Texas Medication Algorithm Project, Phase 3 (TMAP-3): Rationale and Study Design

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Background: Medication treatment algorithms may improve clinical outcomes, uniformity of treatment, quality of care, and efficiency. However, such benefits have never been evaluated for patients with severe, persistent mental illnesses. This study compared clinical and economic outcomes of an algorithm-driven disease management program (ALGO) with treatment-as-usual (TAU) for adults with DSM-IV schizophrenia (SCZ), bipolar disorder (BD), and major depressive disorder (MDD) treated in public mental health outpatient clinics in Texas.

Discussion: The disorder-specific intervention ALGO included a consensually derived and feasibility-tested medication algorithm, a patient/family educational program, ongoing physician training and consultation, a uniform medical documentation system with routine assessment of symptoms and side effects at each clinic visit to guide ALGO implementation, and prompting by on-site clinical coordinators. A total of 19 clinics from 7 local authorities were matched by authority and urban status, such that 4 clinics each offered ALGO for only 1 disorder (SCZ, BD, or MDD). The remaining 7 TAU clinics offered no ALGO and thus served as controls (TAUnonALGO). To determine if ALGO for one disorder impacted care for another disorder within the same clinic ("culture effect"), additional TAU subjects were selected from 4 of the ALGO clinics offering ALGO for another disorder (TAUinALGO). Patient entry occurred over 13 months, beginning March 1998 and concluding with the final active patient visit in April 2000. Research outcomes assessed at baseline and periodically for at least 1 year included (1) symptoms, (2) functioning, (3) cognitive functioning (for SCZ), (4) medication side effects, (5) patient satisfaction, (6) physician satisfaction, (7) quality of life, (8) frequency of contacts with criminal justice and state welfare system, (9) mental health and medical service utilization and cost, and (10) alcohol and substance abuse and supplemental substance use information. Analyses were based on hierarchical linear models designed to test for initial changes and growth in differences between ALGO and TAU patients over time in this matched clinic design.

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A complete list of the members of the TMAP Research Group is given at the end of this article.

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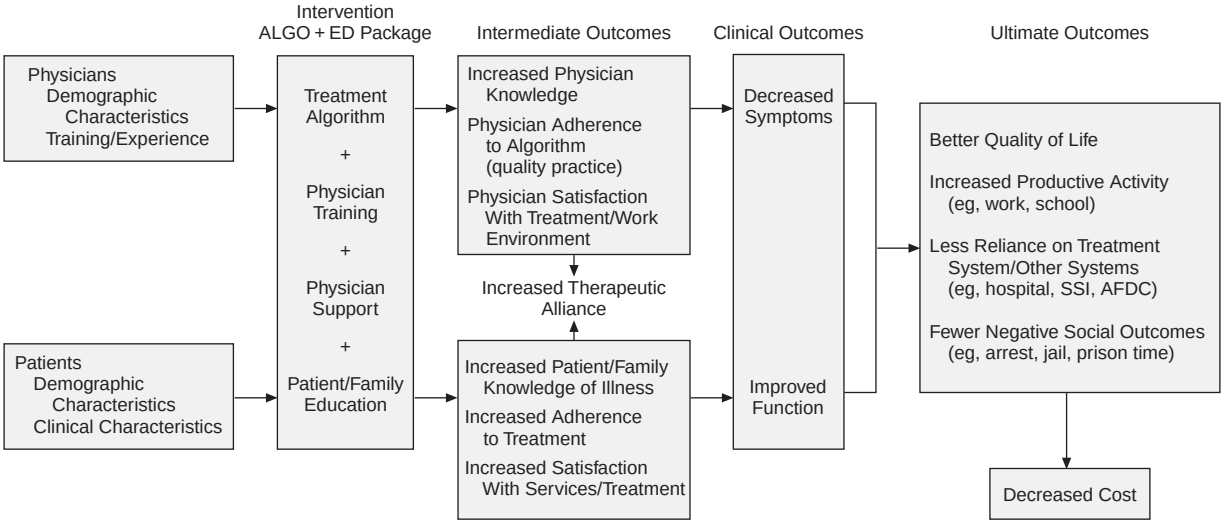
In late 1995, the Texas Department of Mental Health and Mental Retardation (MHMR) decided to develop and evaluate medication algorithms for the treatment of patients with DSM-IV schizophrenia (SCZ), bipolar disorder (BD), and major depressive disorder (MDD) in the Texas public mental health system. This decision was the result, in part, of having observed significant variance across physicians and clinics in the medication management of severe mental illness, an emerging emphasis on managed care and reducing health care costs, the desire to implement "best practices" for the delivery of care, and the recognition that a consistent care plan across different sites and providers would improve the quality of care.

The use of algorithms to address these challenges was based on the assumption that decreasing practice variance and increasing proper selection and dosing of medications would improve clinical outcomes and/or contain costs.[1–3] An algorithmic approach assumes that sufficient homogeneity exists among patients with a given disorder that a relatively uniform approach to treatment can be utilized in most patients. Algorithms should provide clinicians with

Figure 1. Texas Medication Algorithm Project (TMAP) Logic Model[a]



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Abbreviations: AFDC = Aid to Families with Dependent Children, ALGO = algorithm-driven disease management program, ED = education, SSI = Social Security Insurance.

the framework to make consistent decisions given similar patient scenarios, while also allowing for the necessary flexibility to address differences among patients.[1,2]

Medication algorithms provide a framework for decision making that allows multiple clinicians serving the same patient to provide consistent care over time. The net result is expected to improve clinical outcomes. The rationale for developing and implementing treatment algorithms in the public mental health sector has been discussed elsewhere.[3] In spite of their theoretical allure, algorithm-based practices have not been evaluated in the care of those with severe and persistent mental illnesses.

