seriously mentally ill veterans who, as a group, are consumers of large amounts of services, making optimal treatment of this population a high priority for the VA system. For instance, between 405,000 and 630,000 veterans suffer from serious mental illness, and about 326,000 of these veterans use VA services each year.[5] These seriously mentally ill veterans are 5 times more likely to use VA services than veterans in the general population. During fiscal year 1993, the VA provided 4 million days of inpatient care for these individuals at a cost of approximately $1.3 billion, and 4.5 million outpatient visits costing $225 million.[6] Further, the number of veterans treated in outpatient settings has increased by nearly 20% between 1990 and 1995.[5]

Third, the VA system is centralized and hierarchical and maintains an extensive automated data management system. These characteristics make it feasible both to implement systemwide changes effectively in clinical practice and to monitor their results.

The VA has recognized 3 varieties of clinical guidelines as potentially useful: Clinical Practice Guidelines, Clinical Algorithms, and Clinical Pathways.[7] *Clinical Practice Guidelines* are statements that assist both the practitioner and patient in making the best decisions about appropriate health care in specific circumstances. They take the form of explicit recommendations for the performance or exclusion of specific procedures or services. *Clinical Algorithms*, incorporated into Clinical Practice Guidelines, are explicit decision tools in the form of flow charts or decision trees. They systematically guide the user through a series of steps that describe key elements of treatment, e.g., diagnosis, therapeutic interventions, time and/or length of treatment. This type of algorithm is the core of the VA Bipolar Guidelines. *Clinical Pathways* are locally developed management tools that are based on systemwide Clinical Practice Guidelines and Algorithms. They define key processes and events, which are important to the day-to-day management of care in a given environment.

To date, the VA has developed algorithm-based guidelines for several common health problems of veterans, including heart disease, chronic pulmonary disease, and common surgical diagnoses (available through the VA Office of Performance and Quality). The first guideline developed for a major mental illness was for major depressive disorder and was completed in 1996.[8] Several months later, working groups were convened to establish treatment guidelines for the major psychoses.[9] This document was divided into 4 individual sections on organic psychoses, schizophrenia, bipolar disorder, and psychosocial rehabilitation. The VA Bipolar Guidelines from this family of guidelines are the subject of this review.

The purpose of this article is to introduce readers to the Bipolar Guidelines and to describe their empirically based development. The algorithms are presented in their entirety, with an overview outlining the most salient or controversial decision points. The entire text of the Bipolar Guidelines, comprised of over 50 pages of algorithms and annotations, is available on the *Journal* Web site (http://www.psychiatrist.com). Comparison with other major guidelines for bipolar disorder is found in the Discussion section of this article.

METHOD

Overview of the Developmental Process for VA Mental Health Guidelines

The VA Office of Performance and Quality and the Mental Health Strategic Health Care Group coordinated the development of Major Depressive Disorder[8] and Psychoses Guidelines,[9] with the Bipolar Guidelines a subset of the latter. The principles for development of each of the guidelines were identical. With support from the VA's External Peer Review program, multidisciplinary work groups were created to work on each of the guidelines. Each group consisted of facilitators who were experienced in algorithm development and decision-making processes, content experts, and professionals in general clinical practice in VA, university, and/or private practice venues. The consulting group conducted an extensive literature search using *bipolar affective disorder, schizoaffective disorder,* and related terms, and recent articles were provided to team members for use in the guideline development. Consumer input was solicited from clients and family members by conducting focus groups at 5 medical centers across the nation.

The working groups first met in November 1996 for a 2-day orientation and education session. All members received instruction in formal algorithm methodology and group decision-making methods (e.g., nominal group process, delphi method). The group was also instructed in the U.S. Agency for Health Care Policy and Research (AHCPR)[10] and American College of Cardiologists and American Heart Association (ACC/AHA)[11] methods for evidence evaluation, as summarized in Table 1. The groups were oriented to the framework for the final product, which was to consist of a set of freestanding algorithms supplemented by a series of text annotations that

Table 1. Classification of Evidence and Recommendations According to the AHCPR and ACC/AHA Systems[a]

