Medication Treatment for the Severely and Persistently Mentally Ill: The Texas Medication Algorithm Project

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This article provides an overview of the issues involved in developing, using, and evaluating specific medication guidelines for patients with psychiatric disorders. The potential advantages and disadvantages, as well as the essential elements in the structure of algorithms, are illustrated by experience to date with the Texas Medication Algorithm Project, a public-academic collaboration. Phase 1 entailed assembling research findings on the efficacy of medications for schizophrenic, bipolar, and major depressive disorders. This knowledge was evaluated for its quality and relevance, integrated with expert clinical judgment as well as input by practicing clinicians, family advocates, and patients. Phase 1 (the design and development of the algorithms) was followed by a feasibility test (Phase 2). Phase 3 is an ongoing evaluation comparing the clinical and economic effects of using specific medication guidelines (algorithms) versus treatment as usual in public sector patients with severe and persistent mental illnesses.

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Recent years have witnessed a rush to develop and implement practice guidelines in the care of patients with psychiatric disorders. For example, the Agency for Health Care Policy and Research (AHCPR) provided guidelines for primary care providers,[1] while the American Psychiatric Association (APA) developed similar, albeit less specific, evidence-based guidelines for psychiatrists.[2] The American Pharmaceutical Association (APhA)[3] has also published peer-reviewed treatment protocols for mental disorders for both primary care and nonphysician providers.

In contrast to the above noted evidence-based guidelines, disease management protocols in managed care environments typically rely on medical necessity[4,5] to define preferred care, and often entail limited access to care or to more expensive (on a cost/pill basis) medications.

This article reports our efforts to derive preferred recommendations based first on the scientific literature.[1,2] When scientific evidence was incomplete, we relied on an expert consensus process[6] (for depression) or on published expert consensus reports (for bipolar and schizophrenic disorders).[7,8]

The public sector, with its limited resources and social pressures to both improve quality and serve more people, is perhaps the most in need of methodologies to reliably

Table 1. Potential Benefits of Algorithms

Benefit	Explanation
Facilitate clinical decision making	Clinicians must regularly sort through hundreds of research articles, evaluate the quality, integrate the findings into a coherent model, and incorporate this into their practices. Algorithms, appropriately developed and regularly updated, aid clinicians in this task
Reduce clinically inappropriate or cost-inefficient variation in clinical practice patterns	Research has documented large inconsistencies in the rate in which specific procedures are performed by physicians.[10–14] Algorithms can help clinicians reduce the magnitude of this variation and improve quality of treatment
Provide consistent treatment across different environments	With shorter inpatient stays, clinicians are unlikely to know at discharge whether the treatment selected is the best for the patient. Algorithms provide a basis for developing consistent medication plans to communicate treatments across different treatment venues and practitioners
Individualize treatment	One treatment is not best for all patients. By incorporating the concept of different treatment paths depending on individual response (symptoms, functioning, and side effects), algorithms inform treatment decision making to achieve, if possible, full remission
Increase cost-efficiency of treatment	Costs may decrease if the point of treatment shifts from efficiency of emergency room and hospitals. Indirect costs are likely to decrease as reflected in a faster return to work and a positive impact for nonmedication treatments especially if treatment response is more complete[15]
Make clinical decisions explicit	Algorithms enable clinicians to identify the components and pathways of their clinical judgments, which makes clinical decision making explicit.[16] This facilitates communication among physicians, enhancing treatments
Provide a metric to compare patient progress	Algorithms that use patient outcome as basis for recommending key treatment decisions enable clinicians to compare the progress of treatment
Provide a metric for evaluating when and whether to adopt new medications	New psychotropic agents may have equal or greater efficacy and be better tolerated, safer in overdose, or effective for patients failing to respond to other agents. Algorithms can define empirically where, in the sequence of steps, the new agent may afford the most clinical benefit, thus informing physicians in their use of new medications
Provide a framework for defining cost of treatment	As a framework for clinical decision making, algorithms are a means to document the costs associated with care, which allows mental health systems to delineate the costs associated with specific treatment interventions and to link costs with patient outcomes

align clinical knowledge and therapeutic interventions so that patient outcomes are based on the best possible care, delivered as efficiently as possible. Tables 1 and 2 highlight the *potential* benefits and dangers of developing and using such tools to assist clinical decision making. However, with rare exception,[9] such guidelines have not been prospectively evaluated with regard to either their clinical or economic effects on the care of such patients.