Algorithm dissemination does not imply that clinicians can or will use them. In fact, studies in other areas of medicine have revealed that merely disseminating guidelines to physicians often results in minimal effects on daily practice behaviors.[4,5] Support systems must be put in place to facilitate the use of algorithms, including clinician education and training, clinician prompting regarding algorithm use, uniform chart documentation, chart auditing, clinician feedback, education and other modalities to improve patient and family understanding of the disease state and treatment, and improved follow-up systems to enhance treatment adherence.[4,6–11]

It was hypothesized that improved symptom outcomes should lead to healthier patients who require fewer mental and general medical services in the long term—thus offsetting part of the program costs and enhancing cost effectiveness.

In utilizing a systematic approach to evaluating outcomes with algorithms, one can also define those variables (e.g., concurrent general medical or psychiatric conditions) that influence the variance in treatment approaches (e.g., under what circumstances do clinicians depart from the algorithm?). The assumptions that underpin this project are:

1. Medication is an essential treatment for SCZ, MDD, and BD.[12–14]
2. No single medication is a panacea for any disorder.[12,15–18]
3. Many patients do not respond to or cannot tolerate one medication, but many respond to 1 or more alternative medications or combinations.[19–24]
4. Wide variations in medication practices exist within the public mental health sector. Some patients do not receive the proper medications, the optimal doses, or a sufficient duration of treatment, with a consequence of not achieving maximal benefit. For some, this results in increased crisis encounters, emergency room visits, hospitalizations, or contact with the criminal justice system.
5. Prespecified sequences of medication options and dosages will improve the likelihood of maximal medication benefit for more patients.[20,23]
6. Additional time spent educating patients, answering their concerns, and empowering them and their families to become actively involved in their care will increase adherence to treatment.[25–30]

Figure 1 shows the conceptual framework to evaluate the disease management program. The program itself contains (1) medication algorithms, (2) patient education,

(3) medical documentation enhancements, (4) expert consultation, and (5) clinical support. The framework begins with the characteristics of patients, clinicians, and their interactions. Physicians receive education and clinical and technical support to enhance algorithm implementation and adherence. Patients and family members receive education about mental illness and its treatment to increase their involvement in treatment decisions and adherence to treatment. Physician and patient characteristics influence algorithm implementation, which, in turn, leads to intermediate outcomes, including (1) improvements in physician knowledge of medications, (2) process of medication management, (3) physician adherence to recommended treatment sequences, (4) patient and family understanding of the illness and treatment procedures, (5) patient adherence to recommended treatments, and (6) clinician and consumer satisfaction. These intermediate outcomes, in turn, lead to enhanced clinical outcomes (e.g., decreased symptomatology, improved functioning), better quality of life (e.g., work, school, household activities, less involvement with criminal justice system including arrests and incarceration time, less reliance on treatment and service systems), and ultimately improved cost effectiveness of health care.

INTERVENTION

Overview

The intervention tested in this project was an algorithm-driven disease management program (ALGO) for the treatment of severe and persistent mental illnesses. This intervention package included the following elements:

1. Evidence-based, consensually derived, and feasibility-tested medication algorithms.
2. Clinical coordinators to enhance patient care, assist the physician in algorithm implementation, and provide algorithm prompting.
3. Initial and ongoing education for physicians and clinical coordinators.
4. Ongoing clinical and technical consultation for algorithm implementation.
5. Uniform assessment and documentation of symptoms and side effects at each clinic visit to guide treatment adjustments.
6. Medical documentation system including chart auditing, technical assistance, and prompting from on-site clinical coordinators.
7. Comprehensive patient/family psychoeducation program.

The algorithm development processes and the specific algorithm content (TMAP Phases 2 and 3) are detailed elsewhere.[23,31–34] The goal of treatment is symptom remission and, when remission is not possible, as much improvement as possible. The algorithms provide a framework for clinical decision making. Strategies (i.e., the specific medications recommended at each stage) and tactics (e.g., the preferred oral doses or serum concentrations, the time to remain at the dose, frequency of clinical visits, and how to evaluate treatment response) were provided for each algorithm. Critical decision points provided prompts for revising either the tactics or the strategies.

The algorithms identify treatment options at each stage that are relatively equivalent in expected overall efficacy, medical safety, and tolerability. The earlier treatment stages in each algorithm are typically simpler to implement, while the later stages or steps are more complicated. Medication regimens in the earlier stages tend to have fewer potential significant side effects than those in later stages. The early stages are also based more upon scientific evidence while the later stages depend more on expert consensus. Additionally, a basic premise of the algorithm philosophy is that patients, and when possible, families, should be actively involved in the decision-making process.