AHCPR[10] Classification of Strength of Evidence
Class A: Randomized controlled trials
Class B: Well-designed clinical studies
Class C: Panel consensus
ACC/AHA[11] Classification of Strength of Recommendations
Class I: Usually indicated, always acceptable, and considered useful and effective
Class II: Acceptable, of uncertain efficacy, and may be controversial
IIa: Weight of evidence in favor of usefulness/efficacy
IIb: Not well established by evidence, can be helpful and probably not harmful
Class III: Not indicated and may be harmful

[a]Abbreviations: AHCPR = U.S. Agency for Health Care Policy and Research, ACC/AHA = American College of Cardiologists and American Heart Association.

would include expansion of the recommendations and scholarly reviews of evidence. Thus, the content is similar to that of the AHCPR guidelines, but the algorithms and text were to be separated for ease of use. During the initial meeting, the work groups responsible for developing the 4 psychosis guidelines also met separately to formulate plans and strategies for how to best accomplish their task of having a draft algorithm completed by February 1997. The second and final face-to-face meeting of all participants took place in March 1997. During this 2-day meeting, the individual draft guidelines were reviewed and critiqued by all of the groups working on the psychosis guidelines in order to identify and reconcile interface and coordination issues among the guidelines.

During the entire process of algorithm development, the empirical basis for their construction was recorded in a series of text annotations that were associated with the relevant algorithm steps. These annotations were used to expand on instructions presented in skeletal form in the algorithm itself, to provide references for further information, and, importantly, to present the scientific basis for each specific algorithm step. In this last endeavor, the work groups recorded their evaluation of the scientific evidence based on AHCPR standards and indicated the confidence of the resulting recommendation based on ACC/AHA standards. The primary source references that served as the basis for the recommendations were typically summarized in the form of evidence tables for easy reference by the users.

Specific Developmental Process for the Bipolar Guidelines

The Bipolar Guidelines work group consisted of both content experts and practitioners in general clinical practice. Individuals were by design drawn from several disciplines (7 M.D.s, 3 Ph.D.s, 3 R.N.s, and 1 L.C.S.W.) and was led by M.D. and Ph.D. cochairs. The majority of participants were not acquainted and/or had not worked together prior to the initial meeting.

Given the complexity of bipolar disorder, each content expert was given responsibility for each of several key areas, which were to be developed into separate but linked algorithms. In addition to the core diagnostic module, which was developed by the entire group, the 4 key areas designated for individual modules were Manic/Hypomanic/Mixed Episode, Bipolar Depressive Episode, Rapid Cycling, and Bipolar with Psychotic Features (including schizoaffective disorder). The content expert solicited assistance from other members, such as performing literature searches, critiquing, editing, and revising. In addition to the 2 face-to-face meetings, approximately 16 hours of conference calls were devoted to these activities. In addition, group members communicated with each other as needed via e-mail, fax, and personal telephone calls.

The resultant Bipolar Guidelines draft was then sent to 10 content experts (predominantly non-VA), who provided written or verbal critiques. Version 1.0 was released to the field in September 1997 as part of the Clinical Guidelines for Management of Persons with Psychoses,[9] which also included the other 3 guidelines noted above. Minor text and algorithm corrections and clarifications were then incorporated in the subsequent several months, with Version 1.1 (the version summarized in this article) released in early 1998.