Table 2. Potential Risks Associated With Algorithms[a]

Risk	Explanation
Insufficient evidence	Poorly developed guidelines (i.e., those with insufficient reliance on empirical evidence) may lead to poor quality of care and inferior clinical outcomes.
Biased opinions	Guidelines developed by consensus panels may not always reflect a broader consensus of experts.
Increased cost and utilization of services	Algorithms may increase costs, with or without increasing benefits.[18]
Substitute for clinical judgment	If an algorithm is too rigid and inflexible, clinicians may not be able to use appropriate expertise and judgment in making decisions in the best interest of the individual patient.
Poor standard of care	Ill-conceived guidelines may render poor treatment care outcomes.
Inappropriate use by administrators	Administrators may inappropriately assume that algorithms can be used by inadequately educated and trained clinicians.
Used by lawyers to sue	Malpractice attorneys may use deviation from algorithms as evidence in malpractice cases.

[a]Adapted from reference 17.

OVERVIEW OF THE TEXAS MEDICATION ALGORITHM PROJECT

In October 1995, the state of Texas began a unique, public-academic collaboration to develop medication treatment algorithms for patients with schizophrenic, bipolar, and major depressive disorders receiving services in the public mental health system. Discussions between the Texas Department of Mental Health and Mental Retardation (TDMHMR) and the Department of Psychiatry at the University of Texas Southwestern Medical Center in Dallas about improving the quality of medication treatment for patients with severe and persistent mental illness in the TDMHMR system led to a collaborative relationship among TDMHMR, 5 Texas medical schools, the University of Texas at Austin College of Pharmacy, physicians, patients, families, and advocacy groups throughout the state of Texas.

This effort recognized the importance of developing clinically sound algorithms that are simple to implement and that maximize patient adherence to and collaboration with recommended treatment. Collectively, this collaborative effort, which was implemented to include practicing public sector physicians, is known as the Texas Medication Algorithm Project (TMAP). This article presents an overview of TMAP, detailing each phase: Phase 1 focused on the development of medication algorithms; Phase 2 evaluated the feasibility of algorithm use in the public sector; and Phase 3 consists of a prospective evalu-

ation of the clinical and economic impact of algorithm-based treatment as compared with treatment-as-usual.

PHASE 1

Phase 1 (October 1995 through September 1996) developed the algorithms and accompanying patient/family education materials. Major depressive, bipolar, and schizophrenic disorders were selected for algorithm development since they account for 36%, 14%, and 26%, respectively, of the adult patients utilizing services provided by TDMHMR in 1996.

Algorithm Development

The first algorithm developed was for major depressive disorder. Using the formal consensus conference method,[6] a consensus panel was convened that included national experts, TDMHMR practitioners who were going to implement the algorithm(s), administrators, patients, and family members.

The development of the schizophrenia and bipolar algorithms took a different course. For these disorders, results of the Tri-University Project[7,8] were used as the basis for algorithm development. These consensus guidelines, utilizing a modified RAND Corporation survey methodology of large numbers of academic experts and clinicians, attempted to add additional specificity to treatment recommendations and to fill gaps in the existing literature, including those in the AHCPR and APA evidence-based guidelines.[1,2] To use these documents, 2 consensus conferences were held, 1 each for bipolar and schizophrenic disorders. The Tri-University investigators presented their findings to TDMHMR practitioners, as well as academic experts, administrators, families, advocates, and patients. Based on feedback from these participants, the guideline recommendations were adapted into algorithms (or clinical treatment decision trees) for the Phase 2 bipolar and schizophrenic modules.