Adherence: Implementing the Algorithms

The tools used by clinicians to help assess clinical status at each clinic visit included patient and clinician global symptom and side effect ratings and specific symptom rating scale(s) for each disorder. The clinicians made several symptom cluster ratings (0–6) and received patient global self-report ratings for both symptoms (0–4) and side effects (0–4) at each visit. The specific symptom rating scales used at each clinic visit to inform the clinical implementation of the ALGO and treatment decision making were the 30-item Inventory of Depressive Symptomatology-Clinician Rating (IDS-C-30) and Self-Report (IDS-SR-30)[35] for MDD; the 24-item Brief Psychiatric Rating Scale (BPRS-24)[36–38] (overall symptoms) and the Clinician-Administered Rating Scale for Mania (CARS-M),[39] IDS-SR-30, and BPRS-24 (manic symptoms) for BD; and the 4-item positive (from the BPRS) and negative (from the Negative Symptom Assessment Scale) for SCZ as described by Miller et al.[33]

Patient/Family Education

The psychoeducational program and the materials used in TMAP were developed by a task force (Patient Advocacy Team) composed of consumers, advocates, family members, and providers to help patients and families better understand their illness and to become more actively involved in treatment decisions with their providers. Educational materials for each of the disorders were either created specifically for the program or adapted from other sources. All materials were available in English and Spanish. The program was implemented in a phased fashion, with multiple educational modalities (e.g., written ma-

terials, videos, group interactions). The program was designed to improve the therapeutic alliance between patients and clinicians, improve patient/family knowledge of the disorder and its management, promote patient involvement in decision making, and promote patient adherence. Details of this program are described elsewhere.[40]

Clinician Training

Prior to patient enrollment, investigators spent 4 months hiring and training clinical coordinators, research coordinators, and staff; advising site medical directors and administrative staff; and consulting with clinical staff regarding study protocol and procedures.

STUDY ORGANIZATION

Figure 2 shows the TMAP administrative structure. The Steering Committee was composed of Texas mental health and academic stakeholders and provided general project oversight and direction. The Scientific Review Group included a multidisciplinary cadre of national experts on outcomes research who reviewed the protocol, making suggestions for revisions and advising on data analyses.

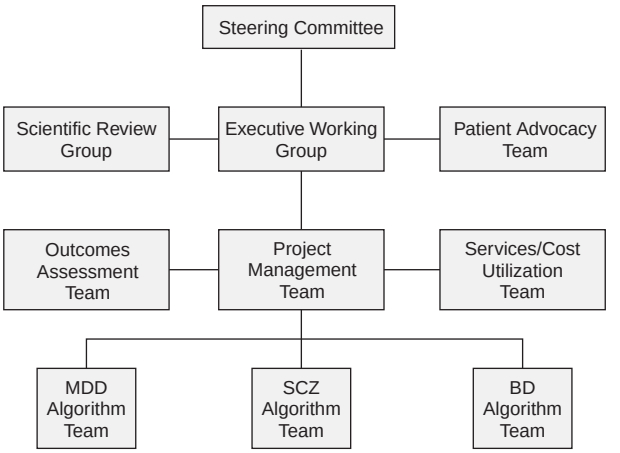
The Executive Working Group oversaw the implementation of the protocol, made decisions about any changes or adaptation in methodology, oversaw day-to-day operations, solved problems rapidly, anticipated and responded to administrative changes in the Central Office or at the clinical sites, and ensured smooth day-to-day functioning.

The Project Management Team was responsible for the development and implementation of all aspects of the project. This team oversaw all aspects of the protocol, management of the algorithm implementation process, management of data collection, data analysis, and reporting of results.

There were 3 Algorithm Management Teams, 1 each for MDD, BD, and SCZ. Each team was composed of a director, an assistant director, and a research coordinator who oversaw the implementation of each algorithm package, along with M.L.C. from the Executive Working Group. Each research coordinator, supervised by the director, was responsible for day-to-day oversight and for immediate consultation with the clinical coordinators and physicians at each clinical site implementing an algorithm.

The physicians and clinical coordinators were responsible for recruiting and treating patients utilizing the algorithms, as well as for ensuring accurate clinical data entry into charts. Each physician had the final responsibility and full authority for patient care. The ALGO physician had to judge the suitability of the ALGO for each individual patient, and was responsible for implementing it to the best of his/her ability.

Figure 2. Texas Medication Algorithm Project (TMAP) Administrative Structure[a]



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Abbreviations: BD = bipolar disorder, MDD = major depressive disorder, SCZ = schizophrenia.

The clinical coordinator had several responsibilities: assisting physicians with providing care and implementing the algorithm package, performing relevant clinical assessments at each visit, ensuring proper documentation of relevant clinical data, maintaining interim contacts with patients, and implementing the patient/family psychoeducation program. The clinical coordinator was also responsible for following up with all ALGO patients who failed to show for their appointments and for implementing the "no-show" procedure at each site. Finally, the clinical coordinator provided physicians with prompts to increase the likelihood that the algorithm was followed.

The Outcome Assessment Team oversaw research data collection, faxing, entry, and interim audits. They trained all research coordinators to perform outcome assessments based upon a "gold standard," and they performed reliability assessments on a quarterly basis. They assured accurate and timely acquisition of data; assured data were accurate, complete, and correctly entered; and answered questions from the sites with respect to proper collection and coding of information.

The research coordinator was responsible for conducting the quarterly, independent, but nonblinded, clinical and utilization outcomes evaluations with patients in ALGO, TAUinALGO, and TAUnonALGO. The research administrator was responsible for coordinating administrative activities and providing assistance to the research coordinators and to the Data Center in Dallas, Tex., to assure that the highest level of quality and reliability was achieved.

The Service/Cost Utilization Team was responsible for the planning, data collection, and analysis of treatment and nontreatment system utilization and cost data.

The Patient Advocacy Team included representatives of the National Alliance for the Mentally Ill, Texas, the Texas Depressive and Manic-Depressive Association, Texas Mental Health Consumers, and the Mental Health Association in Texas, as well as some Executive Working Group members and some site representatives. Many of these individuals were actively involved in the development and adoption of patient/family education materials and creation of the total psychoeducation program,[40] and some were involved in training and guiding implementation of the package. The Patient Advocacy Team was briefed periodically throughout the study.

