Introduction

The medical specialties have increasingly adopted the use of guidelines to direct the treatment and management of severe and chronic illness. In psychiatry, guidelines have been published to address treatment of major psychiatric disorders in both adults and children. Despite a paucity of evidence regarding the relative efficacy of guidelines versus traditional pharmacologic management, professional groups and organizations are adopting them into practice with increasing frequency.

Guidelines should be geared to 1) produce symptom reduction in a majority of patients, 2) establish minimum expectations for healthcare delivery, and 3) assist physicians in making more informed decisions [1-4]. The implementation of treatment guidelines could produce multiple benefits, including increased consistency, integration of innovative treatments and new medications into existing treatment practices, and improved accountability of care, which may affect payment, reimbursement, and legal defense [5-7].

Patients with a history of mania (including diagnoses of schizoaffective illness, bipolar type [SABP] and bipolar I disorder [BPI]) comprise more than 2% of the adult population in the United States [8,9] and an estimated 30% of the population served by departments of Mental Health and Mental Retardation [10]. These disorders are particularly suited for application of treatment guidelines due to the 1) recent proliferation of new medication treatments, and 2) the chronicity and severity of symptomatic and functional impairment necessitating immediate translation of promising new treatments into practice. Given the limited utility of monotherapy for this population, all published guidelines move quickly to the use of combination therapies [11•,12•]. Limited prospective data have been published addressing combinations of standard mood stabilizers (lithium, valproate, carbamazepine), or combination therapies that cut across drug categories [13–22]. It is extremely unlikely that scientifically rigorous studies of all combination therapies will ever be completed because multiple trials would be required to evaluate the variety of potentially efficacious combinations for this patient population. Research that evaluates the use of a clinical practice guideline for treatment of these disorders may, among other goals, preliminarily evaluate the effectiveness of varied medication treatments.

There are risks and benefits in applying treatment guidelines and algorithms to any psychiatric disorder. In general medicine, a number of benefits of implementing guidelines have been cited, including potentially more rapid translation of scientific findings into clinical practice, the use of guidelines as a tool to facilitate decision making, and the opportunity to ensure greater uniformity of care and potentially increase the quality of care across broad treatment settings [1,4]. A potential risk is that treatment algorithms may limit options for individualizing treatment. In the treatment of patients with a history of mania, there are few controlled studies to inform a detailed algorithm, and there is a great deal of reliance on expert consensus methods. Other concerns revolve around the need to update treatment algorithms frequently to keep pace with the introduction of new medications and research findings. Once updated, it is critical that changed guidelines be disseminated effectively, in order that they remain reflective of current clinical practice and maintain credibility with clinicians. Rather than serving as direct markers for therapeutic efficacy (which in many cases, is incomplete or preliminary), guidelines for the treatment of bipolar disorder may be best considered as a method of codifying and prioritizing many treatment options.

Medication guidelines are being incorporated into psychiatric care, and may serve multiple functions, including ensuring consistent quality care, minimizing or managing costs, integration of new treatments, and providing clinicians with information necessary to make informed clinical decisions. Methods of guideline development and the published guidelines for the medication treatment of bipolar disorder are briefly reviewed. Despite limited research on the clinical efficacy of using guidelines, they serve other useful functions such as prioritizing multiple treatment options and providing a framework for treatment. The future role of treatment algorithms in psychiatric practice will be determined, in part, by results of studies evaluating the clinical impact of their use.

Guidelines for Treatment of Bipolar Disorder
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How Are Algorithms or Guidelines Developed?

In the development of evidence-based guidelines, developers evaluate currently available data in support of treatment options. Consistent with the Agency for Health Care Policy and Research Depression Guidelines [2, 3] a rating system of A, B, and C is generally used to evaluate the quality of data available to support a recommendation: A representing randomized, blinded, and placebo-controlled trials; B representing open, controlled trials and large case series; and C representing early findings on smaller case reports and case series. In general, those treatments with more A-level positive data are placed as early choices in the algorithm. However, this is sometimes mediated by the ease and relative safety of using a certain medication. For example, a medication option with greater scientific weight may be placed below some other option because of patient and clinician opposition to the superior medication or treatment due to complicated dosing requirements or significant side effects associated with its use.