General Overview of the Algorithms

When conceptualizing the algorithms, we divided the recommendations into strategies (what treatments to use) and tactics (how to use the recommended strategies). Thus, which drug(s) to use first, second, or third constitute strategies. How long to continue a particular drug, what dose to use, and when to go on to the next step(s) are tactics. These algorithms also incorporated a commonly accepted principle of medical practice to start with safer, less complex treatments (assuming similar efficacy), subsequently moving to more complex interventions should the simpler treatments fail or be found intolerable. This principle, along with empirical evidence as to which treatment(s) work when prior treatment(s) have failed, allows specification of the strategic steps in an algorithmic format. By including options among "medically equivalent" interventions within each stage in the algorithm, the danger of inappropriate and unsubstantiated specificity, which may narrow the applicability of algorithms to an ever-smaller group of patients, is avoided.

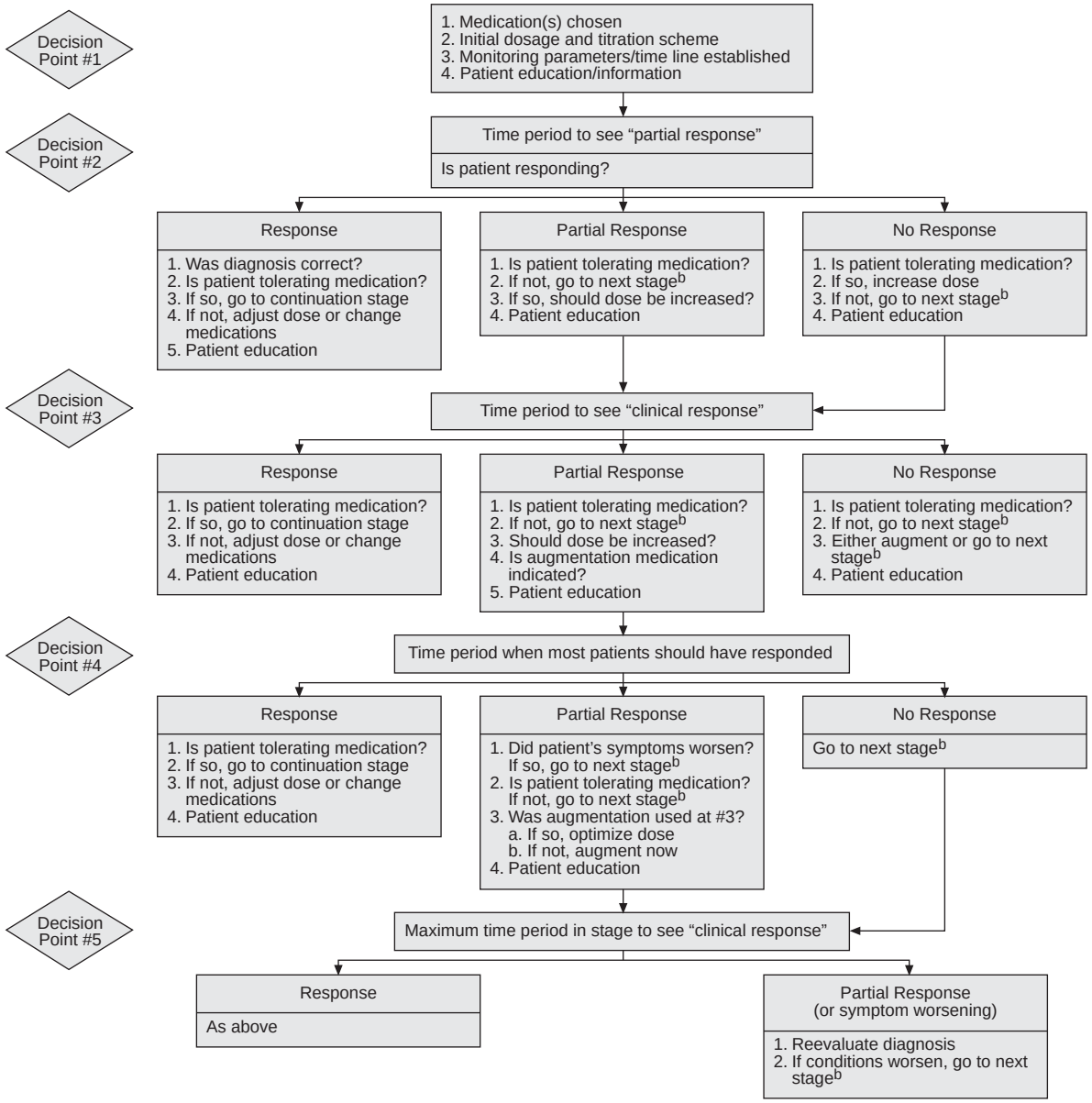
Two algorithms were developed for major depressive disorder, 1 each for psychotic and nonpsychotic forms of the illness. The former has 4 stages, while the latter has 7. The schizophrenia algorithm has 4 stages, plus algorithms for side effects and management of coexisting symptoms (e.g., insomnia, agitation, depressive symptoms). The bipolar disorder algorithms have 6 stages for mania or rapid cycling and 6 stages for the depressed phase.