The study protocol and consent forms were reviewed and approved by the internal review boards at University of Texas Southwestern and University of Texas Austin, as well as by each local internal review board or Human Subjects Committee where applicable. Annual reports were submitted to the respective internal review boards as required.

METHOD

Aim

This project was designed to evaluate the clinical outcomes and costs of ALGO as compared to TAU for SCZ, BD, and MDD. The program included medication algorithms, clinical and technical support for physicians, clinical assessment of symptoms and side effects at each clinic visit to guide ALGO implementation, uniform documentation, and a patient/family education program.

Specifically, we hypothesized that compared to their TAU counterparts, patients treated with ALGO would experience (1) better clinical outcomes (fewer symptoms, better mental and physical functioning, and fewer medication side effects), (2) fewer acute mental health services (fewer crisis visits, emergency room visits, psychiatric admissions, and psychiatric inpatient days), (3) fewer general medical services (fewer outpatient visits, hospital admissions, or hospital days), and (4) fewer encounters with the criminal justice system. Secondary analyses were planned to assess response rates for each medication step in each ALGO, to determine which types of patients preferentially benefit from each ALGO step, and to examine if implementing ALGO for one disorder in a clinic will impact care for another disorder in the same clinic (culture effect).

Study Plan

For each disorder (SCZ, BD, MDD), we evaluated whether the use of ALGO would impact overall clinical outcomes by comparing patients who received care at clinics offering ALGO with those who received care at clinics not offering ALGO to any patient (TAUnonALGO). Patients were assessed at baseline and at 3-month follow-up intervals for at least 1 year but no more than 27 months. Secondarily, we evaluated if clinics that offered ALGO for one disorder would also improve outcomes of care for other clinic patients treated for a non-ALGO condition. These "culture effects" were assessed by comparing outcomes of patients receiving TAU for a given disorder in clinics not offering ALGO to any patient (TAUnonALGO) with those offering ALGO to patients with other disorders (TAUinALGO).

Study assignment to ALGO or TAU was by clinic, rather than by physician or patient. Study assignment (i.e., randomization) by patient would have required physicians to follow the ALGO with some patients, but not others with the same diagnosis. Assignment by physician would have required some physicians in the same clinic to use ALGO while others would deliver TAU. This method would require that physicians avoid sharing experiences with one another and not crossover for each other to avoid contaminating TAU with ALGO treatments ("water cooler" effect).

A limited number of clinics were available for study participation, and in order to reflect the geographic and demographic diversity of Texas, the clinics were chosen to be diverse by design. Given these factors, study cell assignments by clinic were matched, rather than randomly assigned. When possible, clinics were matched in order to have an ALGO clinic and a TAU clinic for the same disorder within the same local mental health authority. This was often not possible for rural authorities with limited numbers of clinics. In such cases, we attempted to match ALGO with a similar type TAU clinic (i.e., rural ALGO with rural TAU). After this, we tried to match a given ALGO clinic with a TAU clinic that was similar in ethnic representation.

Nonphysician clinical staff (clinical coordinators) were added to perform clinical duties required for ALGO (but not TAU), such as collecting symptom and side effect measures at each clinic visit to assist physicians in implementing ALGO, prompting physicians as to ALGO decision points, implementing the patient/family education program, and following patients who missed appointments. Clinical coordinators also performed research tasks (recruiting patients, administering consent, gathering adherence data), though such time was not included in calculating patient care costs.

Study Site and Sample

Clinics. The study was conducted at 19 outpatient mental health clinics operated by 7 local community authorities. Local mental health authorities were selected to maximize the likelihood of administrative, budgetary, and political support for the project and to ensure geographic and ethnic diversity. Selected clinics also had active caseloads that were determined adequate to achieve our enrollment goals. Among these 19 clinics, 12 were selected to offer ALGO (i.e., 4 clinics for each disorder),

Table 1. Inclusion/Exclusion Criteria for Texas Medication Algorithm Project, Phase 3 Study Entry

Inclusion Criteria
ALGO patient
Has the requisite disorder (ie, SCZ, BD, MDD).
Sufficiently symptomatic for medication treatment.
Intolerant or insufficiently responsive to current medication, such that a medication initiation or change (not a simple dose change) is needed (ie, either initiation of a new medication or a change in the type of current medication).
Adult patient (18 years or older).
TAU patient
Requires a psychotropic medication initiation or change (not simply dosage adjustment), excluding sleep and sedative hypnotic medications.
BPRS-24 screening score greater than the median for the clinic and not more than 1 SD below the mean for each ALGO group.
Adult patient (18 years or older).
Exclusion Criteria
ALGO and TAU patients
Currently participating in another psychiatric treatment study.
Receiving treatment via an Assertive Community Treatment program.
Receiving mental health mental retardation services.
Need for acute treatment for alcohol or substance abuse withdrawal (ie, acute detoxification).

Abbreviations: ALGO = algorithm-driven disease management program, BD = bipolar disorder, BPRS-24 = 24-item Brief Psychiatric Rating Scale, MDD = major depressive disorder, SCZ = schizophrenia, TAU = treatment as usual.

with the remaining 7 to continue offering TAU. Three among these 7 were small rural clinics in the same mental health authority, and we combined these 3 clinics to form 1 TAU group. Clinics offering ALGO were allowed to offer the protocol for only 1 disorder. Thus, 4 ALGO clinics were selected per disorder from among the original 19 to produce the best matches with respect to authority, urban/rural mix, and whenever feasible, possible ethnic composition. Each ALGO clinic also served as a TAUinALGO site for a disorder other than the one in that clinic being treated with ALGO.