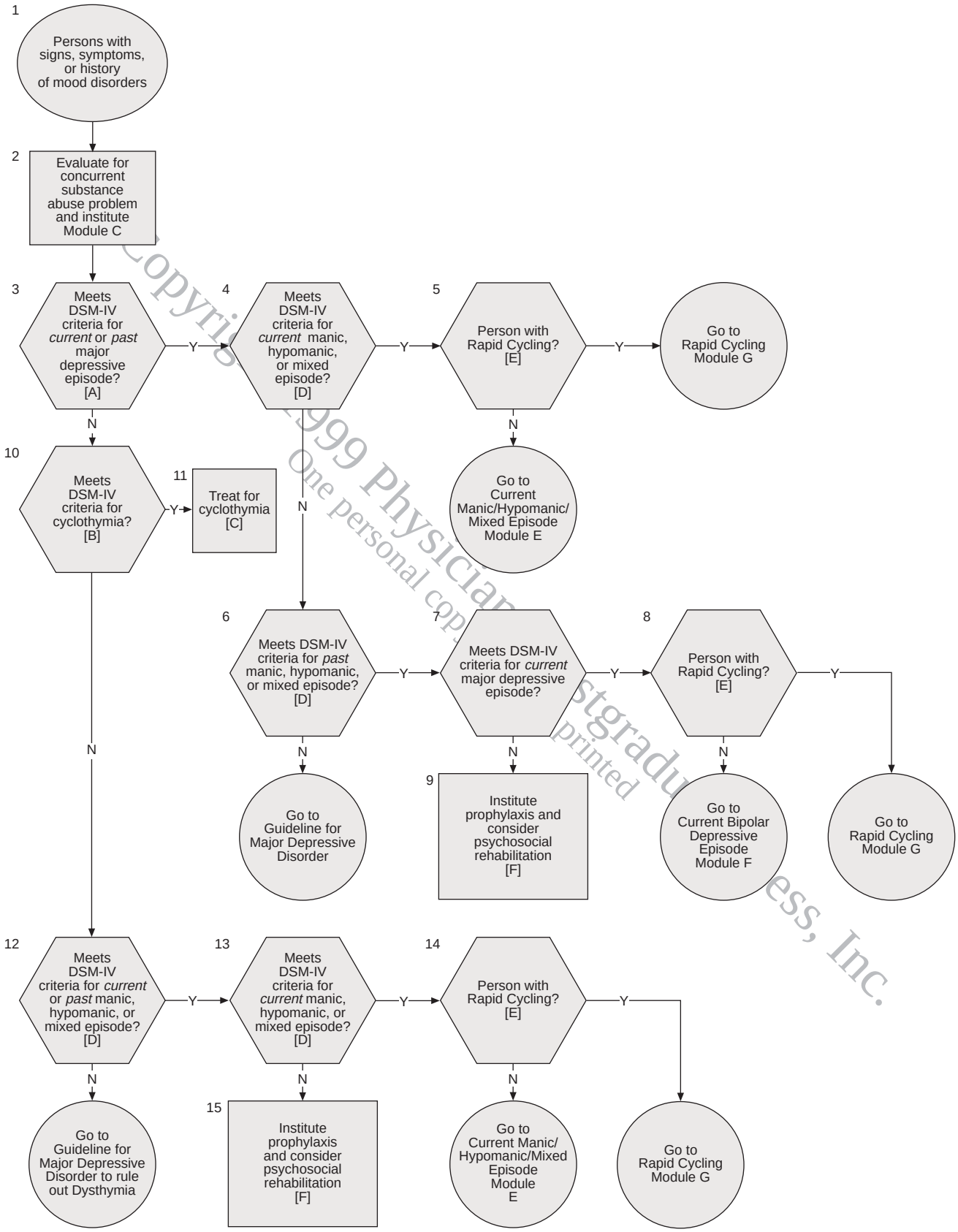
The results section of this article serves several functions. First, it provides an overview of the structure and use of the Bipolar Guidelines; these are similar to the other VA guidelines for mental illnesses. Second, the content of the Bipolar Guidelines is summarized. Third, any particularly controversial or important point is noted and briefly reviewed. A more extensive review of these issues can be found in the annotations of the guidelines themselves, located in their entirety on the *Journal* Web site; reference to specific annotations in the text of this article points the reader to the appropriate section of the appropriate module of the guidelines for further review.

RESULTS

Core Diagnostic Module

The Core Module (Module D) is intended to guide clinicians in assessing a patient's current mood state and episode history so that individuals with suspected bipolar disorder can be routed into the appropriate algorithm for future assessment and treatment. It is assumed that individuals entering the Core Module have been screened in the base module of the overall Psychoses Guidelines for (1) the presence of a mood disturbance and (2) the absence of secondary medical or substance abuse/dependence that might account for the mood disturbance. On the basis of the current episode, individuals are triaged through a series of specific algorithm steps into 1 of the 4 diagnosis-specific modules. Individuals with

Figure 1. Bipolar Disorder Core Module (Module D)



suspected bipolar disorder who are found to have major depressive disorder or dysthymia are screened out and referred to the VA Major Depression Guidelines.[8]

The Core Module algorithm (Figure 1) serves as a prototype for the algorithms for the other 4 modules; thus, it is explained here in somewhat greater detail. The starting place for the algorithm is an oval called the "clinical state box," which describes the presenting problem. The algorithm then guides the reader through a series of yes/no decision-making steps (hexagons). Steps that require some clinical action for all individuals are denoted as "do boxes" (rectangles). The "go to" circles at the various terminal steps of the algorithms indicate that DSM-IV[12]-based diagnostic criteria for a particular condition have been met, and the user is then routed to the appropriate diagnosis-specific module. An alphabetical letter appearing within a box indicates that there is an accompanying text annotation, as described in the Method section above.