The treatment algorithms specify the particular medication options recommended at each stage; the preferred dose (or serum concentration) ranges for each medication; the recommended number of weeks for conducting each stage; the acceptable or unacceptable outcomes that recommend continuing, adjusting dose, discontinuing, or augmenting the medication at each stage; management of side effects; and recommended adjunctive medication(s) for treatment of associated symptoms such as insomnia or agitation. The algorithms also recommend frequency of outpatient visits. Figures 1 and 2 show exemplar templates to illustrate the organization of the strategies and tactics within each algorithm.

The operative assumptions underlying the development and specification of these strategies and tactics are as follows:

1. Scientific evidence should support the treatment recommendations whenever possible (e.g., randomized controlled clinical trials represent the highest level of evidence).
2. Expert clinical consensus is used only when data are lacking or incomplete (i.e., scientific evidence trumps clinical opinion).
3. Initial stages should be less complex, easier to implement, and safer than later stages.
4. When strategies are medically equivalent, patient preference plays a pivotal role in choice of strategies.
5. Symptom response (as well as side effects) assessments and the time in the treatment stage dictate when and whether to proceed to the next stage.
6. Tactics are suggested, not required, as appropriate to ensure applicability to a wide range of patients.
7. Costs should be assessed with respect to patient outcomes (i.e., to specify the benefits accrued and associated costs). This information is important so program managers can make budget decisions that center on the purchase of patient outcomes. From a management perspective, this is the most important objective, especially in a public sector environment marked by a history of purchasing services (or processes) rather than outcomes.

Figure 1. Exemplar Algorithm Showing Tactical Recommendations[a]

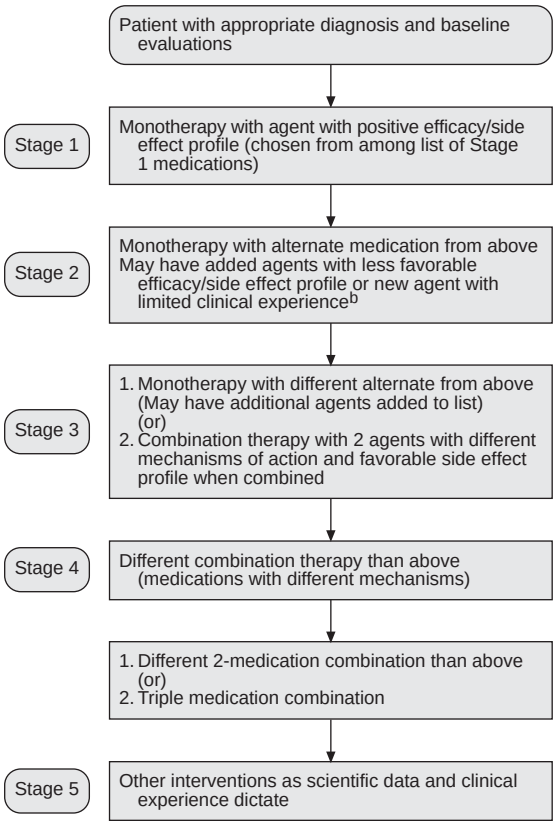


[a]This material is in the public domain and can be reproduced without permission.
[b]Refer to Figure 2 for the next stage.