Physicians and patients. The unit of analysis is the patient, nested within the physician who, in turn, was nested within study clinics. For each disorder (SCZ, BD, MDD), patients were assigned to TAU or ALGO depending on the clinic they attended. Patients attending 1 of the 12 ALGO clinics were enrolled in the ALGO clinical protocol. Patients attending TAU clinics were by definition among study controls (TAUnonALGO).

It was anticipated as a working hypothesis that patients attending ALGO clinics who were receiving TAU, i.e., TAUinALGO, may have better outcomes, even though the ALGO program at their clinic was targeting a different disorder. To test for culture effects, we evaluated additional TAU patients selected from among the 12 ALGO clinics (TAUinALGO).

To be eligible for the study, physicians had to be employed by, and assigned to, either an ALGO or TAU clinic, but not both, with at least a 20% full-time commitment. Physicians hired in ALGO clinics during the study were trained by TMAP staff in the same manner as the original ALGO physicians.

Patients were at least 18 years old, and all gave written informed consent before entry into the study. None were excluded for prior or current comorbid general medical, psychiatric, or substance abuse problems, though patients receiving mental retardation services were excluded (Table 1). Outpatients enrolled in an Assertive Community Treatment (ACT)[41] program were excluded because (1) treatment was provided by different physician/staff teams, (2) high intensity staffing and home visits would introduce noise/confounds to estimates of ALGO impact on outcomes, and (3) many ACT patients might have already gone through most, if not all, ALGO steps.

To qualify for ALGO, the patient had to be treated by a physician in the ALGO clinic, have a diagnosis of the requisite condition as determined by the attending physician (i.e., MDD, BD, SCZ), and start a new, "syndrome-targeted" medication (e.g., a mood stabilizer or antidepressant for BD, an antidepressant for MDD, or an antipsychotic for SCZ). Adjusting the dose of the ongoing syndrome-targeted medication or modifying adjunctive medications (e.g., sedative-hypnotics) or medications for side effects (e.g., anticholinergics for extrapyramidal symptoms) was not sufficient to qualify the patient. (Antipsychotic medications were viewed as adjuncts when used to treat psychotic symptoms in BD or MDD; however, atypical antipsychotics and agents used for mood stabilization in BD were not viewed as adjuncts, i.e., they were viewed as syndrome-targeted agents.) Patients with schizoaffective disorder were eligible for either the bipolar or schizophrenia algorithms, depending on the type of schizoaffective disorder. For schizoaffective disorder (bipolar subtype), the BD ALGO was used. All other patients with schizoaffective disorder were eligible for the SCZ ALGO.

Consenting TAU patients were entered into the study within 14 days of a medication change by the physician. Since medication changes in the TAU groups may not have resembled those in ALGO, any change in psychotropic medications (except those as a hypnotic only) for the given disorder made a patient eligible for enrollment in TAU. To account for TAU physician behavior to frequently maintain partially responding patients on the same medication regimen, patients with a BPRS-24 score above the median of all BPRS-24 scores for all patients with the given disorder, at the given clinic, within the previous 6 months, were also approached for study participation. Upon assessment by the study research coordinator, these patients must have had a BPRS-24 score within 1 standard deviation of the mean for the ALGO group.

Recruitment, enrollment, and retention. Patients were entered over a 13-month period beginning March 1998 and concluding with the final active patient visit in April 2000. TMAP consisted of 9 study cells (ALGO, TAUinALGO,

Table 2. Schedule of Baseline and Follow-Up (outcome) Assessments for the Texas Medication Algorithm Project, Phase 3

Outcome Assessment Measure	Administrator	Disorder	Schedule: Baseline and Every 3 Months	Schedule: Baseline and Every 6 Months	Schedule: Baseline and at 3 and 9 Months
Symptoms					
Brief Psychiatric Rating Scale	RC	MDD, BD, SCZ	✓		
Inventory of Depressive Symptomatology, Clinician-Rated	RC	MDD, BD	✓		
Inventory of Depressive Symptomatology, Self-Report	SR	MDD	✓		
Clinician-Administered Rating Scale for Mania	RC	BD	✓		
Scale for the Assessment of Negative Symptoms	RC	SCZ	✓		
Calgary Depression Scale	RC	SCZ	✓		
Modified Internal State Scale	SR	BD	✓		
Functioning and quality of life					
Lehman Work and Productive Activity subscale	SR	MDD, BD, SCZ	✓		
Quality of Life Interview-Brief Version Terrible-Delighted subscale	RC	MDD, BD, SCZ	✓		
12-item Short-Form Health Survey	SR	MDD, BD, SCZ	✓		
Trail Making Test, Part A	RC	SCZ			✓
Trail Making Test, Part B	RC	SCZ			✓
Verbal Fluency Test	RC	SCZ			✓
Hopkins Verbal Learning Test	RC	SCZ			✓
Patient and physician satisfaction and knowledge					
40-item Texas MHMR Mental Health Consumer Survey	SR	MDD, BD, SCZ		✓	
Drug Attitude Inventory	SR	MDD, BD, SCZ		✓	
Patient Perception of Benefits	SR	MDD, BD, SCZ		✓	
Service and nontreatment utilization/costs					
Utilization and Cost Patient Questionnaire	RC	MDD, BD, SCZ	✓		
Adherence					
Modified Medication Compliance Scale	RC	MDD, BD, SCZ	✓		
Side effects					
Modified Systematic Assessment for Treatment Emergent Events	RC	MDD, BD, SCZ	✓		
Barnes Rating Scale for Drug-Induced Akathisia	RC	SCZ	✓		
Drug and alcohol use					
Drug Abuse Screening Test	SR	MDD, BD, SCZ	✓		
Michigan Alcohol Screening Test	SR	MDD, BD, SCZ	✓		
Supplemental Substance Use Information	SR	MDD, BD, SCZ	✓		

Abbreviations: BD = bipolar disorder, MDD = major depressive disorder, MHMR = Mental Health and Mental Retardation, RC = research coordinator, SCZ = schizophrenia, SR = self-report.