The Core Module algorithm is sufficiently comprehensive and flexible to meet clinicians' needs in assessing all individuals with suspected bipolar spectrum conditions. Specifically, it is designed to triage individuals who present for treatment with or without current medications, to evaluate individuals with cyclothymia, and to accommodate individuals with bipolar disorder who present for treatment while not in a major mood episode. With regard to this last group, the relevant annotations (annotations E and F) indicate the necessity of long-term treatment with mood stabilizers for individuals with bipolar disorder. Accordingly, the data for prophylactic efficacy of the available agents are reviewed in detail along with a discussion of the costs and benefits.

The Core Module also presents an overview of psychosocial interventions for bipolar disorder. These include psychoeducation, formal psychotherapy, and psychosocial rehabilitation. The guidelines specify psychoeducation for all individuals and formal psychotherapy or psychosocial rehabilitation for selected individuals, depending on the clinical situation.

Manic, Hypomanic, or Mixed Episode Module

As seen in Figure 2, the clinical state oval indicates that individuals in the Manic, Hypomanic, or Mixed Episode Module (Module E) meet DSM-IV[12] criteria for one of these episodes and are free of causative general medical condition, substance intoxication, or substance withdrawal. The clinician must then determine the appropriate setting of care, initiate psychoeducational tasks, evaluate for other psychosocial interventions, and ensure normal thyroid functioning. Subsequent actions involve evaluating the status of current medications, making medication adjustments, and monitoring additional symptoms such as insomnia and anxiety.

The guidelines recommend that if an individual is in a manic, hypomanic, or mixed state and is receiving antidepressants, these medications should be discontinued. If there is a history of response to a previous mood-stabilizing regimen that has been stopped, that regimen should be restarted; if there has been no previous treatment with a mood stabilizer, one should be initiated (annotation J). If, after 3 weeks of treatment, there is no response to the optimal dose of the initial mood stabilizer, or if there is a clear history of nonresponse to the current mood stabilizer, the guidelines recommend starting a different mood stabilizer and tapering off the initial one (annotation K). If there is only a partial response, or if none of the mood stabilizers prove to be efficacious, a combination of different mood stabilizers (preferably lithium plus one of the anticonvulsants) is recommended treatment. In the event that mood stabilizers, either singly or in combination, do not control the acute manic symptoms, other agents with possible antimanic properties (e.g., clozapine, lamotrigine, or gabapentin) should be tried (annotation K). Once the acute manic symptoms are under control, prophylactic treatments and psychoeducation should be initiated, along with psychosocial rehabilitation if indicated (annotation F).

One of the more controversial aspects of the guidelines is their assessment of the relative strength of evidence for the available mood stabilizers—lithium, valproate, and carbamazepine—as antimanic agents. Based on the strength of evidence review of the literature, lithium is recommended as the first-line agent for both acute antimanic and prophylactic use for treating manic and mixed episodes, although some recent evidence indicates that valproate may be more effective than lithium in mixed episodes (annotation J). Also of relevance is the fact that lithium is the only agent to date for which efficacy has been established as a prophylactic agent for management after the acute episode has resolved, adding to the strength of recommendation that lithium should be the first-line antimanic agent.

While there is currently considerable enthusiasm for using the anticonvulsant valproate as a first-line acute treatment, only a relatively small number of controlled trials exist compared with the more extensive data on lithium. Those data that do exist indicate that its overall efficacy is comparable with that of lithium.[13,14] Valproate may be particularly useful in treating individuals with mania who fail to respond to lithium[14,15] or individuals with mania with concurrent depressive features (mixed manics).[15,16] Evidence for the efficacy of carbamazepine in treating acute mania is less extensive than that for lithium. Electroconvulsive therapy (ECT) may also be efficacious as a treatment for acute mania, have a role in the treatment of selected individuals, and be used as a maintenance treatment if there are compelling reasons for not using the mood-stabilizing medications. Clearly, though, additional controlled studies are in progress, and this issue will have to be revisited in later revisions of the guidelines.

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