8. Patients do not have to enter only at stage 1 if an accurate history is available to support entry at later (more complex) treatment stages.
9. With appropriate documentation, the clinician can choose to skip 1 or more strategic steps, or even not use the algorithm, depending on the patient's prior treatment history, general medical health, and associated comorbidities, patient preference, and other factors (e.g., response to a treatment option).
10. Concise but informative chart documentation of treatment strategies, tactics, and patient outcomes insures continuity in care across treatment environments and providers.

In the development of the algorithms, strategies for a given treatment stage were identified that are equivalent in their expected efficacy, safety, and feasibility (as determined by the scientific literature and expert clinical consensus). As there is a dearth of research available examining the cost effectiveness of "medically equivalent" alternatives, it would be imprudent to make preferred recommendations based upon medication acquisition costs. In general, one alternative may be as valuable as another and,

Figure 2. Exemplar Algorithm Showing Strategic Recommendations[a]



[a]This material is in the public domain and can be reproduced without permission.
[b]This step is skipped for bipolar disorder unless initial monotherapy is not tolerated.

therefore, either may be chosen at a particular stage. When clinically equivalent, these strategies are presented to patients and clinicians as options for a particular treatment decision.

Clinician Ratings and Patient Self-Reports

Because algorithms specify sequenced treatment steps, each of which depends on the clinical benefit and side effects of the prior step(s) (as well as other patient factors such as prior history of treatment response, general medical status, and concomitant nonpsychotropic medications), TMAP incorporated the use of specific clinician and patient self-report ratings to gauge both the benefits and adverse effects of each critical decision point before moving on to the next. Such outcome assessments should reduce inappropriately large variation among clinicians (i.e., some may be reluctant to take the next step in the algorithm, whereas others may be more aggressive and move prematurely to the next step). By providing practitioners with a common set of symptom and side effect ratings, we anticipate greater consistency across clinicians in deciding, "Shall I take the next step?"

Patient/Family Education Materials

For patients to make informed choices, and to become participants and collaborators in the long-term management of these often persistent, lifelong illnesses, they should be knowledgeable about the potential benefits, side effects, and inconveniences (e.g., once- versus twice-daily dosing) associated with each medication. Thus, TMAP engaged patients, families, and advocates in developing educational materials (in both English and Spanish) to describe the illnesses, medications used, anticipated benefits, and side effects. By engaging patients and families, we hope not only to improve adherence but to provide quality, timely information to inform the clinical decisions called for in the algorithms.

Initial education consists of simple information about the symptoms of the illness and the medication prescribed, and a method for self-report of symptoms and side effects cued by the ongoing provision of symptom information. Once patients are more stable, information is provided regarding overall prognosis, self-help aids, detection of symptomatic exacerbation, and basic medication and psychosocial remediation of their condition. As stabilization is more complete, and as appropriate, patients are introduced to the long-term issues that can be anticipated and addressed (e.g., pursuit of employment, management of interpersonal relationships, intercurrent life events, general medical conditions, pregnancy). The final element includes videotapes that can be used at any time depending on patient and family status and clinician preference. These videotapes provide essential discussion points for patients and their families to address basic questions about managing these illnesses. These materials are incorporated into an educational plan that encompasses both individual communications between clinician and patient as well as groups facilitated by both professional staff and consumers.

PHASE 2

Phase 2 (October 1996 through September 1997), the feasibility trial, involved 40 physicians located at 16 inpatient and outpatient sites across Texas. At each site, a 2-physician team was asked to implement the proposed algorithms and patient education materials with 5 to 15 patients who they felt needed a medication change. The enrollment period lasted from October 1996 through April 1997. Patients were followed for 4 months whenever feasible (data collection ended August 1997). Altogether, 239 patients were enrolled in 3 algorithms: 95 with schizophrenia, 71 with bipolar disorder, and 73 with major depressive disorder.