TAUnonALGO) for each of the 3 disorders. Enrollment goals were 180 patients per group with SCZ, 225 per group for MDD, and 180 per group for patients with BD. Physicians determined whether a patient was suitable for medication treatment in general, and for ALGO in particular. Each study physician used only 1 specific ALGO for the designated disorder, selected on the basis of the clinician's diagnosis.

Patients were able to discontinue from the study, or from services, at any time. If they discontinued from services, patients were asked to continue with their quarterly outcome assessments. To reduce the likelihood of attrition from the quarterly outcome assessments, the following procedures were implemented:

1. Two "significant others" were identified at entry who could be contacted to locate the patient.
2. Research coordinators visited the patient's residence if the patient could not meet at the clinic.
3. All patients (both TAU and ALGO) were paid for the time and effort required for research-outcome assessments ($20 for each completed assessment).
4. Appointment cards were provided, noting the next research-outcome assessment visit, with the coordinator's phone number to facilitate rescheduling if needed.
5. Postcards were mailed at the fourth and eighth weeks following each research-outcome assessment visit.
6. Reminder telephone calls were initiated 2 days prior to each quarterly research-outcome assessment.

Study measures. Study measures are described below, with testing schedules described in Table 2. Measures were administered by research coordinators who received training from, and were supervised by, Ph.D.-level psychologists.

1. Symptoms. Different primary symptom measures were used to evaluate symptomatic outcomes for each disorder. For SCZ, the primary symptom outcome measure was the BPRS-18.[37] Secondary symptom outcome measures included the Scale for the Assessment of Negative Symptoms (SANS)[42] and the Calgary Depression

Scale (CDS).[43] For BD, the primary symptom outcome measure was the BPRS-24.[38] Secondary outcome measures included the mania and psychosis subscales of the CARS-M[39] and the IDS-C-30.[35] For MDD, the primary symptom outcome measure was the IDS-C-30. Secondary outcome measures included the BPRS-24 and the IDS-SR-30.

2. Functioning and quality of life. All patients were administered the 12-item Short-Form Health Survey (SF-12)[44] to assess function outcomes. Secondary function outcome measures included the 2-item Terrible-Delighted subscale from the brief version of the Quality of Life Interview (QOLI)[45] and the modified 7-item Lehman Work and Productive Activity subscale, also derived from the QOLI.[45] In addition, SCZ had 4 cognitive function tests: Trail Making Test, Parts A and B,[46,47] Verbal Fluency Test,[48] and the Hopkins Verbal Learning Test.[49]

3. Side effects. Self-rated side effect burden was assessed using a modified Systematic Assessment for Treatment Emergent Events (SAFTEE)[50,51] and, for SCZ only, the Barnes Rating Scale for Drug-Induced Akathisia.[52] Subjects were also asked about global burden from medication side effects that either "bothered or interfered with daily functioning." Mild to no side effects were considered not significant. Significant side effects included those that respondents reported as (1) "bothering but tolerable," (2) "requiring a medication change or something for the side effect," or (3) "requiring hospitalization."

4. Patient and physician satisfaction and knowledge. Patient satisfaction with care was assessed using the 40-item Texas Mental Health Consumer Survey (TMHCS),[53] based on the Mental Health Statistics Improvement Program (MHSIP) Consumer Survey.[54,55] The measure assessed 4 components: access, quality/appropriateness, outcomes, and general satisfaction. To examine if ALGO improved physician-patient relationships to help patients adhere to treatment regimens, the therapeutic alliance between patients and physicians was assessed using the "quality appropriateness" subscale of the TMHCS.[53,54]

Physician satisfaction with ALGO experiences was assessed on the Termination Form for each patient, in which physicians described their satisfaction with the algorithm in terms of patient progress and helpfulness in guiding treatment process. At the end of the study, physicians participated in debriefing interviews, planned conference calls, and site visits and completed a 41-item questionnaire regarding their overall satisfaction with ALGO.

Clinical staff in all clinics completed the Community Program Philosophy Scale (CPPS)[56] at baseline and at 1 year to evaluate attitudes about their work environment and their ability to treat patients in a therapeutic manner.

5. Physician adherence to the algorithms. For TAU and ALGO, prescribing practices were characterized by medication type and doses. The status of patients (e.g., symptom severity, side effect burden) could not be reliably deciphered in many TAU records. Thus, a detailed analysis of the comparative appropriateness of the strategies and tactics for TAU was not possible. In order to measure adherence, the uniform documentation acquired by the Clinical Record Form for ALGO patients allowed an appraisal of the degree of physician adherence to the ALGO and the relationship between adherence and patient outcomes.

Physicians were allowed to deviate from the algorithm (e.g., skip a treatment stage, modify any tactic) on the basis of the patient's general medical or psychiatric history, prior treatment response, patient preference, and clinical judgment. In these cases, physicians provided brief, written explanations of significant deviations (e.g., skipping stages, not tactics) from algorithm recommendations in the chart.