Consensus guidelines are derived from consensus of expert opinion, sometimes in combination with practitioners, and may or may not include review of available research data in support of specific treatment options. The derivation of the expert opinion is based on a variety of subjective and objective sources, and these are not always specified. It is possible for guidelines to be developed using a combination of evidence-based review and consensus opinions.

The published guidelines for the treatment of bipolar disorder include the International Psychopharmacology Algorithm Project [23], the American Psychiatric Association (APA) guidelines [24], the Expert Consensus Guidelines [25••], Texas Medication Algorithm Project (TMAP) [7], Canadian Network for Mood and Anxiety Treatments (CANMAT) [27–32], European Algorithm Project [33, 34], and the Department of Veterans Affairs (VA) guidelines [35••]. The history and details of recommendations from published treatment algorithms for patients with bipolar disorder are reviewed in Suppes et al. [11•] and Dennehy and Suppes [12•].

General Characteristics of Guidelines for Bipolar Disorder

Algorithms are generally made up of a series of steps that involve switching drugs within the same drug class (e.g., antidepressants), or between different versions of similar drug classes (e.g., antipsychotics). Algorithms for treatment of bipolar disorder differ in that the majority of recommendations concern how to combine medications that may cut across classes of drugs (e.g., lithium and anticonvulsants). Generally, the treatment of bipolar disorder moves to the use of combination therapies by step 2 [11•]. However, in terms of the available scientific information, there are scant controlled data beyond the first step (i.e., the use of monotherapy) for the treatment and management of patients with bipolar illness. As a consequence, bipolar treatment algorithms and guidelines are typically based on a consensus of experts. As a summary of the general recommendations for treatment of bipolar disorder is published elsewhere [12•], we do not review the specific contents of these algorithms in this paper. However, it is worth noting that the existing guidelines for treatment of bipolar disorder possess many similarities and overlap. In order to provide a sample of a medication guideline for treatment of bipolar disorder, the guidelines used in phase 3 of the TMAP are included in Figures 1 and 2.

In the treatment of mania and hypomania, all existing guidelines recommend monotherapy with an established mood stabilizer (lithium, divalproex sodium, and carbamazepine are discussed) as a first step. Some specify preferences or rank order these mood stabilizers for different symptoms or presentation. All guidelines move to the use of combination mood stabilizers as a next option, should monotherapy fail to reduce symptoms sufficiently. Antipsychotic medications are often mentioned as either adjunctive treatments, or for their possible mood-stabilizing benefits. The guidelines vary in their recommendations regarding electroconvulsive therapy (ECT), use of adjunctive medications, and management of antidepressant medications in a manic/hypomanic patient. The paucity of data in this area is evidenced by the fact that many of the guidelines present preliminary steps, and then offer an unranked array of other options that can be considered.

The published algorithms in this area tend to separately address the treatment and management of patients with a history of mania who are currently in a depressive episode. Guidelines in this area contain very few concrete recommendations, a direct reflection of the continuing debate regarding use of antidepressants in patients with a history of mania and the extremely limited research into the treatment of bipolar depression. Use of lithium, antidepressants, psychotherapy, and ECT are frequently mentioned as treatment options. With one exception, the guidelines recommend that mood stabilizing medications be at optimal levels before initiation of antidepressant treatment.

Some of the published guidelines for treatment of patients with a history of mania include recommendations for the treatment of mixed episodes and rapid cycling. Suggestions for continuation and maintenance treatment are sometimes included. Again, for a review of specific recommendations contained in the published guidelines for treatment of patients with bipolar disorder, see Dennehy and Suppes [12•]. Importantly, the available guidelines contain much similarity and overlap in recommendations. Additionally, it is clear that patients with bipolar disorder would benefit from additional research to inform empirically-driven treatment recommendations and strategies.

Additional recommendations

The focus on medication treatment does not preclude consideration of nonpharmacologic interventions in the