Phase 2 determined whether the recommended algorithms were applicable and suitable to patients, practitioners, and clinical circumstances in TDMHMR and estimated the resources (e.g., staff time, formulary costs) needed to implement them (Table 3). This phase sought to

Table 3. TMAP Phase 2 Questions

1. Are the algorithms as recommended by expert consensus methodologies suitable for TDMHMR patients, or do they need to be partially or significantly revised?
2. Are the clinical diagnoses rendered by routine care in the TDMHMR system sufficiently accurate to implement the algorithms?
3. To what degree are physicians in general satisfied with the algorithms?
4. To what degree did the physicians implement the algorithms as planned?
5. What resources (e.g., physician, staff time, medication costs) are needed to implement algorithms?
6. To what degree are patients satisfied with the algorithm treatment?
7. How long did patients stay in the algorithms?
8. What is the overall benefit of using algorithms in terms of symptom reduction and improved functioning?
9. Which algorithm stages were used first?
10. Which medications were used?
11. What doses were used?
12. Did patients who received multiple steps need them?

develop impressions regarding whether tactical or strategic revisions in each algorithm should be undertaken and to provide preliminary estimates of response (based on symptoms and disability) to each algorithm and to individual stages within each algorithm. Also evaluated was the need for training and/or education of physicians, staff, patients, and families. Finally, Phase 2 determined whether physician or patient global ratings or itemized symptom ratings are preferred methods to estimate response to each step at key decision points, and whether the algorithms should be revised. In the course of conducting the feasibility trial, we recognized a greater-than-anticipated need to provide clinicians not only with basic information about the structure and use of the algorithms and associated medications, but also with ongoing clinical consultation and/or advice.

PHASE 3

Phase 3 is a prospective evaluation of the clinical and economic impact of algorithm-based treatment as compared with treatment-as-usual. Phase 3 will (1) determine the clinical outcomes of algorithm-informed treatment by measuring its impact on patient symptoms, functioning, and quality of life and (2) identify the economic impact of algorithm-informed treatment as reflected in direct treatment costs (e.g., physician time; medications; psychosocial services; residential, hospital, and crisis services), nontreatment costs, (e.g., welfare, Social Security disability insurance, police contacts, courts, jails), and opportunity costs.

Phase 3 will enroll approximately 1200 patients in either an algorithm or treatment-as-usual control condition, following each for a minimum of 12 and maximum of 24 months. The impact of both algorithm and treatment-as-usual on patients' symptoms, side effects, function, and quality of life will be assessed quarterly using instruments appropriate to the particular disorder. Physician and patient satisfaction will also be assessed.

Since Phase 3 evaluates both patient functioning and symptomatology within the treatment context established by the algorithms, detailed information on the appropriateness of each algorithm stage will be available to determine the clinical impact on individuals.

A major evaluation issue will be determining physician adherence to the algorithms. How to measure the degree of adherence to algorithms is an unresolved issue. The greater the specificity and the fewer the options in an algorithm, the easier it is to measure adherence, but the more clinically narrow its utility. (For example, if there is only a single medication to be used at a single dose for a given disorder, then either the practitioner did or did not use the medication at the proper dose for the proper duration of time.) Thus, this simple practice can be rated either as being in adherence with or not in adherence with the recommendation(s).

However, most algorithms are more complex and must be more flexible. In TMAP, practitioners can skip stages based on a patient's prior treatment history or clinical presentation, patient preference, or administrative availability of treatments. The rationale for skipping a stage can be provided by a simple checklist. As algorithms list more clinical options, the rationale for selecting a particular strategy or tactic must be weighed in the context of complex background information. Incomplete documentation of the clinical decision-making process further obscures the identification of errors of either omission or commission with regard to both strategies and tactics. Thus, both increasing algorithm complexity and incomplete clinical data create problems in assessing algorithm adherence.