Patients were provided with information to make choices about their treatment whenever possible, particularly when multiple strategies or tactics are available at a given step or stage in the algorithm. Patients could also decline any stage in the algorithm (e.g., the patient might decline a particular medication because of recent negative media coverage).

6. Patient adherence to treatment. Patient adherence was measured by determining how long patients remained in treatment and by kept-appointment rates. Medication adherence was assessed by asking patients to give a global impression of their medication adherence. Although some authors report that patients overestimate their adherence rates,[27] others have shown most patients to be relatively honest in reporting nonadherence.[57]

7. Utilization/cost questionnaire. The quarterly-administered 15-item Utilization and Cost Patient Questionnaire (UAC-PQ-15) solicited factual information about the services patients received and the identities of those health care providers.[58,59] Once identified, providers were located and asked to provide patient medical and billing records describing clinical encounters and procedures. Use of services was compiled from hybrid sources, including (1) billing and medical records from patients' health care providers, including MHMR and other mental/general medical providers; (2) administrative files from community MHMR centers, state hospitals, and Medicaid; and (3) patient self-reports. Services were classified by specialty (mental health or general medical care), source of financing, and treatment setting (inpatient, outpatient clinic, emergency room, home care, and day hospitals). Costs were computed by multiplying the number of services the patient consumed by a unit cost for the service and then summing the costs for each service over all services.[58] Unit costs were based on price schedules computed from provider billing charges, Medicare fees, and Medicaid rates.[58,59]

8. Contacts with criminal justice system. Frequency of arrests and incarceration days were obtained from patient

self-reports (UAC-PQ-15) and from computerized files obtained through the Texas Department of Public Safety and the Texas Department of Criminal Justice.

9. Demographic and baseline characteristics. Patient demographic characteristics (ethnicity, race, gender, family size, insurance status, income status) were obtained by face-to-face interviews administered at baseline by research coordinators. Included was a 10-item Patient Perception of Benefits (PPB) questionnaire developed for this study to measure whether patients believe they will see improved functioning if they get needed care. Scores ranged from 10 to 50, with higher values indicating disbelief that care will help (Kashner et al., unpublished rating scale, 1996).

STATISTICAL ANALYSES

Sample Size Estimation

Sample size was determined only for the primary outcome measure for each disorder to provide a power of 90% ($\beta = .1$ and $\alpha = .05$) based on a 2-sample t test of the change from baseline to end of study for the intent-to-treat sample. Standard deviations were based on a feasibility study (TMAP Phase 2).[3,23,31–34] For SCZ, a beginning BPRS-18 score of 61 was assumed with a 15% (9-point) improvement in the ALGO group and 5% (3-point) improvement in the TAU group (SD = 14), requiring 107 patients per group. A baseline BPRS-24 score of 54 was assumed for BD with a 15% (8-point) and 5.5% (3-point) improvement in the ALGO and TAU groups (SD = 12), respectively, requiring 122 patients per group. For MDD, a baseline IDS-C-30 score of 39 was assumed with a 20% (8-point) improvement in the ALGO group and 10% (4-point) improvement in the TAU group (SD = 12), leading to a need for 190 patients per group. Altogether, 1257 patients were required for ALGO, TAUnonALGO, and TAUinALGO groups for all modules (SCZ: N = 321; BD: N = 366; MDD: N = 570). In fact, 1421 patients were enrolled in the study (SCZ: N = 465; BD: N = 409; MDD: N = 547).

Creation of Analytic Sample

Patients in the analytic sample included TAUnonALGO and ALGO patients who had a primary outcome measure assessed at baseline and at least 1 follow-up for SCZ and BD. Excluding TAUinALGO patients from analyses for SCZ and BD patients was necessary to prevent a clinically meaningful culture effect causing a downward bias in the estimated ALGO effects.

In the MDD sample, ALGO patients had more severe depression symptoms that reached clinical significance (IDS-C-30) than their TAUnonALGO counterparts. Using change scores to adjust for baseline differences, regression to the mean would lead to an upward bias in estimated ALGO effect sizes. To equalize baseline values, the MDD analytic sample was constructed by matching ALGO patients to TAU patients, which were obtained by combining TAUinALGO and TAUnonALGO patients and matching with respect to IDS-C-30 (score ≤ 2) and IDS-SR-30 (score ≤ 10) and length of illness. The final analytic sample was 926 patients (SCZ: N = 309, BD: N = 267, MDD: N = 350).

Estimates of ALGO Effects

ALGO effects were computed by comparing differences in outcomes between ALGO and TAU patients over time. The a priori defined primary symptom outcome measure for each disorder was the BPRS-18 for SCZ, BPRS-24 for BD, and IDS-C-30 for MDD. Since TAU patients also received treatment, ALGO effects were estimated using a declining effects approach[60] based on hierarchical linear models[61] as adopted to access ALGO-driven disease management programs.[62] For a patient cohort (level 2) followed longitudinally by repeatedly assessing outcomes (level 1) at baseline and 3-month intervals, these models describe the course of illness for each subject as an initial change in outcomes between baseline and 3 months and for the remainder of follow-up, a growth rate or change in outcome per quarter. ALGO effects were represented by 2 parameters describing ALGO versus TAU differences in initial changes (initial effect) and in growth rates (growth-rate effect). These approaches did not depend on fixed intervals between observations, and they handled missing observations; permitted more flexible covariance structures for a better model fit[62]; and handled continuous,[63] bivariate, and ordinal[64] psychiatric outcome data. This approach determined the impact of ALGO on patient outcomes and ascertained if these initial differences increased, remained constant, or declined during the remainder of follow-up.

Since the number of clinics by disorder was small (14 for MDD, with 4 in ALGO and 10 in TAU; 11 for BD, with 4 in ALGO and 7 in TAU; and 11 for SCZ, with 4 in ALGO and 7 in TAU), with treatment groups assigned by clinic, no clinic random variate was entered into the model. Rather, ALGO versus TAU assignment was described as a patient-level dichotomous variable, with the final model reduced to a single equation with patient- and time-level random variates. To adjust for site-specific differences, outcome measures were represented as change scores to avoid loading baseline differences between ALGO and TAU. Estimates were also adjusted to reflect baseline differences with respect to need for care (symptom severity: IDS-C-30 for MDD, BPRS-24 for BD, and BPRS-18 for SCZ; length of illness: MDD; age: SCZ, BD), enabling factors (family size, disposable monthly income), predisposition to obtain care (years of education, patient perception of benefits from treatment), and other factors (gender, African American status, and Hispanic status).

In addition to the primary analyses described above, the analytic sample for each disorder was divided into 3 groups according to baseline symptom severity for exploratory analyses. This corrected for regression to the mean that results when baseline outcome values differ significantly between the ALGO and TAU groups. Assignment to moderate, severe, and very severe symptom groups used baseline assessments with cutpoints selected a priori to populate clinically meaningful groups:

1. SCZ: moderate symptoms, BPRS-18 score = 18–30; severe symptoms, BPRS-18 score = 31–44; very severe symptoms, BPRS-18 score ≥ 45.
2. BD: moderate symptoms, BPRS-24 score = 24–39; severe symptoms, BPRS-24 score = 40–59; very severe symptoms, BPRS-24 score ≥ 60.
3. MDD: moderate symptoms, IDS-C-30 score ≤ 32; severe symptoms, IDS-C-30 score = 33–49; very severe symptoms, IDS-C-30 score ≥ 50.

In addition to mitigating regression to the mean, dividing the sample into subgroups also helped equalize variances between comparison groups. However, our a priori power analyses and primary hypotheses were based on the total sample.

Unlike SCZ and BD patients, MDD ALGO patients were significantly more symptomatic on baseline IDS-C-30 than MDD TAU patients. For MDD, the subgroup analyses would not have been adequate to resolve the regression to the mean problem, as uncorrected analyses would overstate estimated ALGO effect sizes. To solve this problem, differences in baseline values were narrowed by obtaining a best match for each ALGO patient with a TAU subject, obtained by pooling TAUnonALGO and TAUinALGO groups. A match was completed if for each ALGO patient, the matching TAU was within ± 2 points on the IDS-C-30 score, ± 10 points on the IDS-SR-30 score, and ± 20 years length of illness. The matched sample was then divided into moderate, severe, and very severe subgroups as described above. The matching procedure reduced the MDD sample to 350 patients.

DISCUSSION

TMAP represents the first attempt to evaluate clinical and economic outcomes associated with the implementation of evidence-based treatment algorithms in patients with severe and persistent mental disorders treated in the public mental health sector. Since studies in other areas of medicine have shown that typical guideline dissemination techniques are only minimally effective in obtaining guideline implementation,[65] TMAP provided substantial support to increase the chances of implementation. The result of this effort was to create a disease management program that included medication algorithms to drive clinical decision making. Thus, TMAP is actually a study of a bundle of interventions, and not just the effects of using medication algorithms. As a result, it will not be possible to fully ascertain which of these several components (e.g., medication algorithms, clinical support, patient/family education) substantially account for any differences found between ALGO and TAU.

Performing outcomes research in the public mental health sector is difficult. The patients are often seriously ill and have major functional impairment. Thus, recruiting patients for entry and keeping patients actively involved in treatment and the study can be challenging. The entrance criteria were chosen to reflect the types of patients actually treated, both to maximize enrollment and to increase the generalizability of results. A comprehensive scheme was implemented to keep patients actively involved in the study. While this is helpful to decrease subject attrition rate, it also runs the risk of creating a nonspecific treatment effect in the control group that could potentially make it more difficult to detect a difference between the intervention and the control groups. However, we felt that this latter risk was acceptable in order to maintain our sample size.

The collaboration of the public mental health sector with multiple academic institutions is both novel and challenging. While not possessing the necessary resources to pursue major outcomes research, the Texas Department of MHMR wished to pursue studies that were of significance to the provision of services within its system. Being a historically underresourced system, this presented a major challenge. Its leaders sought out researchers from the academic community in an attempt to address important questions. However, academic psychiatrists and clinical psychopharmacologists are not particularly accustomed to addressing health services–related research questions. Thus, the research effort became a collaborative effort involving clinicians, researchers, and administrators of various backgrounds. The potential problems involved in this type of multidisciplinary, multiinstitutional effort were addressed by the creation of an organizational structure that was able to respond to issues on a daily basis while obtaining broad representation for major policy decisions. The group's expertise was significantly enhanced by the utilization of a cadre of nationally renowned mental health outcomes researchers who ably advised the Project Management Team on both research design and analytical issues.

Hopefully, TMAP will provide useful information regarding the outcomes associated with implementing algorithm-based disease management programs in the public mental health sector and will stimulate others to perform meaningful research in this population. The public mental health sector typically treats the most seriously and chronically mentally ill individuals in our society. We hope that this effort and future collaborative research

efforts will address major services and outcomes issues related to their care. Additional information regarding TMAP can be accessed at the TMAP Web site: http://www.mhmr.state.tx.us/CentralOffice/MedicalDirector/TMAP.html.

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