TMAP has approached this problem by specifying algorithm stages (most with a number of "medically equivalent" options) and specifying a range of selected tactical behaviors (such as dosages and time ranges for treatment durations prior to evaluating response to that stage). Whether practitioners are "inside" or "outside" of these recommended dose and duration ranges can be rated for selected strategies and tactics. For strategic decisions, the rationale for medication use can be divided into those aimed at the core syndrome (e.g., mood stabilizing agents for bipolar disorder), those used as adjuncts to address associated symptoms (e.g., sedative hypnotics for insomnia in major depression), and those used to treat side effects (e.g., anticholinergic agents for patients receiving antipsychotics). The rationale for each medication can be specified in a simple checklist in the clinical record.

By collecting symptomatic outcome data at each critical decision point in the algorithm, the clinician develops a guide with which to assess each patient's progress against what might be "expected." Thus, physicians can use this yardstick to monitor the progress of individual

patients within the treatment algorithm. This information provides physicians with a useful framework for making decisions regarding when to modify, change, or discontinue treatment.

Because treatment outcome must be balanced with costs, service utilization data for both treatment and nontreatment costs are collected every 3 months during Phase 3. In addition, upon the enrollment of a patient in the study, a review of the patient's service usage for the prior 2 years is conducted. By combining algorithm adherence, outcome, and service utilization, TMAP provides the basis for outlining the temporal course of treatment, identifying patient outcomes at key points in the sequence of treatment, and establishing the cost to achieve these outcomes.

SUMMARY

There are both clinical and administrative reasons to suggest that algorithm-driven treatment increases the quality of care and avoids unnecessary practice variations. However, empirical data are few, although Katon et al.[9] recently reported that guideline-based treatment for major depression improved outcome in the primary care setting, but at an increased cost. This cost may be worthwhile, however, when viewed in light of lower long-term treatment costs and lower occupational disability (i.e., increased work productivity).

The public sector behavioral health care system continues to be besieged by conflicting demands to enhance quality, increase access, and improve patient outcomes, while at the same time to contain or reduce costs. Algorithms are attempts to bring these competing expectations into balance. An accepted range of medication options is already known for each of the 3 major mental disorders involved in TMAP. In addition, a reasonable consensus exists regarding preferred sequences of medication use, how to facilitate their implementation, and how to measure clinical outcomes and costs.

The TMAP algorithms and implementation procedures rest upon a treatment philosophy designed to provide quality clinical care yet be sufficiently flexible and explicit to allow individual tailoring of treatment and be budgetarily informative. The following points articulate this treatment philosophy:

1. Incorporate treatment strategies that are based upon demonstrated efficacy in the treatment of the 3 major disorder groups.
2. Use expert clinical consensus to recommend particular strategies and tactics when gaps exist in the evidence base (i.e., scientific literature).
3. Include physicians, patients and their families, advocates, administrators, and other decision makers in the design of the algorithms.
4. Incorporate patient choice of medications with similar efficacy and safety profiles. This choice allows patients to choose among medications largely based on anticipated side effects (i.e., selecting treatments that are both convenient and least disruptive to their lifestyles). When choice is provided, patient adherence to a medication regimen is assumed to be maximized.
5. Provide physicians with choices to utilize their clinical decision making (i.e., algorithms inform but do not replace physician judgment).
6. Develop a consultation support system capable of responding to physician questions and concerns regarding a patient's pharmacotherapy and algorithm implementation.
7. Increase consistency in patient assessment across practitioners using the algorithms (e.g., by using symptom rating scales at key decision points.)
8. Provide physicians, patients, and families an educational support package describing the respective disorders, the specific medications, side effects, and expected outcomes.
9. Ensure that physicians provide adequate frequency of and have ample time to spend with patients during visits.
10. Provide recommendations as to frequency of outpatient visits, average length of an appointment, and the typical personnel needed to implement the algorithms and educational program.
11. Test the feasibility of initial algorithm recommendations and make appropriate revisions based on this evaluation.
12. Specify the costs associated with implementation including medication and physician and other staff time.

It would appear that the time is ripe for the development and empirical evaluation of medication algorithms for patients with severe and persistent mental illnesses. Whether such guideline-driven (algorithm-driven) care is acceptable to physicians and patients, whether it produces substantial clinical benefit over usual care, what it costs, and whether the costs (if increased) are worth it deserve further study in a variety of treatment systems.

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